SEQUENCE LISTING

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<120> MODIFIED UROKINASE-TYPE PLASMINOGEN
ACTIVATOR POLYPEPTIDES AND METHODS OF USE

<130> 33328.04940.WO01/4940

<150> 62/786,302
<151> 2018-12-28

<160> 1044

<170> FastSEQ for Windows Version 4.0

<210> 1
<211> 431
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
pro-peptide

<400> 1
Met Arg Ala Leu Leu Ala Arg Leu Leu Leu Cys Val Leu Val Val Ser
1 5 10 15
Asp Ser Lys Gly Ser Asn Glu Leu His Gln Val Pro Ser Asn Cys Asp
20 25 30
Cys Leu Asn Gly Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile
35 40 45
His Trp Cys Asn Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile
50 55 60
Asp Lys Ser Lys Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly
65 70 75 80
Lys Ala Ser Thr Asp Thr Met Gly Arg Pro Cys Leu Pro Trp Asn Ser
85 90 95
Ala Thr Val Leu Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu

```
            100                 105                 110
Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg
        115                 120                 125
Arg Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln
    130                 135                 140
Glu Cys Met Val His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro
145                 150                 155                 160
Pro Glu Glu Leu Lys Phe Gln Cys Gly Gln Lys Thr Leu Arg Pro Arg
                165                 170                 175
Phe Lys Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp
            180                 185                 190
Phe Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val
        195                 200                 205
Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His
    210                 215                 220
Cys Phe Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly
225                 230                 235                 240
Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val
                245                 250                 255
Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala His
            260                 265                 270
His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys
        275                 280                 285
Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr
    290                 295                 300
Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys
305                 310                 315                 320
Glu Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val
                325                 330                 335
Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly
            340                 345                 350
Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys
        355                 360                 365
Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu
    370                 375                 380
Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys
385                 390                 395                 400
Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu
                405                 410                 415
Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
            420                 425                 430
```

<210> 2
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain

<400> 2

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala His His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 3
<211> 411
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA) mature

<400> 3

```
Ser Asn Glu Leu His Gln Val Pro Ser Asn Cys Asp Cys Leu Asn Gly
 1               5                  10                  15
Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile His Trp Cys Asn
            20                  25                  30
Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile Asp Lys Ser Lys
        35                  40                  45
Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly Lys Ala Ser Thr
    50                  55                  60
Asp Thr Met Gly Arg Pro Cys Leu Pro Trp Asn Ser Ala Thr Val Leu
65                  70                  75                  80
Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu Gln Leu Gly Leu
                85                  90                  95
Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg Arg Arg Pro Trp
            100                 105                 110
Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln Glu Cys Met Val
        115                 120                 125
His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro Pro Glu Glu Leu
    130                 135                 140
Lys Phe Gln Cys Gly Gln Lys Thr Leu Arg Pro Arg Phe Lys Ile Ile
145                 150                 155                 160
Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala Ala Ile
                165                 170                 175
Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val Cys Gly Gly Ser
            180                 185                 190
Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe Ile Asp
        195                 200                 205
Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser Arg Leu
    210                 215                 220
Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn Leu Ile
225                 230                 235                 240
Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala His His Asn Asp Ile
                245                 250                 255
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            260                 265                 270
Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr Asn Asp Pro Gln
        275                 280                 285
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    290                 295                 300
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
305                 310                 315                 320
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                325                 330                 335
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            340                 345                 350
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        355                 360                 365
Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys Asp
    370                 375                 380
```

```
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
385                 390                 395                 400
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                405                 410
```

<210> 4
<211> 431
<212> PRT
<213> Artificial Sequence

<220>
<223> urokinase plasminogen activator (u-PA) pro-peptide
C122S

<400> 4

```
Met Arg Ala Leu Leu Ala Arg Leu Leu Leu Cys Val Leu Val Val Ser
 1               5                  10                  15
Asp Ser Lys Gly Ser Asn Glu Leu His Gln Val Pro Ser Asn Cys Asp
            20                  25                  30
Cys Leu Asn Gly Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile
        35                  40                  45
His Trp Cys Asn Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile
    50                  55                  60
Asp Lys Ser Lys Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly
65                  70                  75                  80
Lys Ala Ser Thr Asp Thr Met Gly Arg Pro Cys Leu Pro Trp Asn Ser
                85                  90                  95
Ala Thr Val Leu Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu
            100                 105                 110
Gln Leu Gly Leu Gly Lys His Asn Tyr Ser Arg Asn Pro Asp Asn Arg
        115                 120                 125
Arg Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln
    130                 135                 140
Glu Cys Met Val His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro
145                 150                 155                 160
Pro Glu Glu Leu Lys Phe Gln Cys Gly Gln Lys Thr Leu Arg Pro Arg
                165                 170                 175
Phe Lys Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp
            180                 185                 190
Phe Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val
        195                 200                 205
Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His
    210                 215                 220
Cys Phe Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly
225                 230                 235                 240
Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val
                245                 250                 255
```

```
Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala His
            260                 265                 270
His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys
        275                 280                 285
Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr
    290                 295                 300
Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys
305                 310                 315                 320
Glu Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val
                325                 330                 335
Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly
            340                 345                 350
Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys
        355                 360                 365
Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu
    370                 375                 380
Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys
385                 390                 395                 400
Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu
                405                 410                 415
Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
            420                 425                 430


<210> 5
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain C122S

<400> 5
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala His His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
```

```
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 6
<211> 411
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA) mature
C122S

<400> 6

```
Ser Asn Glu Leu His Gln Val Pro Ser Asn Cys Asp Cys Leu Asn Gly
 1               5                  10                  15
Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile His Trp Cys Asn
            20                  25                  30
Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile Asp Lys Ser Lys
        35                  40                  45
Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly Lys Ala Ser Thr
    50                  55                  60
Asp Thr Met Gly Arg Pro Cys Leu Pro Trp Asn Ser Ala Thr Val Leu
65                  70                  75                  80
Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu Gln Leu Gly Leu
                85                  90                  95
Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg Arg Arg Pro Trp
            100                 105                 110
Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln Glu Cys Met Val
        115                 120                 125
His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro Pro Glu Glu Leu
    130                 135                 140
```

```
Lys Phe Gln Cys Gly Gln Lys Thr Leu Arg Pro Arg Phe Lys Ile Ile
145                 150                 155                 160
Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala Ala Ile
                165                 170                 175
Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val Cys Gly Gly Ser
            180                 185                 190
Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe Ile Asp
        195                 200                 205
Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser Arg Leu
    210                 215                 220
Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn Leu Ile
225                 230                 235                 240
Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala His His Asn Asp Ile
                245                 250                 255
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            260                 265                 270
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        275                 280                 285
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    290                 295                 300
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
305                 310                 315                 320
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                325                 330                 335
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            340                 345                 350
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        355                 360                 365
Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys Asp
    370                 375                 380
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
385                 390                 395                 400
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                405                 410
```

<210> 7
<211> 1296
<212> DNA
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
pro-peptide

<400> 7
atgagagccc tgctggcgcg cctgcttctc tgcgtcctgg tcgtgagcga ctccaaaggc 60
agcaatgaac ttcatcaagt tccatcgaac tgtgactgtc taaatggagg aacatgtgtg 120

```
tccaacaagt acttctccaa cattcactgg tgcaactgcc caaagaaatt cggagggcag 180
cactgtgaaa tagataagtc aaaaacctgc tatgagggga atggtcactt ttaccgagga 240
aaggccagca ctgacaccat gggccggccc tgcctgccct ggaactctgc cactgtcctt 300
cagcaaacgt accatgccca cagatctgat gctcttcagc tgggcctggg gaaacataat 360
tactgcagga acccagacaa ccggaggcga ccctggtgct atgtgcaggt gggcctaaag 420
ccgcttgtcc aagagtgcat ggtgcatgac tgcgcagatg gaaaaaagcc ctcctctcct 480
ccagaagaat taaaatttca gtgtggccaa aagactctga ggccccgctt taagattatt 540
gggggagaat tcaccaccat cgagaaccag ccctggtttg cggccatcta caggaggcac 600
cgggggggct ctgtcaccta cgtgtgtgga ggcagcctca tcagcccttg ctgggtgatc 660
agcgccacac actgcttcat tgattaccca aagaaggagg actacatcgt ctacctgggt 720
cgctcaaggc ttaactccaa cacgcaaggg gagatgaagt ttgaggtgga aaacctcatc 780
ctacacaagg actacagcgc tgacacgctt gctcaccaca acgacattgc cttgctgaag 840
atccgttcca aggagggcag gtgtgcgcag ccatcccgga ctatacagac catctgcctg 900
ccctcgatgt ataacgatcc ccagtttggc acaagctgtg agatcactgg ctttggaaaa 960
gagaattcta ccgactatct ctatccggag cagctgaaaa tgactgttgt gaagctgatt 1020
tcccaccggg agtgtcagca gccccactac tacggctctg aagtcaccac caaaatgctg 1080
tgtgctgctg acccacagtg gaaaacagat tcctgccagg gagactcagg gggacccctc 1140
gtctgttccc tccaaggccg catgactttg actggaattg tgagctgggg ccgtggatgt 1200
gccctgaagg acaagccagg cgtctacacg agagtctcac acttcttacc ctggatccgc 1260
agtcacacca aggaagagaa tggcctggcc ctctga                           1296

<210> 8
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/V38D/Y40H/V41R/L97bA/H99Q/C122S/M157K

<400> 8
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
```

```
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 9
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36H/H37E/V38E/T39W/Y40H/V41R/Y60bQ/T97a
E/L97bA/H99Q/C122S/Y149K/M157K

<400> 9

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp His Glu Arg Gly Gly Ser Glu Trp His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
```

```
Ser Thr Asp Lys Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 10
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35W/R36H/H37D/V38E/T39Y/Y40F/V41R/T97aI/L97b
      A/H99Q/C122S/Y149R/M157K

<400> 10
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp His Asp Arg Gly Gly Ser Glu Tyr Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
```

```
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 11
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35W/R36H/H37N/V38E/T39F/Y40F/V41R/T97aI/L97bA/H99
      Q/C122S/Y149R/M157K/Q192H

<400> 11
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Trp His Asn Arg Gly Gly Ser Glu Phe Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
```

```
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys His Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 12
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35Y/R36H/H37K/V38E/T39F/Y40F/V41R/T97aI/L97b
      A/H99Q/C122S/Y149R/M157K

<400> 12
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Tyr His Lys Arg Gly Gly Ser Glu Phe Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
```

```
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 13
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36H/H37N/V38E/T39Y/Y40F/V41R/Y60bS/T97a
E/L97bA/H99Q/C122S/Y149K/M157K

<400> 13

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp His Asn Arg Gly Gly Ser Glu Tyr Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Lys Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
```

```
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 14
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36H/H37P/V38E/T39Y/Y40F/V41R/Y60bS/T97a
E/L97bA/H99Q/C122S/Y149K/M157K

<400> 14

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp His Pro Arg Gly Gly Ser Glu Tyr Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Lys Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
```

```
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 15
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38E/Y40Q/V41L/Y60bL/L97bA/H99Q/C122S

<400> 15

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Leu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
```

245 250

<210> 16
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/R36H/H37G/R37aE/V38E/T39F/Y40F/V41R/D60a
P/Y60bS/T97aI/L97bA/H99Q/C122S/Y149R/M157K

<400> 16
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Gln His Gly Glu Gly Gly Ser Glu Phe Phe Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Pro Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 17
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Y/R36H/H37P/R37aQ/V38E/T39Y/Y40F/V41R/Y60b
H/T97aI/L97bA/H99Q/C122S/Y149R/M157K

<400> 17

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Tyr His Pro Gln Gly Gly Ser Glu Tyr Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp His Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 18

<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aT/Y60bT/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 18

Ile	Ile	Gly	Gly	Glu	Phe	Thr	Thr	Ile	Glu	Asn	Gln	Pro	Trp	Phe	Ala
1				5				10						15	
Ala	Ile	Tyr	Gln	Arg	Tyr	Glu	Gly	Gly	Ser	Glu	Tyr	Tyr	Arg	Cys	Gly
			20					25					30		
Gly	Ser	Leu	Ile	Ser	Pro	Cys	Trp	Val	Ile	Ser	Ala	Thr	His	Cys	Phe
		35					40					45			
Ile	Thr	Thr	Pro	Lys	Lys	Glu	Asp	Tyr	Ile	Val	Tyr	Leu	Gly	Arg	Ser
	50					55					60				
Arg	Leu	Asn	Ser	Asn	Thr	Gln	Gly	Glu	Met	Lys	Phe	Glu	Val	Glu	Asn
65					70					75					80
Leu	Ile	Leu	His	Lys	Asp	Tyr	Ser	Ala	Asp	Ile	Ala	Ala	Gln	His	Asn
				85					90					95	
Asp	Ile	Ala	Leu	Leu	Lys	Ile	Arg	Ser	Lys	Glu	Gly	Arg	Cys	Ala	Gln
			100					105					110		
Pro	Ser	Arg	Thr	Ile	Gln	Thr	Ile	Ser	Leu	Pro	Ser	Met	Tyr	Asn	Asp
		115					120					125			
Pro	Gln	Phe	Gly	Thr	Ser	Cys	Glu	Ile	Thr	Gly	Phe	Gly	Lys	Glu	Asn
	130					135					140				
Ser	Thr	Asp	Arg	Leu	Tyr	Pro	Glu	Gln	Leu	Lys	Met	Thr	Val	Val	Lys
145					150					155					160
Leu	Ile	Ser	His	Arg	Glu	Cys	Gln	Gln	Pro	His	Tyr	Tyr	Gly	Ser	Glu
				165					170					175	
Val	Thr	Thr	Lys	Met	Leu	Cys	Ala	Ala	Asp	Pro	Gln	Trp	Lys	Thr	Asp
			180					185					190		
Ser	Cys	Gln	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Cys	Ser	Leu	Gln	Gly
		195					200					205			
Arg	Met	Thr	Leu	Thr	Gly	Ile	Val	Ser	Trp	Gly	Arg	Gly	Cys	Ala	Leu
	210					215					220				
Lys	Asp	Lys	Pro	Gly	Val	Tyr	Thr	Arg	Val	Ser	His	Phe	Leu	Pro	Trp
225					230					235					240
Ile	Arg	Ser	His	Thr	Lys	Glu	Glu	Asn	Gly	Leu	Ala	Leu			
				245					250						

<210> 19
<211> 253
<212> PRT

<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35W/H37P/R37aN/V38E/T39Y/V41R/D60aP/Y60bL/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 19

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Trp Arg Pro Asn Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Leu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 20
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35W/H37D/R37aP/V38E/T39W/V41R/Y60bA/T97aI/L97bA/H
99Q/C122S/Y149R

<400> 20
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Trp Arg Asp Pro Gly Gly Ser Glu Trp Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Ala Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 21
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)

protease domain
R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aP/Y60bQ/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 21
```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 22
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
H37Y/R37aE/V38E/T39Y/V41R/D60aP/Y60bQ/T97aI/L97bA/

H99Q/C122S/Y149R

<400> 22
```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg Tyr Glu Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 23
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/R37aE/V38E/T39Y/V41R/D60aP/Y60bQ/T97aI/L97bA/
H99Q/C122S/Y149R

<400> 23
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Gln Arg His Glu Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 24
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35Q/H37Y/V38E/T39Y/V41R/D60aP/Y60bQ/T97aI/L97bA/H
      99Q/C122S/Y149R

<400> 24
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala

```
 1               5                  10                  15
Ala Ile Tyr Gln Arg Tyr Arg Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 25
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37Y/R37aE/T39Y/V41R/D60aP/Y60bQ/T97aI/L97bA/
H99Q/C122S/Y149R

<400> 25

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Val Tyr Tyr Arg Cys Gly
```

```
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 26
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35Q/H37Y/R37aE/V38E/V41R/D60aP/Y60bQ/T97aI/L97bA/
      H99Q/C122S/Y149R

<400> 26
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
```

```
        35                  40                  45
Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 27
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37Y/R37aE/V38E/T39Y/D60aP/Y60bQ/T97aI/L97bA/
H99Q/C122S/Y149R

<400> 27

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Tyr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
```

```
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 28
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37Y/R37aE/V38E/T39Y/V41R/Y60bQ/T97aI/L97bA/H
99Q/C122S/Y149R

<400> 28

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
```

```
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 29
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aP/T97aI/L97bA/H
99Q/C122S/Y149R

<400> 29

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
```

```
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 30
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aP/Y60bQ/L97bA/H
99Q/C122S/Y149R

<400> 30

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
```

```
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 31
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aP/Y60bQ/T97aI/H
      99Q/C122S/Y149R

<400> 31
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Leu Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
```

```
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 32
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aP/Y60bQ/T97aI/L
97bA/C122S/Y149R

<400> 32

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala His His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
```

```
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 33
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aP/Y60bQ/T97aI/L
97bA/H99Q/C122S

<400> 33

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
```

```
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 34
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain Y40Q/V41L/Y60bL/L97bA/H99Q/C122S

<400> 34
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Leu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
```

```
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 35
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38E/Y40Q/Y60bL/L97bA/H99Q/C122S

<400> 35

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Thr Gln Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Leu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
```

```
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 36
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38E/Y40Q/V41L/L97bA/H99Q/C122S

<400> 36

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
```

245 250

<210> 37
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38E/Y40Q/V41L/Y60bL/H99Q/C122S

<400> 37
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Thr Gln Leu Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Leu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 38

<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38E/Y40Q/V41L/Y60bL/L97bA/C122S

<400> 38
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Thr Gln Leu Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Leu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala His His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 39
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain Y40Q/V41L/L97bA/H99Q/C122S

<400> 39
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Gln Leu Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 40
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain Y40Q/V41L/L97bA/C122S

<400> 40
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Gln Leu Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala His His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 41
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain R37aS/V41R/L97bG/H99Q/C122S

<400> 41
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Ser Gly Gly Ser Val Thr Tyr Arg Cys Gly

```
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 42
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain T39Y/V41R/L97bA/H99Q/C122S

<400> 42

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Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
```

```
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 43
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain T39Y/V41R/Y60bQ/L97bA/H99Q/C122S

<400> 43

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Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
```

```
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 44
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain T39Y/V41R/D60aP/L97bA/H99Q/C122S

<400> 44

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
```

```
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 45
<211> 330
<212> PRT
<213> Artificial Sequence

<220>
<223> hIgG1 heavy chain constant

<400> 45

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Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
 1               5                  10                  15
Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
            20                  25                  30
Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
        35                  40                  45
Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50                  55                  60
Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65                  70                  75                  80
Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
                85                  90                  95
Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
            100                 105                 110
Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
        115                 120                 125
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
    130                 135                 140
Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145                 150                 155                 160
```

```
Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
                165                 170                 175
Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
            180                 185                 190
His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
        195                 200                 205
Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
    210                 215                 220
Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
225                 230                 235                 240
Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
                245                 250                 255
Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
            260                 265                 270
Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
        275                 280                 285
Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
    290                 295                 300
Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305                 310                 315                 320
Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330
```

<210> 46
<211> 5132
<212> DNA
<213> Homo sapiens

<220>

<400> 46

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agataaaaag ccagctccag caggcgctgc tcactcctcc ccatcctctc cctctgtccc 60
tctgtccctc tgaccctgca ctgtcccagc accatgggac ccacctcagg tcccagcctg 120
ctgctcctgc tactaaccca cctccccctg gctctgggga gtcccatgta ctctatcatc 180
acccccaaca tcttgcggct ggagagcgag gagaccatgg tgctggaggc ccacgacgcg 240
caaggggatg ttccagtcac tgttactgtc cacgacttcc caggcaaaaa actagtgctg 300
tccagtgaga agactgtgct gacccctgcc accaaccaca tgggcaacgt caccttcacg 360
atcccagcca acagggagtt caagtcagaa aaggggcgca acaagttcgt gaccgtgcag 420
gccaccttcg ggacccaagt ggtggagaag gtggtgctgg tcagcctgca gagcgggtac 480
ctcttcatcc agacagacaa gaccatctac acccctggct ccacagttct ctatcggatc 540
ttcaccgtca accacaagct gctacccgtg ggccggacgg tcatggtcaa cattgagaac 600
ccggaaggca tcccggtcaa gcaggactcc ttgtcttctc agaaccagct tggcgtcttg 660
cccttgtctt gggacattcc ggaactcgtc aacatgggcc agtggaagat ccgagcctac 720
tatgaaaact caccacagca ggtcttctcc actgagtttg aggtgaagga gtacgtgctg 780
cccagtttcg aggtcatagt ggagcctaca gagaaattct actacatcta taacgagaag 840
ggcctggagg tcaccatcac cgccaggttc ctctacggga agaaagtgga gggaactgcc 900
tttgtcatct tcgggatcca ggatggcgaa cagaggattt ccctgcctga atccctcaag 960
```

cgcattccga ttgaggatgg ctcgggggag gttgtgctga gccggaaggt actgctggac 1020
ggggtgcaga acccccgagc agaagacctg gtggggaagt ctttgtacgt gtctgccacc 1080
gtcatcttgc actcaggcag tgacatggtg caggcagagc gcagcgggat ccccatcgtg 1140
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tttgacctca tggtgttcgt gacgaaccct gatggctctc cagcctaccg agtccccgtg 1260
gcagtccagg gcgaggacac tgtgcagtct ctaacccagg gagatggcgt ggccaaactc 1320
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gagctctcgg aggcagagca ggctaccagg accatgcagg ctctgcccta cagcaccgtg 1440
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tacatcacag agctgcggcg gcagcacgcg cgggccagcc acctgggcct ggccaggagt 2340
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tgcagagaag ccctgaagct ggaggagaag aaacactacc tcatgtgggg tctctcctcc 4920
gatttctggg gagagaagcc caacctcagc tacatcatcg ggaaggacac ttgggtggag 4980
cactggcccg aggaggacga atgccaagac gaagagaacc agaaacaatg ccaggacctc 5040
ggcgccttca ccgagagcat ggttgtcttt gggtgcccca actgaccaca cccccattcc 5100
cccactccag ataaagcttc agttatatct ca   5132

<210> 47
<211> 1663
<212> PRT
<213> Homo sapiens

<220>
<223> Complement Protein C3

<400> 47
Met Gly Pro Thr Ser Gly Pro Ser Leu Leu Leu Leu Leu Leu Thr His
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Leu Pro Leu Ala Leu Gly Ser Pro Met Tyr Ser Ile Ile Thr Pro Asn
            20   25   30
Ile Leu Arg Leu Glu Ser Glu Glu Thr Met Val Leu Glu Ala His Asp
        35   40   45
Ala Gln Gly Asp Val Pro Val Thr Val Thr Val His Asp Phe Pro Gly
    50   55   60
Lys Lys Leu Val Leu Ser Ser Glu Lys Thr Val Leu Thr Pro Ala Thr
65   70   75   80
Asn His Met Gly Asn Val Thr Phe Thr Ile Pro Ala Asn Arg Glu Phe
                85   90   95
Lys Ser Glu Lys Gly Arg Asn Lys Phe Val Thr Val Gln Ala Thr Phe
            100   105   110

```
Gly Thr Gln Val Val Glu Lys Val Val Leu Val Ser Leu Gln Ser Gly
        115                 120                 125
Tyr Leu Phe Ile Gln Thr Asp Lys Thr Ile Tyr Thr Pro Gly Ser Thr
    130                 135                 140
Val Leu Tyr Arg Ile Phe Thr Val Asn His Lys Leu Leu Pro Val Gly
145                 150                 155                 160
Arg Thr Val Met Val Asn Ile Glu Asn Pro Glu Gly Ile Pro Val Lys
                165                 170                 175
Gln Asp Ser Leu Ser Ser Gln Asn Gln Leu Gly Val Leu Pro Leu Ser
            180                 185                 190
Trp Asp Ile Pro Glu Leu Val Asn Met Gly Gln Trp Lys Ile Arg Ala
        195                 200                 205
Tyr Tyr Glu Asn Ser Pro Gln Gln Val Phe Ser Thr Glu Phe Glu Val
    210                 215                 220
Lys Glu Tyr Val Leu Pro Ser Phe Glu Val Ile Val Glu Pro Thr Glu
225                 230                 235                 240
Lys Phe Tyr Tyr Ile Tyr Asn Glu Lys Gly Leu Glu Val Thr Ile Thr
                245                 250                 255
Ala Arg Phe Leu Tyr Gly Lys Lys Val Glu Gly Thr Ala Phe Val Ile
            260                 265                 270
Phe Gly Ile Gln Asp Gly Glu Gln Arg Ile Ser Leu Pro Glu Ser Leu
        275                 280                 285
Lys Arg Ile Pro Ile Glu Asp Gly Ser Gly Glu Val Val Leu Ser Arg
    290                 295                 300
Lys Val Leu Leu Asp Gly Val Gln Asn Pro Arg Ala Glu Asp Leu Val
305                 310                 315                 320
Gly Lys Ser Leu Tyr Val Ser Ala Thr Val Ile Leu His Ser Gly Ser
                325                 330                 335
Asp Met Val Gln Ala Glu Arg Ser Gly Ile Pro Ile Val Thr Ser Pro
            340                 345                 350
Tyr Gln Ile His Phe Thr Lys Thr Pro Lys Tyr Phe Lys Pro Gly Met
        355                 360                 365
Pro Phe Asp Leu Met Val Phe Val Thr Asn Pro Asp Gly Ser Pro Ala
    370                 375                 380
Tyr Arg Val Pro Val Ala Val Gln Gly Glu Asp Thr Val Gln Ser Leu
385                 390                 395                 400
Thr Gln Gly Asp Gly Val Ala Lys Leu Ser Ile Asn Thr His Pro Ser
                405                 410                 415
Gln Lys Pro Leu Ser Ile Thr Val Arg Thr Lys Lys Gln Glu Leu Ser
            420                 425                 430
Glu Ala Glu Gln Ala Thr Arg Thr Met Gln Ala Leu Pro Tyr Ser Thr
        435                 440                 445
Val Gly Asn Ser Asn Asn Tyr Leu His Leu Ser Val Leu Arg Thr Glu
    450                 455                 460
Leu Arg Pro Gly Glu Thr Leu Asn Val Asn Phe Leu Leu Arg Met Asp
465                 470                 475                 480
Arg Ala His Glu Ala Lys Ile Arg Tyr Tyr Thr Tyr Leu Ile Met Asn
                485                 490                 495
```

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Lys Gly Arg Leu Leu Lys Ala Gly Arg Gln Val Arg Glu Pro Gly Gln
            500                 505                 510
Asp Leu Val Val Leu Pro Leu Ser Ile Thr Thr Asp Phe Ile Pro Ser
        515                 520                 525
Phe Arg Leu Val Ala Tyr Tyr Thr Leu Ile Gly Ala Ser Gly Gln Arg
    530                 535                 540
Glu Val Val Ala Asp Ser Val Trp Val Asp Val Lys Asp Ser Cys Val
545                 550                 555                 560
Gly Ser Leu Val Val Lys Ser Gly Gln Ser Glu Asp Arg Gln Pro Val
                565                 570                 575
Pro Gly Gln Gln Met Thr Leu Lys Ile Glu Gly Asp His Gly Ala Arg
            580                 585                 590
Val Val Leu Val Ala Val Asp Lys Gly Val Phe Val Leu Asn Lys Lys
        595                 600                 605
Asn Lys Leu Thr Gln Ser Lys Ile Trp Asp Val Val Glu Lys Ala Asp
    610                 615                 620
Ile Gly Cys Thr Pro Gly Ser Gly Lys Asp Tyr Ala Gly Val Phe Ser
625                 630                 635                 640
Asp Ala Gly Leu Thr Phe Thr Ser Ser Ser Gly Gln Gln Thr Ala Gln
                645                 650                 655
Arg Ala Glu Leu Gln Cys Pro Gln Pro Ala Ala Arg Arg Arg Arg Ser
            660                 665                 670
Val Gln Leu Thr Glu Lys Arg Met Asp Lys Val Gly Lys Tyr Pro Lys
        675                 680                 685
Glu Leu Arg Lys Cys Cys Glu Asp Gly Met Arg Glu Asn Pro Met Arg
    690                 695                 700
Phe Ser Cys Gln Arg Arg Thr Arg Phe Ile Ser Leu Gly Glu Ala Cys
705                 710                 715                 720
Lys Lys Val Phe Leu Asp Cys Cys Asn Tyr Ile Thr Glu Leu Arg Arg
                725                 730                 735
Gln His Ala Arg Ala Ser His Leu Gly Leu Ala Arg Ser Asn Leu Asp
            740                 745                 750
Glu Asp Ile Ile Ala Glu Glu Asn Ile Val Ser Arg Ser Glu Phe Pro
        755                 760                 765
Glu Ser Trp Leu Trp Asn Val Glu Asp Leu Lys Glu Pro Pro Lys Asn
    770                 775                 780
Gly Ile Ser Thr Lys Leu Met Asn Ile Phe Leu Lys Asp Ser Ile Thr
785                 790                 795                 800
Thr Trp Glu Ile Leu Ala Val Ser Met Ser Asp Lys Lys Gly Ile Cys
                805                 810                 815
Val Ala Asp Pro Phe Glu Val Thr Val Met Gln Asp Phe Phe Ile Asp
            820                 825                 830
Leu Arg Leu Pro Tyr Ser Val Val Arg Asn Glu Gln Val Glu Ile Arg
        835                 840                 845
Ala Val Leu Tyr Asn Tyr Arg Gln Asn Gln Glu Leu Lys Val Arg Val
    850                 855                 860
Glu Leu Leu His Asn Pro Ala Phe Cys Ser Leu Ala Thr Thr Lys Arg
865                 870                 875                 880
```

```
Arg His Gln Gln Thr Val Thr Ile Pro Pro Lys Ser Ser Leu Ser Val
                885                 890                 895
Pro Tyr Val Ile Val Pro Leu Lys Thr Gly Leu Gln Glu Val Glu Val
            900                 905                 910
Lys Ala Ala Val Tyr His His Phe Ile Ser Asp Gly Val Arg Lys Ser
        915                 920                 925
Leu Lys Val Val Pro Glu Gly Ile Arg Met Asn Lys Thr Val Ala Val
    930                 935                 940
Arg Thr Leu Asp Pro Glu Arg Leu Gly Arg Glu Gly Val Gln Lys Glu
945                 950                 955                 960
Asp Ile Pro Pro Ala Asp Leu Ser Asp Gln Val Pro Asp Thr Glu Ser
                965                 970                 975
Glu Thr Arg Ile Leu Leu Gln Gly Thr Pro Val Ala Gln Met Thr Glu
            980                 985                 990
Asp Ala Val Asp Ala Glu Arg Leu Lys His Leu Ile Val Thr Pro Ser
        995                 1000                1005
Gly Cys Gly Glu Gln Asn Met Ile Gly Met Thr Pro Thr Val Ile Ala
    1010                1015                1020
Val His Tyr Leu Asp Glu Thr Glu Gln Trp Glu Lys Phe Gly Leu Glu
1025                1030                1035                1040
Lys Arg Gln Gly Ala Leu Glu Leu Ile Lys Lys Gly Tyr Thr Gln Gln
                1045                1050                1055
Leu Ala Phe Arg Gln Pro Ser Ser Ala Phe Ala Ala Phe Val Lys Arg
            1060                1065                1070
Ala Pro Ser Thr Trp Leu Thr Ala Tyr Val Val Lys Val Phe Ser Leu
        1075                1080                1085
Ala Val Asn Leu Ile Ala Ile Asp Ser Gln Val Leu Cys Gly Ala Val
    1090                1095                1100
Lys Trp Leu Ile Leu Glu Lys Gln Lys Pro Asp Gly Val Phe Gln Glu
1105                1110                1115                1120
Asp Ala Pro Val Ile His Gln Glu Met Ile Gly Gly Leu Arg Asn Asn
                1125                1130                1135
Asn Glu Lys Asp Met Ala Leu Thr Ala Phe Val Leu Ile Ser Leu Gln
            1140                1145                1150
Glu Ala Lys Asp Ile Cys Glu Glu Gln Val Asn Ser Leu Pro Gly Ser
        1155                1160                1165
Ile Thr Lys Ala Gly Asp Phe Leu Glu Ala Asn Tyr Met Asn Leu Gln
    1170                1175                1180
Arg Ser Tyr Thr Val Ala Ile Ala Gly Tyr Ala Leu Ala Gln Met Gly
1185                1190                1195                1200
Arg Leu Lys Gly Pro Leu Leu Asn Lys Phe Leu Thr Thr Ala Lys Asp
                1205                1210                1215
Lys Asn Arg Trp Glu Asp Pro Gly Lys Gln Leu Tyr Asn Val Glu Ala
            1220                1225                1230
Thr Ser Tyr Ala Leu Leu Ala Leu Leu Gln Leu Lys Asp Phe Asp Phe
        1235                1240                1245
Val Pro Pro Val Val Arg Trp Leu Asn Glu Gln Arg Tyr Tyr Gly Gly
    1250                1255                1260
```

```
Gly Tyr Gly Ser Thr Gln Ala Thr Phe Met Val Phe Gln Ala Leu Ala
1265                1270                1275                1280
Gln Tyr Gln Lys Asp Ala Pro Asp His Gln Glu Leu Asn Leu Asp Val
                1285                1290                1295
Ser Leu Gln Leu Pro Ser Arg Ser Ser Lys Ile Thr His Arg Ile His
            1300                1305                1310
Trp Glu Ser Ala Ser Leu Leu Arg Ser Glu Glu Thr Lys Glu Asn Glu
        1315                1320                1325
Gly Phe Thr Val Thr Ala Glu Gly Lys Gly Gln Gly Thr Leu Ser Val
    1330                1335                1340
Val Thr Met Tyr His Ala Lys Ala Lys Asp Gln Leu Thr Cys Asn Lys
1345                1350                1355                1360
Phe Asp Leu Lys Val Thr Ile Lys Pro Ala Pro Glu Thr Glu Lys Arg
                1365                1370                1375
Pro Gln Asp Ala Lys Asn Thr Met Ile Leu Glu Ile Cys Thr Arg Tyr
            1380                1385                1390
Arg Gly Asp Gln Asp Ala Thr Met Ser Ile Leu Asp Ile Ser Met Met
        1395                1400                1405
Thr Gly Phe Ala Pro Asp Thr Asp Asp Leu Lys Gln Leu Ala Asn Gly
    1410                1415                1420
Val Asp Arg Tyr Ile Ser Lys Tyr Glu Leu Asp Lys Ala Phe Ser Asp
1425                1430                1435                1440
Arg Asn Thr Leu Ile Ile Tyr Leu Asp Lys Val Ser His Ser Glu Asp
                1445                1450                1455
Asp Cys Leu Ala Phe Lys Val His Gln Tyr Phe Asn Val Glu Leu Ile
            1460                1465                1470
Gln Pro Gly Ala Val Lys Val Tyr Ala Tyr Tyr Asn Leu Glu Glu Ser
        1475                1480                1485
Cys Thr Arg Phe Tyr His Pro Glu Lys Glu Asp Gly Lys Leu Asn Lys
    1490                1495                1500
Leu Cys Arg Asp Glu Leu Cys Arg Cys Ala Glu Glu Asn Cys Phe Ile
1505                1510                1515                1520
Gln Lys Ser Asp Asp Lys Val Thr Leu Glu Glu Arg Leu Asp Lys Ala
                1525                1530                1535
Cys Glu Pro Gly Val Asp Tyr Val Tyr Lys Thr Arg Leu Val Lys Val
            1540                1545                1550
Gln Leu Ser Asn Asp Phe Asp Glu Tyr Ile Met Ala Ile Glu Gln Thr
        1555                1560                1565
Ile Lys Ser Gly Ser Asp Glu Val Gln Val Gly Gln Gln Arg Thr Phe
    1570                1575                1580
Ile Ser Pro Ile Lys Cys Arg Glu Ala Leu Lys Leu Glu Glu Lys Lys
1585                1590                1595                1600
His Tyr Leu Met Trp Gly Leu Ser Ser Asp Phe Trp Gly Glu Lys Pro
                1605                1610                1615
Asn Leu Ser Tyr Ile Ile Gly Lys Asp Thr Trp Val Glu His Trp Pro
            1620                1625                1630
Glu Glu Asp Glu Cys Gln Asp Glu Glu Asn Gln Lys Gln Cys Gln Asp
        1635                1640                1645
```

Leu Gly Ala Phe Thr Glu Ser Met Val Val Phe Gly Cys Pro Asn
1650 1655 1660

<210> 48
<211> 157
<212> PRT
<213> Artificial Sequence

<220>
<223> uPA a chain long

<400> 48
Ser Asn Glu Leu His Gln Val Pro Ser Asn Cys Asp Cys Leu Asn Gly
1 5 10 15
Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile His Trp Cys Asn
20 25 30
Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile Asp Lys Ser Lys
35 40 45
Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly Lys Ala Ser Thr
50 55 60
Asp Thr Met Gly Arg Pro Cys Leu Pro Trp Asn Ser Ala Thr Val Leu
65 70 75 80
Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu Gln Leu Gly Leu
85 90 95
Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg Arg Arg Pro Trp
100 105 110
Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln Glu Cys Met Val
115 120 125
His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro Pro Glu Glu Leu
130 135 140
Lys Phe Gln Cys Gly Gln Lys Thr Leu Arg Pro Arg Phe
145 150 155

<210> 49
<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<223> uPA a chain short

<400> 49
Lys Pro Ser Ser Pro Pro Glu Glu Leu Lys Phe Gln Cys Gly Gln Lys
1 5 10 15
Thr Leu Arg Pro Arg Phe
20

<210> 50
<211> 231
<212> PRT
<213> Artificial Sequence

<220>
<223> hIgG1 Fc

<400> 50
Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
 1   5   10   15
Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
            20   25   30
Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
        35   40   45
Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
    50   55   60
Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
65   70   75   80
Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
                85   90   95
Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
            100   105   110
Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
        115   120   125
Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
    130   135   140
Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
145   150   155   160
Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
                165   170   175
Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
            180   185   190
Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
        195   200   205
Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
    210   215   220
Leu Ser Leu Ser Pro Gly Lys
225   230

<210> 51
<211> 414
<212> PRT
<213> Artificial Sequence

<220>
<223> u-PA isoform 2

<400> 51

```
Met Val Phe His Leu Arg Thr Arg Tyr Glu Gln Ala Asn Cys Asp Cys
 1               5                  10                  15
Leu Asn Gly Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile His
            20                  25                  30
Trp Cys Asn Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile Asp
        35                  40                  45
Lys Ser Lys Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly Lys
    50                  55                  60
Ala Ser Thr Asp Thr Met Gly Arg Pro Cys Leu Pro Trp Asn Ser Ala
65                  70                  75                  80
Thr Val Leu Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu Gln
                85                  90                  95
Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg Arg
            100                 105                 110
Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln Glu
        115                 120                 125
Cys Met Val His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro Pro
    130                 135                 140
Glu Glu Leu Lys Phe Gln Cys Gly Gln Lys Thr Leu Arg Pro Arg Phe
145                 150                 155                 160
Lys Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe
                165                 170                 175
Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val Cys
            180                 185                 190
Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys
        195                 200                 205
Phe Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg
    210                 215                 220
Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu
225                 230                 235                 240
Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala His His
                245                 250                 255
Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala
            260                 265                 270
Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr Asn
        275                 280                 285
Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu
    290                 295                 300
Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val
305                 310                 315                 320
Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser
                325                 330                 335
Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr
            340                 345                 350
```

```
Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln
        355                 360                 365
Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala
    370                 375                 380
Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro
385                 390                 395                 400
Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                405                 410


<210> 52
<211> 433
<212> PRT
<213> Mus musculus

<220>
<223> u-PA precursor

<400> 52
Met Lys Val Trp Leu Ala Ser Leu Phe Leu Cys Ala Leu Val Val Lys
 1               5                  10                  15
Asn Ser Glu Gly Gly Ser Val Leu Gly Ala Pro Asp Glu Ser Asn Cys
            20                  25                  30
Gly Cys Gln Asn Gly Gly Val Cys Val Ser Tyr Lys Tyr Phe Ser Arg
        35                  40                  45
Ile Arg Arg Cys Ser Cys Pro Arg Lys Phe Gln Gly Glu His Cys Glu
    50                  55                  60
Ile Asp Ala Ser Lys Thr Cys Tyr His Gly Asn Gly Asp Ser Tyr Arg
65                  70                  75                  80
Gly Lys Ala Asn Thr Asp Thr Lys Gly Arg Pro Cys Leu Ala Trp Asn
                85                  90                  95
Ala Pro Ala Val Leu Gln Lys Pro Tyr Asn Ala His Arg Pro Asp Ala
            100                 105                 110
Ile Ser Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn
        115                 120                 125
Gln Lys Arg Pro Trp Cys Tyr Val Gln Ile Gly Leu Arg Gln Phe Val
    130                 135                 140
Gln Glu Cys Met Val His Asp Cys Ser Leu Ser Lys Lys Pro Ser Ser
145                 150                 155                 160
Ser Val Asp Gln Gln Gly Phe Gln Cys Gly Gln Lys Ala Leu Arg Pro
                165                 170                 175
Arg Phe Lys Ile Val Gly Gly Glu Phe Thr Glu Val Glu Asn Gln Pro
            180                 185                 190
Trp Phe Ala Ala Ile Tyr Gln Lys Asn Lys Gly Gly Ser Pro Pro Ser
        195                 200                 205
Phe Lys Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ala Ser Ala
    210                 215                 220
Ala His Cys Phe Ile Gln Leu Pro Lys Lys Glu Asn Tyr Val Val Tyr
```

```
225                 230                 235                 240
Leu Gly Gln Ser Lys Glu Ser Ser Tyr Asn Pro Gly Glu Met Lys Phe
                245                 250                 255
Glu Val Glu Gln Leu Ile Leu His Glu Tyr Tyr Arg Glu Asp Ser Leu
            260                 265                 270
Ala Tyr His Asn Asp Ile Ala Leu Leu Lys Ile Arg Thr Ser Thr Gly
        275                 280                 285
Gln Cys Ala Gln Pro Ser Arg Ser Ile Gln Thr Ile Cys Leu Pro Pro
    290                 295                 300
Arg Phe Thr Asp Ala Pro Phe Gly Ser Asp Cys Glu Ile Thr Gly Phe
305                 310                 315                 320
Gly Lys Glu Ser Glu Ser Asp Tyr Leu Tyr Pro Lys Asn Leu Lys Met
                325                 330                 335
Ser Val Val Lys Leu Val Ser His Glu Gln Cys Met Gln Pro His Tyr
            340                 345                 350
Tyr Gly Ser Glu Ile Asn Tyr Lys Met Leu Cys Ala Ala Asp Pro Glu
        355                 360                 365
Trp Lys Thr Asp Ser Cys Lys Gly Asp Ser Gly Gly Pro Leu Ile Cys
    370                 375                 380
Asn Ile Glu Gly Arg Pro Thr Leu Ser Gly Ile Val Ser Trp Gly Arg
385                 390                 395                 400
Gly Cys Ala Glu Lys Asn Lys Pro Gly Val Tyr Thr Arg Val Ser His
                405                 410                 415
Phe Leu Asp Trp Ile Gln Ser His Ile Gly Glu Glu Lys Gly Leu Ala
            420                 425                 430
Phe
```

<210> 53
<211> 432
<212> PRT
<213> Rattus norvegicus

<220>
<223> u-PA precursor

<400> 53

```
Met Arg Val Trp Leu Ala Ser Leu Phe Leu Cys Ala Leu Val Ala Asn
 1               5                  10                  15
Ser Glu Gly Gly Ser Glu Leu Glu Ala Ser Asp Glu Ser Asn Cys Gly
            20                  25                  30
Cys Gln Asn Gly Gly Val Cys Val Ser Tyr Lys Tyr Phe Ser Ser Ile
        35                  40                  45
Arg Arg Cys Ser Cys Pro Lys Lys Phe Lys Gly Glu His Cys Glu Ile
    50                  55                  60
Asp Thr Ser Lys Thr Cys Tyr His Gly Asn Gly Gln Ser Tyr Arg Gly
65                  70                  75                  80
```

```
Lys Ala Asn Thr Asp Thr Lys Gly Arg Pro Cys Leu Ala Trp Asn Ser
                85                  90                  95
Pro Ala Val Leu Gln Gln Thr Tyr Asn Ala His Arg Ser Asp Ala Leu
            100                 105                 110
Ser Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Gln
        115                 120                 125
Arg Arg Pro Trp Cys Tyr Val Gln Ile Gly Leu Lys Gln Phe Val Gln
    130                 135                 140
Glu Cys Met Val Gln Asp Cys Ser Leu Ser Lys Lys Pro Ser Ser Thr
145                 150                 155                 160
Val Asp Gln Gln Gly Phe Gln Cys Gly Gln Lys Ala Leu Arg Pro Arg
                165                 170                 175
Phe Lys Ile Val Gly Gly Glu Phe Thr Val Val Glu Asn Gln Pro Trp
            180                 185                 190
Phe Ala Ala Ile Tyr Leu Lys Asn Lys Gly Gly Ser Pro Pro Ser Phe
        195                 200                 205
Lys Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ala Ser Ala Thr
    210                 215                 220
His Cys Phe Val Asn Gln Pro Lys Lys Glu Glu Tyr Val Val Tyr Leu
225                 230                 235                 240
Gly Gln Ser Lys Arg Asn Ser Tyr Asn Pro Gly Glu Met Lys Phe Glu
                245                 250                 255
Val Glu Gln Leu Ile Leu His Glu Asp Phe Ser Asp Glu Thr Leu Ala
            260                 265                 270
Phe His Asn Asp Ile Ala Leu Leu Lys Ile Arg Thr Ser Thr Gly Gln
        275                 280                 285
Cys Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Pro Arg
    290                 295                 300
Phe Gly Asp Ala Pro Phe Gly Ser Asp Cys Glu Ile Thr Gly Phe Gly
305                 310                 315                 320
Gln Glu Ser Ala Thr Asp Tyr Phe Tyr Pro Lys Asp Leu Lys Met Ser
                325                 330                 335
Val Val Lys Ile Ile Ser His Glu Gln Cys Lys Gln Pro His Tyr Tyr
            340                 345                 350
Gly Ser Glu Ile Asn Tyr Lys Met Leu Cys Ala Ala Asp Pro Glu Trp
        355                 360                 365
Lys Thr Asp Ser Cys Ser Gly Asp Ser Gly Gly Pro Leu Ile Cys Asn
    370                 375                 380
Ile Asp Gly Arg Pro Thr Leu Ser Gly Ile Val Ser Trp Gly Ser Gly
385                 390                 395                 400
Cys Ala Glu Lys Asn Lys Pro Gly Val Tyr Thr Arg Val Ser Tyr Phe
                405                 410                 415
Leu Asn Trp Ile Gln Ser His Ile Gly Glu Glu Asn Gly Leu Ala Phe
            420                 425                 430
```

<210> 54
<211> 433

<212> PRT
<213> Bos taurus

<220>
<223> u-PA precursor

<400> 54
```
Met Arg Val Leu Leu Ala Cys Leu Leu Val Cys Ala Leu Val Val Ser
 1               5                  10                  15
Asp Ser Asp Gly Ser Asn Glu Val His Lys Glu Ser Gly Glu Ser Asn
            20                  25                  30
Cys Gly Cys Leu Asn Gly Gly Lys Cys Val Thr Tyr Lys Tyr Phe Ser
        35                  40                  45
Asn Ile Gln Arg Cys Ser Cys Pro Lys Lys Phe Gln Gly Glu His Cys
    50                  55                  60
Glu Ile Asp Thr Ser Lys Thr Cys Tyr Gln Gly Asn Gly His Ser Tyr
65                  70                  75                  80
Arg Gly Lys Ala Asn Arg Asp Leu Ser Gly Arg Pro Cys Leu Ala Trp
                85                  90                  95
Asp Ser Pro Thr Val Leu Leu Lys Met Tyr His Ala His Arg Ser Asp
            100                 105                 110
Ala Ile Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp
        115                 120                 125
Asn Gln Arg Arg Pro Trp Cys Tyr Val Gln Ile Gly Leu Lys Gln Phe
    130                 135                 140
Val Gln Phe Cys Met Val Gln Asp Cys Ser Val Gly Lys Ser Pro Ser
145                 150                 155                 160
Ser Pro Arg Glu Lys Glu Glu Phe Gln Cys Gly Gln Lys Ala Leu Arg
                165                 170                 175
Pro Arg Phe Lys Ile Val Gly Gly Gln Val Thr Asn Ala Glu Asn Gln
            180                 185                 190
Pro Trp Phe Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Ile Thr
        195                 200                 205
Tyr Leu Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Val Ser Ala
    210                 215                 220
Thr His Cys Phe Ile Asp His Pro Lys Lys Glu Asn Tyr Ile Val Tyr
225                 230                 235                 240
Leu Gly Gln Ser Arg Leu Asn Ser Asp Thr Arg Gly Glu Met Gln Phe
                245                 250                 255
Glu Val Glu Lys Leu Ile Leu His Glu Asp Tyr Ser Ala Glu Ser Leu
            260                 265                 270
Ala His His Asn Asp Ile Ala Leu Leu Lys Ile Arg Thr Ser Arg Gly
        275                 280                 285
Gln Cys Ala Gln Pro Ser Arg Ser Ile Gln Thr Ile Cys Leu Pro Pro
    290                 295                 300
Glu His Glu Asp Ala His Ser Arg Thr Arg Cys Glu Ile Thr Gly Phe
305                 310                 315                 320
Gly Lys Glu Asn Pro Ser Asp Tyr Arg Tyr Ser Asp Glu Leu Lys Met
```

```
                325                 330                 335
Thr Phe Val Ser Leu Val Ser His Glu Val Cys Gln Gln Pro His Tyr
            340                 345                 350
Tyr Gly Ala Glu Val Thr Asp Lys Met Leu Cys Ala Ala Asp Pro Gln
        355                 360                 365
Trp Glu Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys
    370                 375                 380
Thr Ile Gln Gly Arg Leu Thr Leu Thr Gly Ile Val Ser Trp Gly Arg
385                 390                 395                 400
Asp Cys Ala Met Lys Tyr Lys Pro Gly Val Tyr Thr Arg Val Ser Lys
                405                 410                 415
Phe Leu Pro Trp Ile Asn Thr His Thr Arg Gly Glu Ile Asn Leu Val
            420                 425                 430
Leu
```

<210> 55
<211> 442
<212> PRT
<213> Sus scrofa

<220>
<223> u-PA precursor

<400> 55

```
Met Arg Val Leu Arg Ala Cys Leu Ser Leu Cys Val Leu Val Val Ser
 1               5                  10                  15
Asp Ser Lys Gly Ser His Glu Leu His Gln Glu Ser Gly Ala Ser Asn
            20                  25                  30
Cys Gly Cys Leu Asn Gly Gly Lys Cys Val Ser Tyr Lys Tyr Phe Ser
        35                  40                  45
Asn Ile Gln Arg Cys Ser Cys Pro Lys Lys Phe Gln Gly Glu His Cys
    50                  55                  60
Glu Ile Asp Thr Ser Gln Thr Cys Phe Glu Gly Asn Gly His Ser Tyr
65                  70                  75                  80
Arg Gly Lys Ala Asn Thr Asn Thr Gly Gly Arg Pro Cys Leu Pro Trp
                85                  90                  95
Asn Ser Ala Thr Val Leu Leu Asn Thr Tyr His Ala His Arg Pro Asp
            100                 105                 110
Ala Leu Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp
        115                 120                 125
Asn Gln Arg Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Gln Leu
    130                 135                 140
Val Gln Glu Cys Met Val Pro Asn Cys Ser Gly Gly Glu Ser His Arg
145                 150                 155                 160
Pro Ala Tyr Asp Gly Lys Asn Pro Phe Ser Thr Pro Glu Lys Val Glu
                165                 170                 175
```

```
Phe Gln Cys Gly Gln Lys Ala Leu Arg Pro Arg Phe Lys Ile Val Gly
            180                 185                 190
Gly Lys Ser Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala Ala Ile Tyr
        195                 200                 205
Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val Cys Gly Gly Ser Leu
    210                 215                 220
Ile Ser Pro Cys Trp Val Val Ser Ala Thr His Cys Phe Ile Asn Tyr
225                 230                 235                 240
Gln Gln Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Gln Thr Leu His
                245                 250                 255
Ser Ser Thr His Gly Glu Met Lys Phe Glu Val Glu Lys Leu Ile Leu
            260                 265                 270
His Glu Asp Tyr Ser Ala Asp Ser Leu Ala His His Asn Asp Ile Ala
        275                 280                 285
Leu Leu Lys Ile Arg Thr Asp Lys Gly Gln Cys Ala Gln Pro Ser Arg
    290                 295                 300
Ser Ile Gln Thr Ile Cys Leu Pro Pro Val Asn Gly Asp Ala His Phe
305                 310                 315                 320
Gly Ala Ser Cys Glu Ile Val Gly Phe Gly Lys Glu Asp Pro Ser Asp
                325                 330                 335
Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Val Ser
            340                 345                 350
His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr Thr
        355                 360                 365
Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys Gln
    370                 375                 380
Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Thr Gln Gly Arg Leu Thr
385                 390                 395                 400
Leu Thr Gly Ile Val Ser Trp Gly Arg Glu Cys Ala Met Lys Asp Lys
                405                 410                 415
Pro Gly Val Tyr Thr Arg Val Ser Arg Phe Leu Thr Trp Ile His Thr
            420                 425                 430
His Val Gly Gly Glu Asn Gly Leu Ala His
        435                 440


<210> 56
<211> 433
<212> PRT
<213> Oryctolagus cuniculus

<220>
<223> u-PA precursor

<400> 56
Met Arg Val Leu Leu Val Cys Leu Leu Leu Cys Ala Leu Val Val Ser
 1               5                  10                  15
Asp Ser Glu Gly Ser His Glu Leu His Gly Val Ser Asp Ala Ser Asn
```

```
            20                  25                  30
Cys Gly Cys Leu Asn Gly Gly Thr Cys Val Thr Tyr Lys Tyr Phe Ser
        35                  40                  45
Asn Ile Trp Arg Cys Asn Cys Pro Lys Lys Phe Gln Gly Glu His Cys
    50                  55                  60
Glu Ile Asp Thr Leu Lys Thr Cys Tyr His Gly Asp Gly His Ser Tyr
65                  70                  75                  80
Arg Gly Lys Ala Asn Thr Asp Ile Met Asp Arg Pro Cys Leu Ala Trp
                85                  90                  95
Asn Ser Ala Asn Val Leu Thr Lys Thr Tyr His Ala His Arg Pro Asp
            100                 105                 110
Ala Leu Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp
        115                 120                 125
His Gln Arg Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Gln Leu
    130                 135                 140
Ile Gln Glu Cys Lys Val His Asp Cys Ser Ser Gly Lys Lys Pro Ala
145                 150                 155                 160
Leu Pro Pro Gly Lys Leu Glu Phe Gln Cys Gly Gln Lys Ala Leu Arg
                165                 170                 175
Pro Arg Phe Lys Ile Ile Gly Gly Glu Phe Thr Ile Ile Glu Asn Gln
            180                 185                 190
Pro Trp Phe Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr
        195                 200                 205
Tyr Val Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Val Ser Ala
    210                 215                 220
Thr His Cys Phe Ile Asn His Gln Lys Lys Glu Asp Tyr Ile Val Tyr
225                 230                 235                 240
Leu Gly Arg Ser Arg Leu Asn Ser Met Thr Pro Gly Glu Met Lys Phe
                245                 250                 255
Glu Val Glu Gln Leu Ile Leu His Glu Gly Tyr Arg Ala Asp Thr Leu
            260                 265                 270
Ala His His Asn Asp Ile Ala Leu Leu Lys Ile Leu Ser Asn Asn Gly
        275                 280                 285
Gln Cys Ala Gln Pro Ser Arg Ser Ile Gln Thr Ile Cys Leu Pro Pro
    290                 295                 300
Trp Asn Ala Asp Pro Asn Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe
305                 310                 315                 320
Gly Lys Glu Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met
                325                 330                 335
Thr Val Val Lys Leu Val Ser Tyr Gln Glu Cys Gln Gln Pro His Tyr
            340                 345                 350
Tyr Gly Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln
        355                 360                 365
Trp Glu Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys
    370                 375                 380
Ser Val Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg
385                 390                 395                 400
Gly Cys Ala Leu Lys Asn Lys Pro Gly Val Tyr Thr Arg Val Ser Arg
```

```
                405                 410                 415
Phe Leu Pro Trp Ile Arg Ser His Ile Gly Glu Glu Asn Gly Leu Ala
            420                 425                 430
Leu
```

<210> 57
<211> 434
<212> PRT
<213> Gallus gallus

<220>
<223> u-PA precursor

<400> 57

```
Met Lys Leu Ile Ile Phe Leu Thr Val Thr Leu Cys Thr Leu Val Thr
 1               5                  10                  15
Gly Leu Asp Ser Val Tyr Ile Arg Gln Tyr Tyr Lys Leu Ser His Lys
            20                  25                  30
His Arg Pro Gln His Arg Glu Cys Gln Cys Leu Asn Gly Gly Thr Cys
        35                  40                  45
Ile Thr Tyr Arg Phe Phe Ser Gln Ile Lys Arg Cys Leu Cys Pro Glu
    50                  55                  60
Gly Tyr Gly Gly Leu His Cys Glu Ile Asp Thr Asn Ser Ile Cys Tyr
65                  70                  75                  80
Ser Gly Asn Gly Glu Asp Tyr Arg Gly Met Ala Glu Asp Pro Gly Cys
                85                  90                  95
Leu Tyr Trp Asp His Pro Ser Val Ile Arg Trp Gly Asp Tyr His Ala
            100                 105                 110
Asp Leu Lys Asn Ala Leu Gln Leu Gly Leu Gly Lys His Asn Tyr Cys
        115                 120                 125
Arg Asn Pro Asn Gly Arg Ser Arg Pro Trp Cys Tyr Thr Lys Arg Arg
    130                 135                 140
Tyr Ser Ile Gln Glu Thr Pro Cys Ser Thr Ile Glu Lys Cys Glu Arg
145                 150                 155                 160
Thr Cys Gly Gln Arg Ser Phe Ser Lys Tyr Phe Lys Ile Val Gly Gly
                165                 170                 175
Ser Gln Ala Glu Val Glu Thr Gln Pro Trp Ile Ala Gly Ile Phe Gln
            180                 185                 190
Asn Ile Met Gly Thr Asp Gln Phe Leu Cys Gly Gly Ser Leu Ile Asp
        195                 200                 205
Pro Cys Trp Val Leu Thr Ala Ala His Cys Phe Tyr Asn Pro Thr Lys
    210                 215                 220
Lys Gln Pro Asn Lys Ser Val Tyr Lys Val Phe Leu Gly Lys Ser Ile
225                 230                 235                 240
Leu Asn Thr Asn Asp Glu His Glu Gln Val Phe Met Val Asp Glu Ile
                245                 250                 255
```

```
Ile Ser His Pro Asp Phe Thr Asp His Thr Gly Gly Asn Asp Asn Asp
            260                 265                 270
Ile Ala Leu Ile Arg Ile Arg Thr Ala Ser Gly Gln Cys Ala Val Glu
        275                 280                 285
Ser Asn Tyr Val Arg Thr Val Cys Leu Pro Glu Lys Asn Leu Asn Leu
    290                 295                 300
Tyr Asp Asn Thr Trp Cys Glu Ile Ala Gly Tyr Gly Lys Gln Asn Ser
305                 310                 315                 320
Tyr Asp Ile Tyr Tyr Ala Gln Arg Leu Met Ser Ala Thr Val Asn Leu
                325                 330                 335
Ile Ser Gln Asp Asp Cys Lys Asn Lys Tyr Tyr Asp Ser Thr Arg Val
            340                 345                 350
Thr Asp Asn Met Val Cys Ala Gly Asp Pro Leu Trp Glu Thr Asp Ala
        355                 360                 365
Cys Lys Gly Asp Ser Gly Gly Pro Met Val Cys Glu His Asn Gly Arg
    370                 375                 380
Met Thr Leu Tyr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Lys Lys
385                 390                 395                 400
Asn Lys Pro Gly Val Tyr Thr Arg Val Thr Arg Tyr Leu Asn Trp Ile
                405                 410                 415
Asp Ser Asn Met Asn Ala Val Phe Thr Lys Ser Arg Ser Phe Arg Glu
            420                 425                 430
Pro Lys
```

<210> 58
<211> 433
<212> PRT
<213> Papio cynocephalus

<220>
<223> u-PA precursor

<400> 58

```
Met Arg Ala Leu Leu Ala His Leu Leu Leu Cys Val Leu Val Val Ser
 1               5                  10                  15
Ala Ser Lys Gly Ser Arg Glu Leu Gln Val Pro Ser Asp Cys Gly Cys
            20                  25                  30
Leu Asn Gly Gly Thr Cys Met Ser Asn Lys Tyr Phe Ser Ser Ile His
        35                  40                  45
Trp Cys Asn Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile Asp
    50                  55                  60
Lys Ser Lys Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly Lys
65                  70                  75                  80
Ala Ser Thr Asp Thr Met Gly Arg Ser Cys Leu Ala Trp Asn Ser Ala
                85                  90                  95
Thr Val Leu Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu Gln
```

```
            100                 105                 110
Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg Arg
        115                 120                 125
Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Gln Arg Val Gln Glu
    130                 135                 140
Cys Met Val His Asn Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro Pro
145                 150                 155                 160
Glu Glu Leu Gln Phe Gln Cys Gly Gln Arg Thr Leu Arg Pro Arg Phe
                165                 170                 175
Lys Ile Val Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe
            180                 185                 190
Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val Cys
        195                 200                 205
Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Val Ser Ala Thr His Cys
    210                 215                 220
Phe Ile Asn Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg
225                 230                 235                 240
Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu
                245                 250                 255
Asn Leu Ile Leu His Glu Asp Tyr Ser Ala Asp Thr Leu Ala His His
            260                 265                 270
Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala
        275                 280                 285
Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr Asn
    290                 295                 300
Asp Pro Asn Asp Pro Pro Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe
305                 310                 315                 320
Gly Lys Glu Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met
                325                 330                 335
Thr Val Val Lys Leu Val Ser His Gln Lys Cys Gln Gln Pro His Tyr
            340                 345                 350
Tyr Gly Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln
        355                 360                 365
Trp Glu Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys
    370                 375                 380
Ser Ile Gln Gly His Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg
385                 390                 395                 400
Gly Cys Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser Arg
                405                 410                 415
Phe Leu Pro Trp Ile His Ser His Thr Arg Glu Gln Asn Gly Leu Ala
            420                 425                 430
Leu
```

<210> 59
<211> 431
<212> PRT

<213> Pongo abelii

<220>
<223> u-PA precursor

<400> 59

```
Met Arg Ala Leu Leu Ala Arg Leu Leu Leu Cys Val Leu Val Val Ser
 1               5                  10                  15
Asp Ser Lys Gly Ser Asn Glu Leu His Gln Val Pro Ser Asn Cys Asp
            20                  25                  30
Cys Leu Asn Gly Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile
        35                  40                  45
His Trp Cys Asn Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile
    50                  55                  60
Asp Lys Ser Lys Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly
65                  70                  75                  80
Lys Ala Ser Thr Asp Thr Met Gly Arg Pro Cys Leu Ala Trp Asn Ser
                85                  90                  95
Ala Thr Val Leu Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu
            100                 105                 110
Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg
        115                 120                 125
Trp Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln
    130                 135                 140
Glu Cys Met Val His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro
145                 150                 155                 160
Pro Glu Glu Leu Lys Phe Gln Cys Gly Gln Lys Thr Leu Arg Pro Arg
                165                 170                 175
Phe Lys Ile Val Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp
            180                 185                 190
Phe Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val
        195                 200                 205
Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Val Ser Ala Thr His
    210                 215                 220
Cys Phe Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly
225                 230                 235                 240
Arg Ser Arg Leu Asn Ser His Thr Gln Gly Glu Met Lys Phe Glu Val
                245                 250                 255
Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala His
            260                 265                 270
His Asn Asp Ile Ala Leu Leu Lys Ile His Ser Lys Glu Gly Arg Cys
        275                 280                 285
Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr
    290                 295                 300
Asn Asp Pro Pro Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys
305                 310                 315                 320
Glu Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val
                325                 330                 335
```

```
Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly
            340                 345                 350
Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys
        355                 360                 365
Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu
    370                 375                 380
Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys
385                 390                 395                 400
Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser Tyr Phe Leu
                405                 410                 415
Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
            420                 425                 430


<210> 60
<211> 428
<212> PRT
<213> Canus lupus

<220>
<223> u-PA precursor

<400> 60
Met Arg Ala Leu Met Thr Cys Leu Leu Leu Gly Ala Leu Val Gly Ser
 1               5                  10                  15
His Glu Phe His Pro Val Ser Ser Ala Ser Asn Cys Ser Cys Leu Asn
            20                  25                  30
Gly Gly Thr Cys Val Ser Tyr Lys Tyr Phe Ser Asn Ile Gln Arg Cys
        35                  40                  45
Asn Cys Pro Lys Lys Phe Gln Gly Glu His Cys Glu Ile Asp Thr Ser
    50                  55                  60
Lys Thr Cys Tyr Glu Gly Asn Gly His Ser Tyr Arg Gly Lys Ala Asn
65                  70                  75                  80
Thr Asn Thr Arg Gly Arg Pro Cys Leu Ala Trp Asn Ser Ala Ala Val
                85                  90                  95
Leu Leu Lys Gln Tyr His Ala Leu Arg Pro Asp Ala Leu Gln Leu Gly
            100                 105                 110
Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp His Gln Arg Lys Pro
        115                 120                 125
Trp Cys Tyr Val Gln Val Gly Leu Met Gln Leu Val Gln Glu Cys Thr
    130                 135                 140
Val Gln His Cys Ser Phe Glu Lys Asn Pro His Ser Pro Pro Glu Lys
145                 150                 155                 160
Ala Glu Phe Gln Cys Gly Gln Lys Ala Leu Arg Pro Arg Phe Lys Ile
                165                 170                 175
Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala Ala
            180                 185                 190
Ile Tyr Arg Lys His Arg Gly Gly Ser Val Thr Tyr Gln Cys Gly Gly
```

```
        195                 200                 205
Ser Leu Ile Ser Pro Cys Trp Val Val Ser Ala Thr His Cys Phe Ile
    210                 215                 220
Asn Ser Gln Lys Lys Asp Asp Tyr Ile Val Tyr Leu Gly Arg Ser Lys
225                 230                 235                 240
Arg Ile Ser Lys Thr Phe Gly Glu Met Lys Phe Glu Val Glu Lys Leu
                245                 250                 255
Ile Leu His Glu Asp Tyr Ser Ala Asp Ser Leu Ala His His Asn Asp
            260                 265                 270
Ile Ala Leu Leu Lys Ile Arg Ser Asp Glu Gly Gln Cys Ala Gln Pro
        275                 280                 285
Ser Arg Ser Ile Gln Thr Ile Cys Leu Pro Pro Ser Arg Gly Asp Ala
    290                 295                 300
His Phe Gly Ala Ser Cys Glu Ile Ser Gly Phe Gly Lys Glu Asn Ser
305                 310                 315                 320
Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu
                325                 330                 335
Val Ser His Gln Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val
            340                 345                 350
Thr Asp Gln Met Leu Cys Ala Ala Asp Pro Glu Trp Glu Thr Asp Ser
        355                 360                 365
Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Thr Gln Gly Arg
    370                 375                 380
Leu Thr Leu Thr Gly Ile Val Ser Trp Gly Ser Gly Cys Ala Met Lys
385                 390                 395                 400
Asn Lys Pro Gly Val Tyr Thr Arg Val Ser Arg Phe Leu Pro Trp Ile
                405                 410                 415
His Arg His Ile Gly Glu Gln Asn Gly Leu Thr Leu
            420                 425
```

<210> 61
<211> 433
<212> PRT
<213> Ovis aries

<220>
<223> u-PA precursor

<400> 61

```
Met Arg Val Leu Leu Ala Cys Leu Leu Val Cys Ala Leu Val Val Ser
 1               5                  10                  15
Asp Ser Asp Gly Ser Asn Glu Val His Lys Glu Ser Gly Val Ser Asp
            20                  25                  30
Cys Gly Cys Leu Asn Gly Gly Lys Cys Val Ser Tyr Lys Tyr Phe Ser
        35                  40                  45
Asn Ile Gln Arg Cys Ser Cys Pro Lys Lys Phe Gln Gly Glu Tyr Cys
    50                  55                  60
```

```
Glu Ile Asp Thr Ser Lys Thr Cys Tyr Gln Gly Asn Gly His Ser Tyr
65                  70                  75                  80
Arg Gly Lys Ala Asn Thr Asp Leu Arg Gly Arg Pro Arg Leu Ala Trp
                85                  90                  95
Asp Ser Ala Thr Val Leu Leu Lys Met Tyr His Ala His Arg Ser Asp
            100                 105                 110
Ala Ile Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp
        115                 120                 125
Asn Gln Arg Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Gln Phe
    130                 135                 140
Val Gln Glu Cys Met Val Gln Asp Cys Pro Ala Gly Lys Gly Pro Ser
145                 150                 155                 160
Ser Pro Lys Glu Lys Val Glu Phe Gln Cys Gly Gln Lys Ala Leu Arg
                165                 170                 175
Pro Arg Phe Glu Ile Val Gly Gly Glu Phe Thr Thr Ile Glu Ser Gln
            180                 185                 190
Pro Trp Phe Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr
        195                 200                 205
Tyr Leu Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Val Ser Ala
    210                 215                 220
Thr His Cys Phe Thr Asn His Pro Lys Lys Glu Asp Tyr Ile Val Tyr
225                 230                 235                 240
Leu Gly Arg Ser Lys Leu Asn Ser Asp Thr Leu Gly Glu Met Lys Phe
                245                 250                 255
Glu Val Glu Lys Leu Ile Leu His Glu Asp Tyr Ser Ala Asp Ser Leu
            260                 265                 270
Ala His His Asn Asp Ile Ala Leu Leu Lys Ile Arg Thr Ser Arg Gly
        275                 280                 285
Gln Cys Ala Gln Pro Ser Arg Ser Ile Gln Thr Ile Cys Leu Pro Pro
    290                 295                 300
Leu Tyr Gly Asp Ala Arg Phe Gly Thr Arg Cys Glu Ile Thr Gly Phe
305                 310                 315                 320
Gly Lys Glu Asn Pro Ser Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met
                325                 330                 335
Thr Phe Val Asn Leu Val Ser His Glu Glu Cys Gln Gln Pro His Tyr
            340                 345                 350
Tyr Gly Thr Glu Val Thr Asp Lys Met Leu Cys Ala Ala Asp Pro Gln
        355                 360                 365
Trp Glu Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys
    370                 375                 380
Thr Ile Gln Gly Arg Leu Thr Leu Thr Gly Ile Val Ser Trp Gly Arg
385                 390                 395                 400
Glu Cys Ala Met Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser Lys
                405                 410                 415
Phe Leu Pro Trp Ile Tyr Thr His Thr Arg Gly Glu Ile Asp Leu Gly
            420                 425                 430
Leu
```

<210> 62
<211> 430
<212> PRT
<213> Callithrix jacchus

<220>
<223> u-PA

<400> 62
```
Met Arg Thr Leu Leu Val Arg Leu Leu Leu Cys Val Leu Ile Val Ser
 1               5                  10                  15
Asp Ser Lys Gly Arg Arg Glu His Gln Val Pro Ser Asn Cys Asp Cys
            20                  25                  30
Leu Asn Gly Gly Thr Cys Val Ser Ser Lys Tyr Phe Ser Asn Thr Arg
        35                  40                  45
Trp Cys Asn Cys Pro Lys Lys Phe Gly Gly Leu His Cys Glu Ile Asp
    50                  55                  60
Asn Ser Lys Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly Lys
65                  70                  75                  80
Ala Lys Thr Asp Ile Met Gly Arg Ser Cys Leu Ser Trp Asn Ser Ala
                85                  90                  95
Ala Val Leu Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu Gln
            100                 105                 110
Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg Arg
        115                 120                 125
Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Gln Leu Val Gln Glu
    130                 135                 140
Cys Thr Val His Asn Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro Pro
145                 150                 155                 160
Ala Glu Leu Glu Phe Gln Cys Gly Gln Lys Pro Leu Thr Pro Arg Phe
                165                 170                 175
Lys Ile Ile Gly Gly Glu Tyr Thr Thr Ile Glu Asn Gln Pro Trp Phe
            180                 185                 190
Ala Ala Ile Tyr Arg Gln His Arg Gly Gly Ser Val Thr Tyr Leu Cys
        195                 200                 205
Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Val Ser Ala Thr His Cys
    210                 215                 220
Phe Ile Asn His Ala Val Lys Glu Asp Phe Ile Val Tyr Leu Gly Arg
225                 230                 235                 240
Ser Arg Leu Asn Ser Asn Thr Pro Gly Glu Met Arg Phe Asp Val Glu
                245                 250                 255
Asn Leu Ile Leu His Glu Gly Tyr Ser Ala Asp Thr Leu Ala His His
            260                 265                 270
Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Lys Cys Ala
        275                 280                 285
Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Pro Met Leu Asn
```

```
    290                 295                 300
Asp Ala Arg Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu
305                 310                 315                 320
Asn Thr Thr Asp Tyr Phe Tyr Pro Glu Gln Leu Lys Met Thr Val Val
                325                 330                 335
Lys Leu Val Ser His Gln Glu Cys Gln Gln Pro Asn Tyr Tyr Gly Ser
            340                 345                 350
Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Glu Thr
        355                 360                 365
Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Ile Cys Ser Ile Gln
    370                 375                 380
Gly His Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala
385                 390                 395                 400
Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser Arg Phe Leu Pro
                405                 410                 415
Trp Ile Arg Arg His Thr Lys Glu Glu Asn Gly Pro Ala Val
            420                 425                 430


<210> 63
<211> 430
<212> PRT
<213> Macaca mulatta

<220>
<223> u-PA

<400> 63
Met Arg Ala Leu Leu Ala His Leu Leu Leu Cys Val Leu Val Val Ser
 1               5                  10                  15
Asp Ser Lys Gly Ser Arg Glu Leu Gln Val Pro Ser Asp Cys Gly Cys
            20                  25                  30
Leu Asn Gly Gly Thr Cys Met Ser Asn Lys Tyr Phe Ser Ser Ile His
        35                  40                  45
Trp Cys Asn Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile Asp
    50                  55                  60
Lys Ser Lys Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly Lys
65                  70                  75                  80
Ala Ser Thr Asp Thr Met Gly Arg Ser Cys Leu Ala Trp Asn Ser Ala
                85                  90                  95
Thr Val Leu Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu Gln
            100                 105                 110
Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg Arg
        115                 120                 125
Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Gln Leu Val Gln Glu
    130                 135                 140
Cys Met Val Gln Asn Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro Pro
145                 150                 155                 160
```

```
Glu Glu Leu Gln Phe Gln Cys Gly Gln Arg Thr Leu Arg Pro Arg Phe
                165                 170                 175
Lys Ile Val Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe
            180                 185                 190
Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val Cys
        195                 200                 205
Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Val Ser Ala Thr His Cys
    210                 215                 220
Phe Ile Asn Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg
225                 230                 235                 240
Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu
                245                 250                 255
Asn Leu Ile Leu His Glu Asp Tyr Ser Ala Asp Thr Leu Ala His His
            260                 265                 270
Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala
        275                 280                 285
Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Thr Tyr Asn
    290                 295                 300
Asp Pro Pro Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu
305                 310                 315                 320
Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Arg Leu Lys Met Thr Val Val
                325                 330                 335
Lys Leu Val Ser His Gln Lys Cys Gln Gln Pro His Tyr Tyr Gly Ser
            340                 345                 350
Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Glu Thr
        355                 360                 365
Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Ile Gln
    370                 375                 380
Gly His Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala
385                 390                 395                 400
Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser Arg Phe Leu Pro
                405                 410                 415
Trp Ile His Ser His Thr Arg Glu Glu Asn Gly Leu Ala Leu
            420                 425                 430


<210> 64
<211> 345
<212> PRT
<213> Nomascus leucogenys

<220>
<223> u-PA

<400> 64
Met Gly Arg Pro Cys Leu Ala Trp Asn Ser Ala Thr Val Leu Gln Gln
 1               5                  10                  15
Thr Tyr His Ala His Arg Ser Asp Ala Leu Gln Leu Gly Leu Gly Lys
```

```
            20                  25                  30
His Asn Tyr Cys Arg Asn Pro Asp Asn Arg Arg Arg Pro Trp Cys Tyr
        35                  40                  45
Val Gln Val Gly Leu Lys Pro Leu Val Gln Glu Cys Met Val His Asp
    50                  55                  60
Cys Thr Asp Gly Lys Lys Pro Ser Ser Pro Pro Glu Glu Leu Gln Phe
65                  70                  75                  80
Gln Cys Gly Gln Lys Thr Leu Arg Pro Arg Phe Lys Ile Ile Gly Gly
                85                  90                  95
Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala Ala Ile Tyr Arg
            100                 105                 110
Arg His Arg Gly Gly Ser Val Thr Tyr Val Cys Gly Gly Ser Leu Ile
        115                 120                 125
Ser Pro Cys Trp Val Val Ser Ala Thr His Cys Phe Ile Asp Tyr Pro
    130                 135                 140
Lys Lys Glu Asp Tyr Ile Ile Tyr Leu Gly Arg Ser Arg Leu Asn Ser
145                 150                 155                 160
Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn Leu Ile Leu His
                165                 170                 175
Glu Asp Tyr Ser Ala Asp Thr Leu Ala His His Asn Asp Ile Ala Leu
            180                 185                 190
Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser Arg Thr
        195                 200                 205
Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr Asn Asp Pro His Phe Gly
    210                 215                 220
Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr Asp Tyr
225                 230                 235                 240
Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile Ser His
                245                 250                 255
Lys Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr Thr Lys
            260                 265                 270
Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys Gln Gly
        275                 280                 285
Asp Ser Gly Gly Pro Leu Val Cys Ser Ile Arg Gly Arg Met Thr Leu
    290                 295                 300
Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys Asp Lys Pro
305                 310                 315                 320
Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg Ser His
                325                 330                 335
Thr Lys Glu Glu Asn Gly Leu Ala Leu
            340                 345
```

<210> 65
<211> 431
<212> PRT
<213> Pan troglodytes

<220>
<223> u-PA

<400> 65
```
Met Arg Ala Arg Glu Ala Arg Leu Leu Leu Cys Val Leu Val Val Ser
 1               5                  10                  15
Asp Ser Lys Gly Ser Asn Glu Leu His Gln Val Pro Ser Asn Cys Asp
            20                  25                  30
Cys Leu Asn Gly Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile
        35                  40                  45
His Trp Cys Asn Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile
    50                  55                  60
Asp Lys Ser Lys Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly
65                  70                  75                  80
Lys Ala Ser Thr Asp Thr Met Gly Arg Pro Cys Leu Ala Trp Asn Ser
                85                  90                  95
Ala Thr Val Leu Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu
            100                 105                 110
Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg
        115                 120                 125
Arg Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln
    130                 135                 140
Glu Cys Met Val His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro
145                 150                 155                 160
Pro Glu Glu Leu Lys Phe Gln Cys Gly Gln Lys Thr Leu Arg Pro Arg
                165                 170                 175
Phe Lys Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp
            180                 185                 190
Phe Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Leu
        195                 200                 205
Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His
    210                 215                 220
Cys Phe Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly
225                 230                 235                 240
Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val
                245                 250                 255
Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala His
            260                 265                 270
His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys
        275                 280                 285
Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr
    290                 295                 300
Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys
305                 310                 315                 320
Glu Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val
                325                 330                 335
Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly
            340                 345                 350
```

```
Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys
        355                 360                 365
Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu
    370                 375                 380
Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys
385                 390                 395                 400
Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu
                405                 410                 415
Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
            420                 425                 430


<210> 66
<211> 413
<212> PRT
<213> Mus musculus

<220>
<223> u-PA mature protein

<400> 66
Gly Ser Val Leu Gly Ala Pro Asp Glu Ser Asn Cys Gly Cys Gln Asn
 1               5                  10                  15
Gly Gly Val Cys Val Ser Tyr Lys Tyr Phe Ser Arg Ile Arg Arg Cys
            20                  25                  30
Ser Cys Pro Arg Lys Phe Gln Gly Glu His Cys Glu Ile Asp Ala Ser
        35                  40                  45
Lys Thr Cys Tyr His Gly Asn Gly Asp Ser Tyr Arg Gly Lys Ala Asn
    50                  55                  60
Thr Asp Thr Lys Gly Arg Pro Cys Leu Ala Trp Asn Ala Pro Ala Val
65                  70                  75                  80
Leu Gln Lys Pro Tyr Asn Ala His Arg Pro Asp Ala Ile Ser Leu Gly
                85                  90                  95
Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Gln Lys Arg Pro
            100                 105                 110
Trp Cys Tyr Val Gln Ile Gly Leu Arg Gln Phe Val Gln Glu Cys Met
        115                 120                 125
Val His Asp Cys Ser Leu Ser Lys Lys Pro Ser Ser Ser Val Asp Gln
    130                 135                 140
Gln Gly Phe Gln Cys Gly Gln Lys Ala Leu Arg Pro Arg Phe Lys Ile
145                 150                 155                 160
Val Gly Gly Glu Phe Thr Glu Val Glu Asn Gln Pro Trp Phe Ala Ala
                165                 170                 175
Ile Tyr Gln Lys Asn Lys Gly Gly Ser Pro Pro Ser Phe Lys Cys Gly
            180                 185                 190
Gly Ser Leu Ile Ser Pro Cys Trp Val Ala Ser Ala Ala His Cys Phe
        195                 200                 205
Ile Gln Leu Pro Lys Lys Glu Asn Tyr Val Val Tyr Leu Gly Gln Ser
```

```
    210                 215                 220
Lys Glu Ser Ser Tyr Asn Pro Gly Glu Met Lys Phe Glu Val Glu Gln
225                 230                 235                 240
Leu Ile Leu His Glu Tyr Tyr Arg Glu Asp Ser Leu Ala Tyr His Asn
                245                 250                 255
Asp Ile Ala Leu Leu Lys Ile Arg Thr Ser Thr Gly Gln Cys Ala Gln
            260                 265                 270
Pro Ser Arg Ser Ile Gln Thr Ile Cys Leu Pro Pro Arg Phe Thr Asp
        275                 280                 285
Ala Pro Phe Gly Ser Asp Cys Glu Ile Thr Gly Phe Gly Lys Glu Ser
    290                 295                 300
Glu Ser Asp Tyr Leu Tyr Pro Lys Asn Leu Lys Met Ser Val Val Lys
305                 310                 315                 320
Leu Val Ser His Glu Gln Cys Met Gln Pro His Tyr Tyr Gly Ser Glu
                325                 330                 335
Ile Asn Tyr Lys Met Leu Cys Ala Ala Asp Pro Glu Trp Lys Thr Asp
            340                 345                 350
Ser Cys Lys Gly Asp Ser Gly Gly Pro Leu Ile Cys Asn Ile Glu Gly
        355                 360                 365
Arg Pro Thr Leu Ser Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Glu
    370                 375                 380
Lys Asn Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Asp Trp
385                 390                 395                 400
Ile Gln Ser His Ile Gly Glu Glu Lys Gly Leu Ala Phe
                405                 410
```

<210> 67
<211> 413
<212> PRT
<213> Rattus norvegicus

<220>
<223> u-PA mature protein

<400> 67

```
Gly Ser Glu Leu Glu Ala Ser Asp Glu Ser Asn Cys Gly Cys Gln Asn
 1               5                  10                  15
Gly Gly Val Cys Val Ser Tyr Lys Tyr Phe Ser Ser Ile Arg Arg Cys
            20                  25                  30
Ser Cys Pro Lys Lys Phe Lys Gly Glu His Cys Glu Ile Asp Thr Ser
        35                  40                  45
Lys Thr Cys Tyr His Gly Asn Gly Gln Ser Tyr Arg Gly Lys Ala Asn
    50                  55                  60
Thr Asp Thr Lys Gly Arg Pro Cys Leu Ala Trp Asn Ser Pro Ala Val
65                  70                  75                  80
Leu Gln Gln Thr Tyr Asn Ala His Arg Ser Asp Ala Leu Ser Leu Gly
                85                  90                  95
```

```
Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Gln Arg Arg Pro
            100                 105                 110
Trp Cys Tyr Val Gln Ile Gly Leu Lys Gln Phe Val Gln Glu Cys Met
        115                 120                 125
Val Gln Asp Cys Ser Leu Ser Lys Lys Pro Ser Ser Thr Val Asp Gln
    130                 135                 140
Gln Gly Phe Gln Cys Gly Gln Lys Ala Leu Arg Pro Arg Phe Lys Ile
145                 150                 155                 160
Val Gly Gly Glu Phe Thr Val Val Glu Asn Gln Pro Trp Phe Ala Ala
                165                 170                 175
Ile Tyr Leu Lys Asn Lys Gly Gly Ser Pro Pro Ser Phe Lys Cys Gly
            180                 185                 190
Gly Ser Leu Ile Ser Pro Cys Trp Val Ala Ser Ala Thr His Cys Phe
        195                 200                 205
Val Asn Gln Pro Lys Lys Glu Glu Tyr Val Val Tyr Leu Gly Gln Ser
    210                 215                 220
Lys Arg Asn Ser Tyr Asn Pro Gly Glu Met Lys Phe Glu Val Glu Gln
225                 230                 235                 240
Leu Ile Leu His Glu Asp Phe Ser Asp Glu Thr Leu Ala Phe His Asn
                245                 250                 255
Asp Ile Ala Leu Leu Lys Ile Arg Thr Ser Thr Gly Gln Cys Ala Gln
            260                 265                 270
Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Pro Arg Phe Gly Asp
        275                 280                 285
Ala Pro Phe Gly Ser Asp Cys Glu Ile Thr Gly Phe Gly Gln Glu Ser
    290                 295                 300
Ala Thr Asp Tyr Phe Tyr Pro Lys Asp Leu Lys Met Ser Val Val Lys
305                 310                 315                 320
Ile Ile Ser His Glu Gln Cys Lys Gln Pro His Tyr Tyr Gly Ser Glu
                325                 330                 335
Ile Asn Tyr Lys Met Leu Cys Ala Ala Asp Pro Glu Trp Lys Thr Asp
            340                 345                 350
Ser Cys Ser Gly Asp Ser Gly Gly Pro Leu Ile Cys Asn Ile Asp Gly
        355                 360                 365
Arg Pro Thr Leu Ser Gly Ile Val Ser Trp Gly Ser Gly Cys Ala Glu
    370                 375                 380
Lys Asn Lys Pro Gly Val Tyr Thr Arg Val Ser Tyr Phe Leu Asn Trp
385                 390                 395                 400
Ile Gln Ser His Ile Gly Glu Glu Asn Gly Leu Ala Phe
                405                 410
```

<210> 68
<211> 413
<212> PRT
<213> Bos taurus

<220>

<223> u-PA mature protein

<400> 68

```
Ser Asn Glu Val His Lys Glu Ser Gly Glu Ser Asn Cys Gly Cys Leu
 1               5                  10                  15
Asn Gly Gly Lys Cys Val Thr Tyr Lys Tyr Phe Ser Asn Ile Gln Arg
            20                  25                  30
Cys Ser Cys Pro Lys Lys Phe Gln Gly Glu His Cys Glu Ile Asp Thr
        35                  40                  45
Ser Lys Thr Cys Tyr Gln Gly Asn Gly His Ser Tyr Arg Gly Lys Ala
    50                  55                  60
Asn Arg Asp Leu Ser Gly Arg Pro Cys Leu Ala Trp Asp Ser Pro Thr
65                  70                  75                  80
Val Leu Leu Lys Met Tyr His Ala His Arg Ser Asp Ala Ile Gln Leu
                85                  90                  95
Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Gln Arg Arg
            100                 105                 110
Pro Trp Cys Tyr Val Gln Ile Gly Leu Lys Gln Phe Val Gln Phe Cys
        115                 120                 125
Met Val Gln Asp Cys Ser Val Gly Lys Ser Pro Ser Ser Pro Arg Glu
    130                 135                 140
Lys Glu Glu Phe Gln Cys Gly Gln Lys Ala Leu Arg Pro Arg Phe Lys
145                 150                 155                 160
Ile Val Gly Gly Gln Val Thr Asn Ala Glu Asn Gln Pro Trp Phe Ala
                165                 170                 175
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Ile Thr Tyr Leu Cys Gly
            180                 185                 190
Gly Ser Leu Ile Ser Pro Cys Trp Val Val Ser Ala Thr His Cys Phe
        195                 200                 205
Ile Asp His Pro Lys Lys Glu Asn Tyr Ile Val Tyr Leu Gly Gln Ser
    210                 215                 220
Arg Leu Asn Ser Asp Thr Arg Gly Glu Met Gln Phe Glu Val Glu Lys
225                 230                 235                 240
Leu Ile Leu His Glu Asp Tyr Ser Ala Glu Ser Leu Ala His His Asn
                245                 250                 255
Asp Ile Ala Leu Leu Lys Ile Arg Thr Ser Arg Gly Gln Cys Ala Gln
            260                 265                 270
Pro Ser Arg Ser Ile Gln Thr Ile Cys Leu Pro Pro Glu His Glu Asp
        275                 280                 285
Ala His Ser Arg Thr Arg Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    290                 295                 300
Pro Ser Asp Tyr Arg Tyr Ser Asp Glu Leu Lys Met Thr Phe Val Ser
305                 310                 315                 320
Leu Val Ser His Glu Val Cys Gln Gln Pro His Tyr Tyr Gly Ala Glu
                325                 330                 335
Val Thr Asp Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Glu Thr Asp
            340                 345                 350
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Thr Ile Gln Gly
```

```
        355                 360                 365
Arg Leu Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Asp Cys Ala Met
    370                 375                 380
Lys Tyr Lys Pro Gly Val Tyr Thr Arg Val Ser Lys Phe Leu Pro Trp
385                 390                 395                 400
Ile Asn Thr His Thr Arg Gly Glu Ile Asn Leu Val Leu
                405                 410
```

<210> 69
<211> 422
<212> PRT
<213> Sus scrofa

<220>
<223> u-PA mature protein

<400> 69

```
Ser His Glu Leu His Gln Glu Ser Gly Ala Ser Asn Cys Gly Cys Leu
 1               5                  10                  15
Asn Gly Gly Lys Cys Val Ser Tyr Lys Tyr Phe Ser Asn Ile Gln Arg
            20                  25                  30
Cys Ser Cys Pro Lys Lys Phe Gln Gly Glu His Cys Glu Ile Asp Thr
        35                  40                  45
Ser Gln Thr Cys Phe Glu Gly Asn Gly His Ser Tyr Arg Gly Lys Ala
    50                  55                  60
Asn Thr Asn Thr Gly Gly Arg Pro Cys Leu Pro Trp Asn Ser Ala Thr
65                  70                  75                  80
Val Leu Leu Asn Thr Tyr His Ala His Arg Pro Asp Ala Leu Gln Leu
                85                  90                  95
Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Gln Arg Arg
            100                 105                 110
Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Gln Leu Val Gln Glu Cys
        115                 120                 125
Met Val Pro Asn Cys Ser Gly Gly Glu Ser His Arg Pro Ala Tyr Asp
    130                 135                 140
Gly Lys Asn Pro Phe Ser Thr Pro Glu Lys Val Glu Phe Gln Cys Gly
145                 150                 155                 160
Gln Lys Ala Leu Arg Pro Arg Phe Lys Ile Val Gly Gly Lys Ser Thr
                165                 170                 175
Thr Ile Glu Asn Gln Pro Trp Phe Ala Ala Ile Tyr Arg Arg His Arg
            180                 185                 190
Gly Gly Ser Val Thr Tyr Val Cys Gly Gly Ser Leu Ile Ser Pro Cys
        195                 200                 205
Trp Val Val Ser Ala Thr His Cys Phe Ile Asn Tyr Gln Gln Lys Glu
    210                 215                 220
Asp Tyr Ile Val Tyr Leu Gly Arg Gln Thr Leu His Ser Ser Thr His
225                 230                 235                 240
```

```
Gly Glu Met Lys Phe Glu Val Glu Lys Leu Ile Leu His Glu Asp Tyr
                245                 250                 255
Ser Ala Asp Ser Leu Ala His His Asn Asp Ile Ala Leu Leu Lys Ile
            260                 265                 270
Arg Thr Asp Lys Gly Gln Cys Ala Gln Pro Ser Arg Ser Ile Gln Thr
        275                 280                 285
Ile Cys Leu Pro Pro Val Asn Gly Asp Ala His Phe Gly Ala Ser Cys
    290                 295                 300
Glu Ile Val Gly Phe Gly Lys Glu Asp Pro Ser Asp Tyr Leu Tyr Pro
305                 310                 315                 320
Glu Gln Leu Lys Met Thr Val Val Lys Leu Val Ser His Arg Glu Cys
                325                 330                 335
Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr Thr Lys Met Leu Cys
            340                 345                 350
Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys Gln Gly Asp Ser Gly
        355                 360                 365
Gly Pro Leu Val Cys Ser Thr Gln Gly Arg Leu Thr Leu Thr Gly Ile
    370                 375                 380
Val Ser Trp Gly Arg Glu Cys Ala Met Lys Asp Lys Pro Gly Val Tyr
385                 390                 395                 400
Thr Arg Val Ser Arg Phe Leu Thr Trp Ile His Thr His Val Gly Gly
                405                 410                 415
Glu Asn Gly Leu Ala His
            420
```

<210> 70
<211> 417
<212> PRT
<213> Oryctolagus cuniculus

<220>
<223> u-PA mature protein

<400> 70

```
Asp Ser Glu Gly Ser His Glu Leu His Gly Val Ser Asp Ala Ser Asn
 1               5                  10                  15
Cys Gly Cys Leu Asn Gly Gly Thr Cys Val Thr Tyr Lys Tyr Phe Ser
            20                  25                  30
Asn Ile Trp Arg Cys Asn Cys Pro Lys Lys Phe Gln Gly Glu His Cys
        35                  40                  45
Glu Ile Asp Thr Leu Lys Thr Cys Tyr His Gly Asp Gly His Ser Tyr
    50                  55                  60
Arg Gly Lys Ala Asn Thr Asp Ile Met Asp Arg Pro Cys Leu Ala Trp
65                  70                  75                  80
Asn Ser Ala Asn Val Leu Thr Lys Thr Tyr His Ala His Arg Pro Asp
                85                  90                  95
Ala Leu Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp
```

```
            100                 105                 110
His Gln Arg Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Gln Leu
        115                 120                 125
Ile Gln Glu Cys Lys Val His Asp Cys Ser Ser Gly Lys Lys Pro Ala
    130                 135                 140
Leu Pro Pro Gly Lys Leu Glu Phe Gln Cys Gly Gln Lys Ala Leu Arg
145                 150                 155                 160
Pro Arg Phe Lys Ile Ile Gly Gly Glu Phe Thr Ile Ile Glu Asn Gln
                165                 170                 175
Pro Trp Phe Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr
            180                 185                 190
Tyr Val Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Val Ser Ala
        195                 200                 205
Thr His Cys Phe Ile Asn His Gln Lys Lys Glu Asp Tyr Ile Val Tyr
    210                 215                 220
Leu Gly Arg Ser Arg Leu Asn Ser Met Thr Pro Gly Glu Met Lys Phe
225                 230                 235                 240
Glu Val Glu Gln Leu Ile Leu His Glu Gly Tyr Arg Ala Asp Thr Leu
                245                 250                 255
Ala His His Asn Asp Ile Ala Leu Leu Lys Ile Leu Ser Asn Asn Gly
            260                 265                 270
Gln Cys Ala Gln Pro Ser Arg Ser Ile Gln Thr Ile Cys Leu Pro Pro
        275                 280                 285
Trp Asn Ala Asp Pro Asn Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe
    290                 295                 300
Gly Lys Glu Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met
305                 310                 315                 320
Thr Val Val Lys Leu Val Ser Tyr Gln Glu Cys Gln Gln Pro His Tyr
                325                 330                 335
Tyr Gly Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln
            340                 345                 350
Trp Glu Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys
        355                 360                 365
Ser Val Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg
    370                 375                 380
Gly Cys Ala Leu Lys Asn Lys Pro Gly Val Tyr Thr Arg Val Ser Arg
385                 390                 395                 400
Phe Leu Pro Trp Ile Arg Ser His Ile Gly Glu Glu Asn Gly Leu Ala
                405                 410                 415
Leu
```

<210> 71
<211> 414
<212> PRT
<213> Gallus gallus

<220>
<223> u-PA mature protein

<400> 71

```
Val Tyr Ile Arg Gln Tyr Tyr Lys Leu Ser His Lys His Arg Pro Gln
 1               5                  10                  15
His Arg Glu Cys Gln Cys Leu Asn Gly Gly Thr Cys Ile Thr Tyr Arg
            20                  25                  30
Phe Phe Ser Gln Ile Lys Arg Cys Leu Cys Pro Glu Gly Tyr Gly Gly
        35                  40                  45
Leu His Cys Glu Ile Asp Thr Asn Ser Ile Cys Tyr Ser Gly Asn Gly
    50                  55                  60
Glu Asp Tyr Arg Gly Met Ala Glu Asp Pro Gly Cys Leu Tyr Trp Asp
65                  70                  75                  80
His Pro Ser Val Ile Arg Trp Gly Asp Tyr His Ala Asp Leu Lys Asn
                85                  90                  95
Ala Leu Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asn
            100                 105                 110
Gly Arg Ser Arg Pro Trp Cys Tyr Thr Lys Arg Arg Tyr Ser Ile Gln
        115                 120                 125
Glu Thr Pro Cys Ser Thr Ile Glu Lys Cys Glu Arg Thr Cys Gly Gln
    130                 135                 140
Arg Ser Phe Ser Lys Tyr Phe Lys Ile Val Gly Gly Ser Gln Ala Glu
145                 150                 155                 160
Val Glu Thr Gln Pro Trp Ile Ala Gly Ile Phe Gln Asn Ile Met Gly
                165                 170                 175
Thr Asp Gln Phe Leu Cys Gly Gly Ser Leu Ile Asp Pro Cys Trp Val
            180                 185                 190
Leu Thr Ala Ala His Cys Phe Tyr Asn Pro Thr Lys Lys Gln Pro Asn
        195                 200                 205
Lys Ser Val Tyr Lys Val Phe Leu Gly Lys Ser Ile Leu Asn Thr Asn
    210                 215                 220
Asp Glu His Glu Gln Val Phe Met Val Asp Glu Ile Ile Ser His Pro
225                 230                 235                 240
Asp Phe Thr Asp His Thr Gly Gly Asn Asp Asn Asp Ile Ala Leu Ile
                245                 250                 255
Arg Ile Arg Thr Ala Ser Gly Gln Cys Ala Val Glu Ser Asn Tyr Val
            260                 265                 270
Arg Thr Val Cys Leu Pro Glu Lys Asn Leu Asn Leu Tyr Asp Asn Thr
        275                 280                 285
Trp Cys Glu Ile Ala Gly Tyr Gly Lys Gln Asn Ser Tyr Asp Ile Tyr
    290                 295                 300
Tyr Ala Gln Arg Leu Met Ser Ala Thr Val Asn Leu Ile Ser Gln Asp
305                 310                 315                 320
Asp Cys Lys Asn Lys Tyr Tyr Asp Ser Thr Arg Val Thr Asp Asn Met
                325                 330                 335
Val Cys Ala Gly Asp Pro Leu Trp Glu Thr Asp Ala Cys Lys Gly Asp
            340                 345                 350
```

```
Ser Gly Gly Pro Met Val Cys Glu His Asn Gly Arg Met Thr Leu Tyr
        355                 360                 365
Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Lys Lys Asn Lys Pro Gly
    370                 375                 380
Val Tyr Thr Arg Val Thr Arg Tyr Leu Asn Trp Ile Asp Ser Asn Met
385                 390                 395                 400
Asn Ala Val Phe Thr Lys Ser Arg Ser Phe Arg Glu Pro Lys
                405                 410


<210> 72
<211> 413
<212> PRT
<213> Papio cynocephalus

<220>
<223> u-PA mature protein

<400> 72
Ser Arg Glu Leu Gln Val Pro Ser Asp Cys Gly Cys Leu Asn Gly Gly
 1               5                  10                  15
Thr Cys Met Ser Asn Lys Tyr Phe Ser Ser Ile His Trp Cys Asn Cys
            20                  25                  30
Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile Asp Lys Ser Lys Thr
        35                  40                  45
Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly Lys Ala Ser Thr Asp
    50                  55                  60
Thr Met Gly Arg Ser Cys Leu Ala Trp Asn Ser Ala Thr Val Leu Gln
65                  70                  75                  80
Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu Gln Leu Gly Leu Gly
                85                  90                  95
Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg Arg Arg Pro Trp Cys
            100                 105                 110
Tyr Val Gln Val Gly Leu Lys Gln Arg Val Gln Glu Cys Met Val His
        115                 120                 125
Asn Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro Pro Glu Glu Leu Gln
    130                 135                 140
Phe Gln Cys Gly Gln Arg Thr Leu Arg Pro Arg Phe Lys Ile Val Gly
145                 150                 155                 160
Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala Ala Ile Tyr
                165                 170                 175
Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val Cys Gly Gly Ser Leu
            180                 185                 190
Ile Ser Pro Cys Trp Val Val Ser Ala Thr His Cys Phe Ile Asn Tyr
        195                 200                 205
Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser Arg Leu Asn
    210                 215                 220
Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn Leu Ile Leu
```

```
225                 230                 235                 240
His Glu Asp Tyr Ser Ala Asp Thr Leu Ala His His Asn Asp Ile Ala
                245                 250                 255
Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser Arg
            260                 265                 270
Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr Asn Asp Pro Asn Asp
        275                 280                 285
Pro Pro Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    290                 295                 300
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
305                 310                 315                 320
Leu Val Ser His Gln Lys Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                325                 330                 335
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Glu Thr Asp
            340                 345                 350
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Ile Gln Gly
        355                 360                 365
His Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    370                 375                 380
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser Arg Phe Leu Pro Trp
385                 390                 395                 400
Ile His Ser His Thr Arg Glu Gln Asn Gly Leu Ala Leu
                405                 410
```

<210> 73
<211> 411
<212> PRT
<213> Pongo abelii

<220>
<223> u-PA mature protein

<400> 73

```
Ser Asn Glu Leu His Gln Val Pro Ser Asn Cys Asp Cys Leu Asn Gly
 1               5                  10                  15
Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile His Trp Cys Asn
            20                  25                  30
Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile Asp Lys Ser Lys
        35                  40                  45
Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly Lys Ala Ser Thr
    50                  55                  60
Asp Thr Met Gly Arg Pro Cys Leu Ala Trp Asn Ser Ala Thr Val Leu
65                  70                  75                  80
Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu Gln Leu Gly Leu
                85                  90                  95
Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg Trp Arg Pro Trp
            100                 105                 110
```

```
Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln Glu Cys Met Val
        115                 120                 125
His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro Pro Glu Glu Leu
    130                 135                 140
Lys Phe Gln Cys Gly Gln Lys Thr Leu Arg Pro Arg Phe Lys Ile Val
145                 150                 155                 160
Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala Ala Ile
                165                 170                 175
Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val Cys Gly Gly Ser
            180                 185                 190
Leu Ile Ser Pro Cys Trp Val Val Ser Ala Thr His Cys Phe Ile Asp
        195                 200                 205
Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser Arg Leu
    210                 215                 220
Asn Ser His Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn Leu Ile
225                 230                 235                 240
Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala His His Asn Asp Ile
                245                 250                 255
Ala Leu Leu Lys Ile His Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            260                 265                 270
Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr Asn Asp Pro Pro
        275                 280                 285
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    290                 295                 300
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
305                 310                 315                 320
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                325                 330                 335
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            340                 345                 350
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        355                 360                 365
Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys Asp
    370                 375                 380
Lys Pro Gly Val Tyr Thr Arg Val Ser Tyr Phe Leu Pro Trp Ile Arg
385                 390                 395                 400
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                405                 410
```

<210> 74
<211> 404
<212> PRT
<213> Canis lupus

<220>
<223> u-PA mature protein

<400> 74

```
Ala Ser Asn Cys Ser Cys Leu Asn Gly Gly Thr Cys Val Ser Tyr Lys
 1               5                  10                  15
Tyr Phe Ser Asn Ile Gln Arg Cys Asn Cys Pro Lys Lys Phe Gln Gly
            20                  25                  30
Glu His Cys Glu Ile Asp Thr Ser Lys Thr Cys Tyr Glu Gly Asn Gly
        35                  40                  45
His Ser Tyr Arg Gly Lys Ala Asn Thr Asn Thr Arg Gly Arg Pro Cys
    50                  55                  60
Leu Ala Trp Asn Ser Ala Ala Val Leu Leu Lys Gln Tyr His Ala Leu
65                  70                  75                  80
Arg Pro Asp Ala Leu Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg
                85                  90                  95
Asn Pro Asp His Gln Arg Lys Pro Trp Cys Tyr Val Gln Val Gly Leu
            100                 105                 110
Met Gln Leu Val Gln Glu Cys Thr Val Gln His Cys Ser Phe Glu Lys
        115                 120                 125
Asn Pro His Ser Pro Pro Glu Lys Ala Glu Phe Gln Cys Gly Gln Lys
    130                 135                 140
Ala Leu Arg Pro Arg Phe Lys Ile Ile Gly Gly Glu Phe Thr Thr Ile
145                 150                 155                 160
Glu Asn Gln Pro Trp Phe Ala Ala Ile Tyr Arg Lys His Arg Gly Gly
                165                 170                 175
Ser Val Thr Tyr Gln Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val
            180                 185                 190
Val Ser Ala Thr His Cys Phe Ile Asn Ser Gln Lys Lys Asp Asp Tyr
        195                 200                 205
Ile Val Tyr Leu Gly Arg Ser Lys Arg Ile Ser Lys Thr Phe Gly Glu
    210                 215                 220
Met Lys Phe Glu Val Glu Lys Leu Ile Leu His Glu Asp Tyr Ser Ala
225                 230                 235                 240
Asp Ser Leu Ala His His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser
                245                 250                 255
Asp Glu Gly Gln Cys Ala Gln Pro Ser Arg Ser Ile Gln Thr Ile Cys
            260                 265                 270
Leu Pro Pro Ser Arg Gly Asp Ala His Phe Gly Ala Ser Cys Glu Ile
        275                 280                 285
Ser Gly Phe Gly Lys Glu Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Gln
    290                 295                 300
Leu Lys Met Thr Val Val Lys Leu Val Ser His Gln Glu Cys Gln Gln
305                 310                 315                 320
Pro His Tyr Tyr Gly Ser Glu Val Thr Asp Gln Met Leu Cys Ala Ala
                325                 330                 335
Asp Pro Glu Trp Glu Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro
            340                 345                 350
Leu Val Cys Ser Thr Gln Gly Arg Leu Thr Leu Thr Gly Ile Val Ser
        355                 360                 365
Trp Gly Ser Gly Cys Ala Met Lys Asn Lys Pro Gly Val Tyr Thr Arg
```

```
    370                 375                 380
Val Ser Arg Phe Leu Pro Trp Ile His Arg His Ile Gly Glu Gln Asn
385                 390                 395                 400
Gly Leu Thr Leu
```

<210> 75
<211> 413
<212> PRT
<213> Ovis aries

<220>
<223> u-PA mature protein

<400> 75

```
Ser Asn Glu Val His Lys Glu Ser Gly Val Ser Asp Cys Gly Cys Leu
 1               5                  10                  15
Asn Gly Gly Lys Cys Val Ser Tyr Lys Tyr Phe Ser Asn Ile Gln Arg
            20                  25                  30
Cys Ser Cys Pro Lys Lys Phe Gln Gly Glu Tyr Cys Glu Ile Asp Thr
        35                  40                  45
Ser Lys Thr Cys Tyr Gln Gly Asn Gly His Ser Tyr Arg Gly Lys Ala
    50                  55                  60
Asn Thr Asp Leu Arg Gly Arg Pro Arg Leu Ala Trp Asp Ser Ala Thr
65                  70                  75                  80
Val Leu Leu Lys Met Tyr His Ala His Arg Ser Asp Ala Ile Gln Leu
                85                  90                  95
Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Gln Arg Arg
            100                 105                 110
Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Gln Phe Val Gln Glu Cys
        115                 120                 125
Met Val Gln Asp Cys Pro Ala Gly Lys Gly Pro Ser Ser Pro Lys Glu
    130                 135                 140
Lys Val Glu Phe Gln Cys Gly Gln Lys Ala Leu Arg Pro Arg Phe Glu
145                 150                 155                 160
Ile Val Gly Gly Glu Phe Thr Thr Ile Glu Ser Gln Pro Trp Phe Ala
                165                 170                 175
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Leu Cys Gly
            180                 185                 190
Gly Ser Leu Ile Ser Pro Cys Trp Val Val Ser Ala Thr His Cys Phe
        195                 200                 205
Thr Asn His Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    210                 215                 220
Lys Leu Asn Ser Asp Thr Leu Gly Glu Met Lys Phe Glu Val Glu Lys
225                 230                 235                 240
Leu Ile Leu His Glu Asp Tyr Ser Ala Asp Ser Leu Ala His His Asn
                245                 250                 255
```

```
Asp Ile Ala Leu Leu Lys Ile Arg Thr Ser Arg Gly Gln Cys Ala Gln
            260                 265                 270
Pro Ser Arg Ser Ile Gln Thr Ile Cys Leu Pro Pro Leu Tyr Gly Asp
        275                 280                 285
Ala Arg Phe Gly Thr Arg Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    290                 295                 300
Pro Ser Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Phe Val Asn
305                 310                 315                 320
Leu Val Ser His Glu Glu Cys Gln Gln Pro His Tyr Tyr Gly Thr Glu
                325                 330                 335
Val Thr Asp Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Glu Thr Asp
            340                 345                 350
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Thr Ile Gln Gly
        355                 360                 365
Arg Leu Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Glu Cys Ala Met
    370                 375                 380
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser Lys Phe Leu Pro Trp
385                 390                 395                 400
Ile Tyr Thr His Thr Arg Gly Glu Ile Asp Leu Gly Leu
                405                 410


<210> 76
<211> 263
<212> PRT
<213> Artificial Sequence

<220>
<223> mature chymotrypsin polypeptide

<400> 76
Met Ala Phe Leu Trp Leu Leu Ser Cys Trp Ala Leu Leu Gly Thr Thr
 1               5                  10                  15
Phe Gly Cys Gly Val Pro Ala Ile His Pro Val Leu Ser Gly Leu Ser
            20                  25                  30
Arg Ile Val Asn Gly Glu Asp Ala Val Pro Gly Ser Trp Pro Trp Gln
        35                  40                  45
Val Ser Leu Gln Asp Lys Thr Gly Phe His Phe Cys Gly Gly Ser Leu
    50                  55                  60
Ile Ser Glu Asp Trp Val Val Thr Ala Ala His Cys Gly Val Arg Thr
65                  70                  75                  80
Ser Asp Val Val Val Ala Gly Glu Phe Asp Gln Gly Ser Asp Glu Glu
                85                  90                  95
Asn Ile Gln Val Leu Lys Ile Ala Lys Val Phe Lys Asn Pro Lys Phe
            100                 105                 110
Ser Ile Leu Thr Val Asn Asn Asp Ile Thr Leu Leu Lys Leu Ala Thr
        115                 120                 125
Pro Ala Arg Phe Ser Gln Thr Val Ser Ala Val Cys Leu Pro Ser Ala
```

```
    130                 135                 140
Asp Asp Asp Phe Pro Ala Gly Thr Leu Cys Ala Thr Thr Gly Trp Gly
145                 150                 155                 160
Lys Thr Lys Tyr Asn Ala Asn Lys Thr Pro Asp Lys Leu Gln Gln Ala
                165                 170                 175
Ala Leu Pro Leu Leu Ser Asn Ala Glu Cys Lys Lys Ser Trp Gly Arg
            180                 185                 190
Arg Ile Thr Asp Val Met Ile Cys Ala Gly Ala Ser Gly Val Ser Ser
        195                 200                 205
Cys Met Gly Asp Ser Gly Gly Pro Leu Val Cys Gln Lys Asp Gly Ala
    210                 215                 220
Trp Thr Leu Val Gly Ile Val Ser Trp Gly Ser Asp Thr Cys Ser Thr
225                 230                 235                 240
Ser Ser Pro Gly Val Tyr Ala Arg Val Thr Lys Leu Ile Pro Trp Val
                245                 250                 255
Gln Lys Ile Leu Ala Ala Asn
            260
```

<210> 77
<211> 1636
<212> PRT
<213> Artificial Sequence

<220>
<223> mature 2 chain C3 protein

<400> 77

```
Pro Met Tyr Ser Ile Ile Thr Pro Asn Ile Leu Arg Leu Glu Ser Glu
 1               5                  10                  15
Glu Thr Met Val Leu Glu Ala His Asp Ala Gln Gly Asp Val Pro Val
            20                  25                  30
Thr Val Thr Val His Asp Phe Pro Gly Lys Lys Leu Val Leu Ser Ser
        35                  40                  45
Glu Lys Thr Val Leu Thr Pro Ala Thr Asn His Met Gly Asn Val Thr
    50                  55                  60
Phe Thr Ile Pro Ala Asn Arg Glu Phe Lys Ser Glu Lys Gly Arg Asn
65                  70                  75                  80
Lys Phe Val Thr Val Gln Ala Thr Phe Gly Thr Gln Val Val Glu Lys
                85                  90                  95
Val Val Leu Val Ser Leu Gln Ser Gly Tyr Leu Phe Ile Gln Thr Asp
            100                 105                 110
Lys Thr Ile Tyr Thr Pro Gly Ser Thr Val Leu Tyr Arg Ile Phe Thr
        115                 120                 125
Val Asn His Lys Leu Leu Pro Val Gly Arg Thr Val Met Val Asn Ile
    130                 135                 140
Glu Asn Pro Glu Gly Ile Pro Val Lys Gln Asp Ser Leu Ser Ser Gln
145                 150                 155                 160
```

```
Asn Gln Leu Gly Val Leu Pro Leu Ser Trp Asp Ile Pro Glu Leu Val
                165                 170                 175
Asn Met Gly Gln Trp Lys Ile Arg Ala Tyr Tyr Glu Asn Ser Pro Gln
            180                 185                 190
Gln Val Phe Ser Thr Glu Phe Glu Val Lys Glu Tyr Val Leu Pro Ser
        195                 200                 205
Phe Glu Val Ile Val Glu Pro Thr Glu Lys Phe Tyr Tyr Ile Tyr Asn
    210                 215                 220
Glu Lys Gly Leu Glu Val Thr Ile Thr Ala Arg Phe Leu Tyr Gly Lys
225                 230                 235                 240
Lys Val Glu Gly Thr Ala Phe Val Ile Phe Gly Ile Gln Asp Gly Glu
                245                 250                 255
Gln Arg Ile Ser Leu Pro Glu Ser Leu Lys Arg Ile Pro Ile Glu Asp
            260                 265                 270
Gly Ser Gly Glu Val Val Leu Ser Arg Lys Val Leu Leu Asp Gly Val
        275                 280                 285
Gln Asn Pro Arg Ala Glu Asp Leu Val Gly Lys Ser Leu Tyr Val Ser
    290                 295                 300
Ala Thr Val Ile Leu His Ser Gly Ser Asp Met Val Gln Ala Glu Arg
305                 310                 315                 320
Ser Gly Ile Pro Ile Val Thr Ser Pro Tyr Gln Ile His Phe Thr Lys
                325                 330                 335
Thr Pro Lys Tyr Phe Lys Pro Gly Met Pro Phe Asp Leu Met Val Phe
            340                 345                 350
Val Thr Asn Pro Asp Gly Ser Pro Ala Tyr Arg Val Pro Val Ala Val
        355                 360                 365
Gln Gly Glu Asp Thr Val Gln Ser Leu Thr Gln Gly Asp Gly Val Ala
    370                 375                 380
Lys Leu Ser Ile Asn Thr His Pro Ser Gln Lys Pro Leu Ser Ile Thr
385                 390                 395                 400
Val Arg Thr Lys Lys Gln Glu Leu Ser Glu Ala Glu Gln Ala Thr Arg
                405                 410                 415
Thr Met Gln Ala Leu Pro Tyr Ser Thr Val Gly Asn Ser Asn Asn Tyr
            420                 425                 430
Leu His Leu Ser Val Leu Arg Thr Glu Leu Arg Pro Gly Glu Thr Leu
        435                 440                 445
Asn Val Asn Phe Leu Leu Arg Met Asp Arg Ala His Glu Ala Lys Ile
    450                 455                 460
Arg Tyr Tyr Thr Tyr Leu Ile Met Asn Lys Gly Arg Leu Leu Lys Ala
465                 470                 475                 480
Gly Arg Gln Val Arg Glu Pro Gly Gln Asp Leu Val Val Leu Pro Leu
                485                 490                 495
Ser Ile Thr Thr Asp Phe Ile Pro Ser Phe Arg Leu Val Ala Tyr Tyr
            500                 505                 510
Thr Leu Ile Gly Ala Ser Gly Gln Arg Glu Val Val Ala Asp Ser Val
        515                 520                 525
Trp Val Asp Val Lys Asp Ser Cys Val Gly Ser Leu Val Val Lys Ser
    530                 535                 540
```

```
Gly Gln Ser Glu Asp Arg Gln Pro Val Pro Gly Gln Gln Met Thr Leu
545                 550                 555                 560
Lys Ile Glu Gly Asp His Gly Ala Arg Val Val Leu Val Ala Val Asp
                565                 570                 575
Lys Gly Val Phe Val Leu Asn Lys Lys Asn Lys Leu Thr Gln Ser Lys
            580                 585                 590
Ile Trp Asp Val Val Glu Lys Ala Asp Ile Gly Cys Thr Pro Gly Ser
        595                 600                 605
Gly Lys Asp Tyr Ala Gly Val Phe Ser Asp Ala Gly Leu Thr Phe Thr
    610                 615                 620
Ser Ser Ser Gly Gln Gln Thr Ala Gln Arg Ala Glu Leu Gln Cys Pro
625                 630                 635                 640
Gln Pro Ala Ala Ser Val Gln Leu Thr Glu Lys Arg Met Asp Lys Val
                645                 650                 655
Gly Lys Tyr Pro Lys Glu Leu Arg Lys Cys Cys Glu Asp Gly Met Arg
            660                 665                 670
Glu Asn Pro Met Arg Phe Ser Cys Gln Arg Arg Thr Arg Phe Ile Ser
        675                 680                 685
Leu Gly Glu Ala Cys Lys Lys Val Phe Leu Asp Cys Cys Asn Tyr Ile
    690                 695                 700
Thr Glu Leu Arg Arg Gln His Ala Arg Ala Ser His Leu Gly Leu Ala
705                 710                 715                 720
Arg Ser Asn Leu Asp Glu Asp Ile Ile Ala Glu Glu Asn Ile Val Ser
                725                 730                 735
Arg Ser Glu Phe Pro Glu Ser Trp Leu Trp Asn Val Glu Asp Leu Lys
            740                 745                 750
Glu Pro Pro Lys Asn Gly Ile Ser Thr Lys Leu Met Asn Ile Phe Leu
        755                 760                 765
Lys Asp Ser Ile Thr Thr Trp Glu Ile Leu Ala Val Ser Met Ser Asp
    770                 775                 780
Lys Lys Gly Ile Cys Val Ala Asp Pro Phe Glu Val Thr Val Met Gln
785                 790                 795                 800
Asp Phe Phe Ile Asp Leu Arg Leu Pro Tyr Ser Val Val Arg Asn Glu
                805                 810                 815
Gln Val Glu Ile Arg Ala Val Leu Tyr Asn Tyr Arg Gln Asn Gln Glu
            820                 825                 830
Leu Lys Val Arg Val Glu Leu Leu His Asn Pro Ala Phe Cys Ser Leu
        835                 840                 845
Ala Thr Thr Lys Arg Arg His Gln Gln Thr Val Thr Ile Pro Pro Lys
    850                 855                 860
Ser Ser Leu Ser Val Pro Tyr Val Ile Val Pro Leu Lys Thr Gly Leu
865                 870                 875                 880
Gln Glu Val Glu Val Lys Ala Ala Val Tyr His His Phe Ile Ser Asp
                885                 890                 895
Gly Val Arg Lys Ser Leu Lys Val Val Pro Glu Gly Ile Arg Met Asn
            900                 905                 910
Lys Thr Val Ala Val Arg Thr Leu Asp Pro Glu Arg Leu Gly Arg Glu
        915                 920                 925
```

```
Gly Val Gln Lys Glu Asp Ile Pro Pro Ala Asp Leu Ser Asp Gln Val
    930                 935                 940
Pro Asp Thr Glu Ser Glu Thr Arg Ile Leu Leu Gln Gly Thr Pro Val
945                 950                 955                 960
Ala Gln Met Thr Glu Asp Ala Val Asp Ala Glu Arg Leu Lys His Leu
                965                 970                 975
Ile Val Thr Pro Ser Gly Cys Gly Glu Gln Asn Met Ile Gly Met Thr
            980                 985                 990
Pro Thr Val Ile Ala Val His Tyr Leu Asp Glu Thr Glu Gln Trp Glu
        995                 1000                1005
Lys Phe Gly Leu Glu Lys Arg Gln Gly Ala Leu Glu Leu Ile Lys Lys
    1010                1015                1020
Gly Tyr Thr Gln Gln Leu Ala Phe Arg Gln Pro Ser Ser Ala Phe Ala
1025                1030                1035                1040
Ala Phe Val Lys Arg Ala Pro Ser Thr Trp Leu Thr Ala Tyr Val Val
                1045                1050                1055
Lys Val Phe Ser Leu Ala Val Asn Leu Ile Ala Ile Asp Ser Gln Val
            1060                1065                1070
Leu Cys Gly Ala Val Lys Trp Leu Ile Leu Glu Lys Gln Lys Pro Asp
        1075                1080                1085
Gly Val Phe Gln Glu Asp Ala Pro Val Ile His Gln Glu Met Ile Gly
    1090                1095                1100
Gly Leu Arg Asn Asn Asn Glu Lys Asp Met Ala Leu Thr Ala Phe Val
1105                1110                1115                1120
Leu Ile Ser Leu Gln Glu Ala Lys Asp Ile Cys Glu Glu Gln Val Asn
                1125                1130                1135
Ser Leu Pro Gly Ser Ile Thr Lys Ala Gly Asp Phe Leu Glu Ala Asn
            1140                1145                1150
Tyr Met Asn Leu Gln Arg Ser Tyr Thr Val Ala Ile Ala Gly Tyr Ala
        1155                1160                1165
Leu Ala Gln Met Gly Arg Leu Lys Gly Pro Leu Leu Asn Lys Phe Leu
    1170                1175                1180
Thr Thr Ala Lys Asp Lys Asn Arg Trp Glu Asp Pro Gly Lys Gln Leu
1185                1190                1195                1200
Tyr Asn Val Glu Ala Thr Ser Tyr Ala Leu Leu Ala Leu Leu Gln Leu
                1205                1210                1215
Lys Asp Phe Asp Phe Val Pro Pro Val Val Arg Trp Leu Asn Glu Gln
            1220                1225                1230
Arg Tyr Tyr Gly Gly Gly Tyr Gly Ser Thr Gln Ala Thr Phe Met Val
        1235                1240                1245
Phe Gln Ala Leu Ala Gln Tyr Gln Lys Asp Ala Pro Asp His Gln Glu
    1250                1255                1260
Leu Asn Leu Asp Val Ser Leu Gln Leu Pro Ser Arg Ser Ser Lys Ile
1265                1270                1275                1280
Thr His Arg Ile His Trp Glu Ser Ala Ser Leu Leu Arg Ser Glu Glu
                1285                1290                1295
Thr Lys Glu Asn Glu Gly Phe Thr Val Thr Ala Glu Gly Lys Gly Gln
            1300                1305                1310
```

```
Gly Thr Leu Ser Val Val Thr Met Tyr His Ala Lys Ala Lys Asp Gln
        1315                1320                1325
Leu Thr Cys Asn Lys Phe Asp Leu Lys Val Thr Ile Lys Pro Ala Pro
    1330                1335                1340
Glu Thr Glu Lys Arg Pro Gln Asp Ala Lys Asn Thr Met Ile Leu Glu
1345                1350                1355                1360
Ile Cys Thr Arg Tyr Arg Gly Asp Gln Asp Ala Thr Met Ser Ile Leu
                1365                1370                1375
Asp Ile Ser Met Met Thr Gly Phe Ala Pro Asp Thr Asp Asp Leu Lys
            1380                1385                1390
Gln Leu Ala Asn Gly Val Asp Arg Tyr Ile Ser Lys Tyr Glu Leu Asp
        1395                1400                1405
Lys Ala Phe Ser Asp Arg Asn Thr Leu Ile Ile Tyr Leu Asp Lys Val
    1410                1415                1420
Ser His Ser Glu Asp Asp Cys Leu Ala Phe Lys Val His Gln Tyr Phe
1425                1430                1435                1440
Asn Val Glu Leu Ile Gln Pro Gly Ala Val Lys Val Tyr Ala Tyr Tyr
                1445                1450                1455
Asn Leu Glu Glu Ser Cys Thr Arg Phe Tyr His Pro Glu Lys Glu Asp
            1460                1465                1470
Gly Lys Leu Asn Lys Leu Cys Arg Asp Glu Leu Cys Arg Cys Ala Glu
        1475                1480                1485
Glu Asn Cys Phe Ile Gln Lys Ser Asp Asp Lys Val Thr Leu Glu Glu
    1490                1495                1500
Arg Leu Asp Lys Ala Cys Glu Pro Gly Val Asp Tyr Val Tyr Lys Thr
1505                1510                1515                1520
Arg Leu Val Lys Val Gln Leu Ser Asn Asp Phe Asp Glu Tyr Ile Met
                1525                1530                1535
Ala Ile Glu Gln Thr Ile Lys Ser Gly Ser Asp Glu Val Gln Val Gly
            1540                1545                1550
Gln Gln Arg Thr Phe Ile Ser Pro Ile Lys Cys Arg Glu Ala Leu Lys
        1555                1560                1565
Leu Glu Glu Lys Lys His Tyr Leu Met Trp Gly Leu Ser Ser Asp Phe
    1570                1575                1580
Trp Gly Glu Lys Pro Asn Leu Ser Tyr Ile Ile Gly Lys Asp Thr Trp
1585                1590                1595                1600
Val Glu His Trp Pro Glu Glu Asp Glu Cys Gln Asp Glu Glu Asn Gln
                1605                1610                1615
Lys Gln Cys Gln Asp Leu Gly Ala Phe Thr Glu Ser Met Val Val Phe
            1620                1625                1630
Gly Cys Pro Asn
        1635
```

<210> 78
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> C3 convertase cleavage site 748-749

<400> 78
Gly Leu Ala Arg
 1

<210> 79
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Factor I cleavage site 954-955

<400> 79
Arg Leu Gly Arg
 1

<210> 80
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Factor I cleavage site 1303-1304

<400> 80
Leu Pro Ser Arg
 1

<210> 81
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Factor I cleavage site 1320-1321

<400> 81
Ser Leu Leu Arg
 1

<210> 82
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<223> Buforin II

<400> 82
Thr Arg Ser Ser Arg Ala Gly Leu Gln Phe Pro Val Gly Arg Val His
 1   5   10   15
Arg Leu Leu Arg Lys
            20

<210> 83
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> DPV3

<400> 83
Arg Lys Lys Arg Arg Arg Glu Ser Arg Lys Lys Arg Arg Arg Glu Ser
 1   5   10   15

<210> 84
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> DPV6

<400> 84
Gly Arg Pro Arg Glu Ser Gly Lys Lys Arg Lys Arg Lys Arg Leu Lys
 1   5   10   15
Pro

<210> 85
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> DPV7

<400> 85
Gly Lys Arg Lys Lys Lys Gly Lys Leu Gly Lys Lys Arg Asp Pro
 1   5   10   15

<210> 86
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> DPV7b

<400> 86
Gly Lys Arg Lys Lys Lys Gly Lys Leu Gly Lys Lys Arg Pro Arg Ser
 1   5   10   15
Arg

<210> 87
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> DPV3/10

<400> 87
Arg Lys Lys Arg Arg Arg Glu Ser Arg Arg Ala Arg Arg Ser Pro Arg
 1   5   10   15
His Leu

<210> 88
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> DPV10/6

<400> 88
Ser Arg Arg Ala Arg Arg Ser Pro Arg Glu Ser Gly Lys Lys Arg Lys

 1   5   10   15
Arg Lys Arg

<210> 89
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> DPV1047

<400> 89
Val Lys Arg Gly Leu Lys Leu Arg His Val Arg Pro Arg Val Thr Arg
 1   5   10   15
Met Asp Val

<210> 90
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> DPV1048

<400> 90
Val Lys Arg Gly Leu Lys Leu Arg His Val Arg Pro Arg Val Thr Arg
 1   5   10   15
Asp Val

<210> 91
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> DPV10

<400> 91
Ser Arg Arg Ala Arg Arg Ser Pro Arg His Leu Gly Ser Gly
 1   5   10

<210> 92
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> DPV15

<400> 92
Leu Arg Arg Glu Arg Gln Ser Arg Leu Arg Arg Glu Arg Gln Ser Arg
 1   5   10   15

<210> 93
<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<223> DPV15b

<400> 93
Gly Ala Tyr Asp Leu Arg Arg Arg Glu Arg Gln Ser Arg Leu Arg Arg
 1   5   10   15
Arg Glu Arg Gln Ser Arg
            20

<210> 94
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> GALA

<400> 94
Trp Glu Ala Ala Leu Ala Glu Ala Leu Ala Glu Ala Leu Ala Glu His
 1   5   10   15
Leu Ala Glu Ala Leu Ala Glu Ala Leu Glu Ala Leu Ala Ala
            20   25   30

<210> 95
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<223> Fibrinogen beta chain

<400> 95
Lys Gly Ser Trp Tyr Ser Met Arg Lys Met Ser Met Lys Ile Arg Pro
 1   5   10   15
Phe Phe Pro Gln Gln
            20

<210> 96
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Fibrinogen gamma chain precursor

<400> 96
Lys Thr Arg Tyr Tyr Ser Met Lys Lys Thr Thr Met Lys Ile Ile Pro
 1   5   10   15
Phe Asn Arg Leu
            20

<210> 97
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Fibrinogen alpha chain

<400> 97
Arg Gly Ala Asp Tyr Ser Leu Arg Ala Val Arg Met Lys Ile Arg Pro
 1   5   10   15
Leu Val Thr Gln
            20

<210> 98
<211> 24
<212> PRT
<213> Artificial Sequence

<220>
<223> hCT(9-32)

<400> 98
Leu Gly Thr Tyr Thr Gln Asp Phe Asn Lys Phe His Thr Phe Pro Gln
 1   5   10   15
Thr Ala Ile Gly Val Gly Ala Pro
            20

<210> 99
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> HN-1

<400> 99
Thr Ser Pro Leu Asn Ile His Asn Gly Gln Lys Leu
 1   5   10

<210> 100
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Influenza virus nucleoprotein (NLS)

<400> 100
Asn Ser Ala Ala Phe Glu Asp Leu Arg Val Leu Ser
 1   5   10

<210> 101
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> KALA

<400> 101

Trp Glu Ala Lys Leu Ala Lys Ala Leu Ala Lys Ala Leu Ala Lys His
 1   5   10   15
Leu Ala Lys Ala Leu Ala Lys Ala Leu Lys Ala Cys Glu Ala
            20   25   30

<210> 102
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Ku70

<400> 102
Val Pro Met Leu Lys Pro Met Leu Lys Glu
 1   5   10

<210> 103
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> MAP

<400> 103
Lys Leu Ala Leu Lys Leu Ala Leu Lys Ala Leu Lys Ala Ala Leu Lys
 1   5   10   15
Leu Ala

<210> 104
<211> 27
<212> PRT
<213> Artificial Sequence

<220>
<223> MPG

<400> 104
Gly Ala Leu Phe Leu Gly Phe Leu Gly Ala Ala Gly Ser Thr Met Gly
 1   5   10   15
Ala Trp Ser Gln Pro Lys Lys Lys Arg Lys Val
            20   25

<210> 105
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Human Fibroblast growth factor 4 (Kaposi
Fibroblast growth factor)

<400> 105
Ala Ala Val Ala Leu Leu Pro Ala Val Leu Leu Ala Leu Leu Ala Pro
1 5 10 15

<210> 106
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> N50 (NLS of NF-kB P50)

<400> 106
Val Gln Arg Lys Arg Gln Lys Leu Met
1 5

<210> 107
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<223> Pep-1

<400> 107
Lys Glu Thr Trp Trp Glu Thr Trp Trp Thr Glu Trp Ser Gln Pro Lys
1 5 10 15
Lys Lys Arg Lys Val
20

<210> 108
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Pep-7

<400> 108
Ser Asp Leu Trp Glu Met Met Met Val Ser Leu Ala Cys Gln Tyr
 1   5   10   15

<210> 109
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> Penetratin

<400> 109
Arg Gln Ile Lys Ile Trp Phe Gln Asn Arg Arg Met Lys Trp Lys Lys
 1   5   10   15

<210> 110
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Penetratin variant

<400> 110
Gly Arg Gln Ile Lys Ile Trp Phe Gln Asn Arg Arg Met Lys Trp Lys
 1   5   10   15
Lys

<210> 111
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Short Penetratin

<400> 111
Arg Arg Met Lys Trp Lys Lys
 1   5

<210> 112
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Penetratin 42-58

<400> 112
Glu Arg Gln Ile Lys Ile Trp Phe Gln Asn Arg Arg Met Lys Trp Lys
 1   5   10   15
Lys

<210> 113
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Poly Arginine - R7

<400> 113
Arg Arg Arg Arg Arg Arg Arg
 1   5

<210> 114
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Poly Arginine - R9

<400> 114
Arg Arg Arg Arg Arg Arg Arg Arg Arg
 1   5

<210> 115
<211> 16
<212> PRT
<213> Artificial Sequence

<220>

<223> pISL

<400> 115
Arg Val Ile Arg Val Trp Phe Gln Asn Lys Arg Cys Lys Asp Lys Lys
 1   5   10   15

<210> 116
<211> 28
<212> PRT
<213> Artificial Sequence

<220>
<223> Prion mouse PrPc1-28

<400> 116
Met Ala Asn Leu Gly Tyr Trp Leu Leu Ala Leu Phe Val Thr Met Trp
 1   5   10   15
Thr Asp Val Gly Leu Cys Lys Lys Arg Pro Lys Pro
            20   25

<210> 117
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> pVEC

<400> 117
Leu Leu Ile Ile Leu Arg Arg Arg Ile Arg Lys Gln Ala His Ala His
 1   5   10   15
Ser Lys

<210> 118
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> pVEC variant

<400> 118
Leu Leu Ile Ile Leu Arg Arg Arg Ile Arg Lys Gln Ala His Ala His
 1   5   10   15

<210> 119
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> SAP

<400> 119
Val Arg Leu Pro Pro Pro Val Arg Leu Pro Pro Pro Val Arg Leu Pro
 1   5   10   15
Pro Pro

<210> 120
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> SV-40 (NLS)

<400> 120
Pro Lys Lys Lys Arg Lys Val
 1   5

<210> 121
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> SynB1

<400> 121
Arg Gly Gly Arg Leu Ser Tyr Ser Arg Arg Arg Phe Ser Thr Ser Thr
 1   5   10   15
Gly Arg

<210> 122
<211> 10
<212> PRT

<213> Artificial Sequence

<220>
<223> SynB3

<400> 122
Arg Arg Leu Ser Tyr Ser Arg Arg Arg Phe
 1   5   10

<210> 123
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> SynB4

<400> 123
Ala Trp Ser Phe Arg Val Ser Tyr Arg Gly Ile Ser Tyr Arg Arg Ser
 1   5   10   15
Arg

<210> 124
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Tat 47-60

<400> 124
Tyr Gly Arg Lys Lys Arg Arg Gln Arg Arg Arg Pro Pro Gln
 1   5   10

<210> 125
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Tat 47-57

<400> 125
Tyr Gly Arg Lys Lys Arg Arg Gln Arg Arg Arg

 1   5   10

<210> 126
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Tat 47-56

<400> 126
Tyr Gly Arg Lys Lys Arg Arg Gln Arg Arg
 1   5   10

<210> 127
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Tat 48-56

<400> 127
Gly Arg Lys Lys Arg Arg Gln Arg Arg
 1   5

<210> 128
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Tat 48-57

<400> 128
Gly Arg Lys Lys Arg Arg Gln Arg Arg Arg
 1   5   10

<210> 129
<211> 9
<212> PRT
<213> Artificial Sequence

<220>

<223> Tat 49-57

<400> 129
Arg Lys Lys Arg Arg Gln Arg Arg Arg
 1   5

<210> 130
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Tat 49-56

<400> 130
Arg Lys Lys Arg Arg Gln Arg Arg
 1   5

<210> 131
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Tat 48-60

<400> 131
Gly Arg Lys Lys Arg Arg Gln Arg Arg Arg Pro Pro Gln
 1   5   10

<210> 132
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Tat 48-52

<400> 132
Gly Arg Lys Lys Arg
 1   5

<210> 133
<211> 36

<212> PRT
<213> Artificial Sequence

<220>
<223> Tat 37-72

<400> 133
Cys Phe Ile Thr Lys Ala Leu Gly Ile Ser Tyr Gly Arg Lys Lys Arg
 1   5   10   15
Arg Gln Arg Arg Arg Pro Pro Gln Phe Ser Gln Thr His Gln Val Ser
            20   25   30
Leu Ser Lys Gln
        35

<210> 134
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> Tat 38-72

<400> 134
Phe Ile Thr Lys Ala Leu Gly Ile Ser Tyr Gly Arg Lys Lys Arg Arg
 1   5   10   15
Gln Arg Arg Arg Pro Gln Phe Ser Gln Thr His Gln Val Ser Leu Ser
            20   25   30
Lys Gln

<210> 135
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Tat 47-59

<400> 135
Tyr Gly Arg Lys Lys Arg Arg Gln Arg Arg Arg Pro Pro
 1   5   10

<210> 136
<211> 27
<212> PRT

<213> Artificial Sequence

<220>
<223> Transportan

<400> 136
Gly Trp Thr Leu Asn Ser Ala Gly Tyr Leu Leu Gly Lys Ile Asn Leu
 1   5   10   15
Lys Ala Leu Ala Ala Leu Ala Lys Lys Ile Leu
            20   25

<210> 137
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<223> Transportan 10

<400> 137
Ala Gly Tyr Leu Leu Gly Lys Ile Asn Leu Lys Ala Leu Ala Ala Leu
 1   5   10   15
Ala Lys Lys Ile Leu
            20

<210> 138
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Transportan derivative

<400> 138
Gly Trp Thr Leu Asn Ser Ala Gly Tyr Leu Leu Gly
 1   5   10

<210> 139
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Transportan derivative

<400> 139
Ile Asn Leu Lys Ala Leu Ala Ala Leu Ala Lys Lys Ile Leu
 1   5   10

<210> 140
<211> 34
<212> PRT
<213> Artificial Sequence

<220>
<223> VP22

<400> 140
Asp Ala Ala Thr Ala Thr Arg Gly Arg Ser Ala Ala Ser Arg Pro Thr
 1   5   10   15
Glu Arg Pro Arg Ala Pro Ala Arg Ser Ala Ser Arg Pro Arg Arg Pro
            20   25   30
Val Asp

<210> 141
<211> 26
<212> PRT
<213> Artificial Sequence

<220>
<223> VT5

<400> 141
Asp Pro Lys Gly Asp Pro Lys Gly Val Thr Val Thr Val Thr Val Thr
 1   5   10   15
Val Thr Gly Lys Gly Asp Pro Lys Pro Asp
            20   25

<210> 142
<211> 27
<212> PRT
<213> Artificial Sequence

<220>
<223> Signal Sequence-based peptide

<400> 142
Gly Ala Leu Phe Leu Gly Trp Leu Gly Ala Ala Gly Ser Thr Met Gly
 1   5   10   15

Ala Trp Ser Gln Pro Lys Lys Lys Arg Lys Val
            20   25

<210> 143
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> Amphiphilic model peptide

<400> 143
Lys Leu Ala Leu Lys Leu Ala Leu Lys Ala Leu Lys Ala Ala Leu Lys
 1   5   10   15
Leu Ala

<210> 144
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Bacterial cell wall permeating

<400> 144
Lys Phe Phe Lys Phe Phe Lys Phe Phe Lys
 1   5   10

<210> 145
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> LL- 37

<400> 145
Leu Leu Gly Asp Phe Phe Arg Lys Ser Lys Glu Lys Ile Gly Lys Glu
 1   5   10   15
Phe Lys Arg Ile Val Gln Arg Ile Lys Asp Phe Leu Arg Asn Leu Val
            20   25   30
Pro Arg Thr Glu Ser
        35

<210> 146
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Cecropin P1

<400> 146
Ser Trp Leu Ser Lys Thr Ala Lys Lys Leu Glu Asn Ser Ala Lys Lys
 1   5   10   15
Arg Ile Ser Glu Gly Ile Ala Ile Ala Ile Gln Gly Gly Pro Arg
            20   25   30

<210> 147
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> alpha defensin

<400> 147
Ala Cys Tyr Cys Arg Ile Pro Ala Cys Ile Ala Gly Glu Arg Arg Tyr
 1   5   10   15
Gly Thr Cys Ile Tyr Gln Gly Arg Leu Trp Ala Phe Cys Cys
            20   25   30

<210> 148
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> beta defensin

<400> 148
Asp His Tyr Asn Cys Val Ser Ser Gly Gly Gln Cys Leu Tyr Ser Ala
 1   5   10   15
Cys Pro Ile Phe Thr Lys Ile Gln Gly Thr Cys Tyr Arg Gly Lys Ala
            20   25   30
Lys Cys Cys Lys
        35

<210> 149
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Bactenecin

<400> 149
Arg Lys Cys Arg Ile Trp Ile Arg Val Cys Arg
 1   5   10

<210> 150
<211> 42
<212> PRT
<213> Artificial Sequence

<220>
<223> PR- 39

<400> 150
Arg Arg Arg Pro Arg Pro Pro Tyr Leu Pro Arg Pro Arg Pro Pro Pro
 1   5   10   15
Phe Phe Pro Pro Arg Leu Pro Pro Arg Ile Pro Pro Gly Phe Pro Pro
            20   25   30
Arg Phe Pro Pro Arg Phe Pro Gly Lys Arg
        35   40

<210> 151
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Indolicidin

<400> 151
Ile Leu Pro Trp Lys Trp Pro Trp Trp Pro Trp Arg Arg
 1   5   10

<210> 152
<211> 27
<212> PRT
<213> Artificial Sequence

<220>
<223> MPS

<400> 152
Gly Ala Leu Phe Leu Gly Trp Leu Gly Ala Ala Gly Ser Thr Met Gly
 1   5   10   15
Ala Trp Ser Gln Pro Lys Lys Lys Arg Lys Val
            20   25

<210> 153
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> pIs1

<400> 153
Pro Val Ile Arg Arg Val Trp Phe Gln Asn Lys Arg Cys Lys Asp Lys
 1   5   10   15
Lys

<210> 154
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain V38D/T97adel/L97bdel/C122S

<400> 154
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ala His His Asn Asp Ile
                85   90   95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser

```
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 155
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain L73R/L97bG/H99Q/C122S

<400> 155

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Arg Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
```

```
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 156
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain V38D/L73R/L97bG/H99Q/C122S

<400> 156
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Arg Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
```

```
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 157
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain L97bP/H99L/C122S

<400> 157

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Pro Ala Leu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
```

```
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 158
<211> 252
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R37aP/V38D/V41R/A96D/D97G/T97aN/A98G/L97bdel/H99L/
      C122S/M157K/R217F

<400> 158
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Pro Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Asp Gly Asn Gly Leu His Asn Asp
                85                  90                  95
Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro
            100                 105                 110
Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro
        115                 120                 125
Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser
    130                 135                 140
Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys Leu
145                 150                 155                 160
Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val
                165                 170                 175
Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser
            180                 185                 190
Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg
        195                 200                 205
Met Thr Leu Thr Gly Ile Val Ser Trp Gly Phe Gly Cys Ala Leu Lys
```

```
    210                 215                 220
Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile
225                 230                 235                 240
Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 159
<211> 252
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aS/G37bD/V38D/V41R/A96D/D97G/T97aN/A98G/L97bdel
/H99L/C122S/R217F

<400> 159

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Ser Asp Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Asp Gly Asn Gly Leu His Asn Asp
                85                  90                  95
Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro
            100                 105                 110
Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro
        115                 120                 125
Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser
    130                 135                 140
Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu
145                 150                 155                 160
Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val
                165                 170                 175
Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser
            180                 185                 190
Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg
        195                 200                 205
Met Thr Leu Thr Gly Ile Val Ser Trp Gly Phe Gly Cys Ala Leu Lys
    210                 215                 220
Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile
```

225 230 235 240
Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 160
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36H/V38D/V41R/A96D/D97G/A98R/T97adel/H99L/L97bdel
/C122S/M157K/R217D

<400> 160
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Asp Gly Arg Leu His Asn Asp Ile
85 90 95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
100 105 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
115 120 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
130 135 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys Leu Ile
145 150 155 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
165 170 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
180 185 190
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
195 200 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
210 215 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225 230 235 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu

245 250

<210> 161
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aH/V38D/V41R/A96D/D97G/A98G/T97adel/H99L/L97bde
l/C122S/S174P/R217D

<400> 161
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His His Gly Gly Ser Asp Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Asp Gly Gly Leu His Asn Asp Ile
85 90 95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
100 105 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
115 120 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
130 135 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145 150 155 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Pro Glu Val Thr
165 170 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
180 185 190
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
195 200 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
210 215 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225 230 235 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 162
<211> 252
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aH/V38D/V41G/A96G/D97E/T97aA/A98G/L97bdel/H99M/
C122S/Y151N

<400> 162
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His His Gly Gly Ser Asp Thr Tyr Gly Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Gly Glu Ala Gly Met His Asn Asp
85 90 95
Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro
100 105 110
Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro
115 120 125
Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser
130 135 140
Thr Asp Tyr Leu Asn Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu
145 150 155 160
Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val
165 170 175
Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser
180 185 190
Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg
195 200 205
Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys
210 215 220
Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile
225 230 235 240
Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 163

<211> 252
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36S/V38D/Y40L/V41R/A96P/D97V/T97aR/A98G/L97bdel/H
99L/C122S

<400> 163
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Ser His Arg Gly Gly Ser Asp Thr Leu Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Pro Val Arg Gly Leu His Asn Asp
85 90 95
Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro
100 105 110
Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro
115 120 125
Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser
130 135 140
Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu
145 150 155 160
Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val
165 170 175
Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser
180 185 190
Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg
195 200 205
Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys
210 215 220
Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile
225 230 235 240
Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 164
<211> 251
<212> PRT

<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36S/V38D/V41R/A96D/D97G/A98G/T97adel/H99L/L97bdel
/C122S/M157K/R217D

<400> 164

Ile	Ile	Gly	Gly	Glu	Phe	Thr	Thr	Ile	Glu	Asn	Gln	Pro	Trp	Phe	Ala
1				5				10						15	
Ala	Ile	Tyr	Arg	Ser	His	Arg	Gly	Gly	Ser	Asp	Thr	Tyr	Arg	Cys	Gly
			20					25					30		
Gly	Ser	Leu	Ile	Ser	Pro	Cys	Trp	Val	Ile	Ser	Ala	Thr	His	Cys	Phe
		35					40					45			
Ile	Asp	Tyr	Pro	Lys	Lys	Glu	Asp	Tyr	Ile	Val	Tyr	Leu	Gly	Arg	Ser
	50					55					60				
Arg	Leu	Asn	Ser	Asn	Thr	Gln	Gly	Glu	Met	Lys	Phe	Glu	Val	Glu	Asn
65					70					75					80
Leu	Ile	Leu	His	Lys	Asp	Tyr	Ser	Asp	Gly	Gly	Leu	His	Asn	Asp	Ile
				85					90					95	
Ala	Leu	Leu	Lys	Ile	Arg	Ser	Lys	Glu	Gly	Arg	Cys	Ala	Gln	Pro	Ser
			100					105					110		
Arg	Thr	Ile	Gln	Thr	Ile	Ser	Leu	Pro	Ser	Met	Tyr	Asn	Asp	Pro	Gln
		115					120					125			
Phe	Gly	Thr	Ser	Cys	Glu	Ile	Thr	Gly	Phe	Gly	Lys	Glu	Asn	Ser	Thr
	130					135					140				
Asp	Tyr	Leu	Tyr	Pro	Glu	Gln	Leu	Lys	Lys	Thr	Val	Val	Lys	Leu	Ile
145					150					155					160
Ser	His	Arg	Glu	Cys	Gln	Gln	Pro	His	Tyr	Tyr	Gly	Ser	Glu	Val	Thr
				165					170					175	
Thr	Lys	Met	Leu	Cys	Ala	Ala	Asp	Pro	Gln	Trp	Lys	Thr	Asp	Ser	Cys
			180					185					190		
Gln	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Cys	Ser	Leu	Gln	Gly	Arg	Met
		195					200					205			
Thr	Leu	Thr	Gly	Ile	Val	Ser	Trp	Gly	Asp	Gly	Cys	Ala	Leu	Lys	Asp
	210					215					220				
Lys	Pro	Gly	Val	Tyr	Thr	Arg	Val	Ser	His	Phe	Leu	Pro	Trp	Ile	Arg
225					230					235					240
Ser	His	Thr	Lys	Glu	Glu	Asn	Gly	Leu	Ala	Leu					
				245					250						

<210> 165
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41R/A96D/D97G/A98G/T97adel/H99L/L97bdel/C122
S/Q192E/R217D

<400> 165
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Asp Gly Gly Leu His Asn Asp Ile
85 90 95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
100 105 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
115 120 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
130 135 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145 150 155 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
165 170 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
180 185 190
Glu Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
195 200 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
210 215 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225 230 235 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 166
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)

protease domain
F30Y/V38D/V41R/A96D/D97G/A98G/T97adel/H99L/L97bdel
/C122S/M157K/R217D

<400> 166

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Asp Gly Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 167
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38D/Y40P/V41K/L97bA/H99Q/C122S

<400> 167
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Pro Lys Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 168
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/Y40P/V41K/L97bA/H99Q/C122S/M157K

<400> 168
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15

```
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Pro Lys Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 169
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/V41R/A96E/D97G/A98G/T97adel/H99L/L97bdel/C122
      S/Y151L/T178S/Q192E/R217D

<400> 169
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
```

```
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Glu Gly Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Ser Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Glu Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 170
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/V38D/Y40H/V41R/L97bA/H99Q/C122S/M157K/R217D

<400> 170

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
```

```
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 171
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30H/V38D/V41R/L97bA/H99Q/Y151L/M157K

<400> 171
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
```

```
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 172
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/V38D/V41R/L97bV/H99Q/C122S/Y151F/M157K

<400> 172

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Val Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
```

```
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Phe Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 173
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30H/V38D/V41R/L97bV/H99Q/C122S/Y151L/M157K

<400> 173
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Val Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
```

```
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 174
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/V38D/V41R/L97bA/H99Q/C122S/Y151F/M157K

<400> 174

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Phe Pro Glu Gln Leu Lys Lys Thr Val Val Lys
```

145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 175
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/V38D/V41R/L97bA/H99Q/C122S/Y151M/M157K

<400> 175
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Met Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175

```
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 176
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30H/V38D/V41R/L97bA/H99Q/C122S/Y149N/Y151L/M157K

<400> 176
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Asn Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
```

```
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 177
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/V38D/V41R/L97bA/H99Q/C122S/Y149N/Y151F/M157K

<400> 177

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Asn Leu Phe Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
```

Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 178
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/V38D/V41R/L97bV/H99Q/C122S/M157K

<400> 178
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Val Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu

245 250

<210> 179
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/V38D/V41R/L97bV/H99Q/C122S/Y151F/M157K

<400> 179
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Val Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Phe Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 180
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/V38D/V41R/L97bV/H99Q/C122S/Y149N/Y151F/M157K

<400> 180
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Val Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Asn Leu Phe Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 181
<211> 253
<212> PRT

<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/V38D/V41R/L97bV/H99Q/C122S/Y149N/Y151F/M157K

<400> 181

Ile	Ile	Gly	Gly	Glu	Phe	Thr	Thr	Ile	Glu	Asn	Gln	Pro	Trp	Tyr	Ala
1				5				10						15	
Ala	Ile	Tyr	Arg	Arg	His	Arg	Gly	Gly	Ser	Asp	Thr	Tyr	Arg	Cys	Gly
		20					25					30			
Gly	Ser	Leu	Ile	Ser	Pro	Cys	Trp	Val	Ile	Ser	Ala	Thr	His	Cys	Phe
	35					40					45				
Ile	Asp	Tyr	Pro	Lys	Lys	Glu	Asp	Tyr	Ile	Val	Tyr	Leu	Gly	Arg	Ser
50					55					60					
Arg	Leu	Asn	Ser	Asn	Thr	Gln	Gly	Glu	Met	Lys	Phe	Glu	Val	Glu	Asn
65				70					75						80
Leu	Ile	Leu	His	Lys	Asp	Tyr	Ser	Ala	Asp	Thr	Val	Ala	Gln	His	Asn
			85					90					95		
Asp	Ile	Ala	Leu	Leu	Lys	Ile	Arg	Ser	Lys	Glu	Gly	Arg	Cys	Ala	Gln
		100					105					110			
Pro	Ser	Arg	Thr	Ile	Gln	Thr	Ile	Ser	Leu	Pro	Ser	Met	Tyr	Asn	Asp
	115					120					125				
Pro	Gln	Phe	Gly	Thr	Ser	Cys	Glu	Ile	Thr	Gly	Phe	Gly	Lys	Glu	Asn
130					135					140					
Ser	Thr	Asp	Asn	Leu	Phe	Pro	Glu	Gln	Leu	Lys	Lys	Thr	Val	Val	Lys
145				150					155						160
Leu	Ile	Ser	His	Arg	Glu	Cys	Gln	Gln	Pro	His	Tyr	Tyr	Gly	Ser	Glu
			165					170					175		
Val	Thr	Thr	Lys	Met	Leu	Cys	Ala	Ala	Asp	Pro	Gln	Trp	Lys	Thr	Asp
		180					185					190			
Ser	Cys	Gln	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Cys	Ser	Leu	Gln	Gly
	195					200					205				
Arg	Met	Thr	Leu	Thr	Gly	Ile	Val	Ser	Trp	Gly	Arg	Gly	Cys	Ala	Leu
210					215					220					
Lys	Asp	Lys	Pro	Gly	Val	Tyr	Thr	Arg	Val	Ser	His	Phe	Leu	Pro	Trp
225				230					235						240
Ile	Arg	Ser	His	Thr	Lys	Glu	Glu	Asn	Gly	Leu	Ala	Leu			
			245					250							

<210> 182
<211> 253
<212> PRT
<213> Artificial Sequence

<220>

<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/V38D/Y40H/V41R/L97bA/H99Q/C122S/M157K/R217G

<400> 182
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Gly Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 183
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/V38D/Y40H/V41R/L97bA/H99Q/C122S/M157K/R217E

<400> 183
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 184
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30H/V38D/V41R/L97bA/H99Q/C122S/Y151L/M157K/R217D

<400> 184
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala

```
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 185
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/V38D/Y40H/V41R/L97bA/H99Q/C122S/Y149L/M157K/R
217G

<400> 185

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
```

```
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Leu Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Gly Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 186
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/V38D/Y40H/V41R/L97bA/H99Q/C122S/Y149L/M157K/R
217E

<400> 186

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
```

```
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Leu Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 187
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/V38D/Y40H/V41R/L97bA/H99Q/C122S/Y149L/M157K/R
217D

<400> 187

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
```

```
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Leu Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 188
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/V38D/Y40H/V41R/L97bA/H99Q/C122S/Y149F/M157K/R
      217G

<400> 188
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
```

65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Phe Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Gly Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 189
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/V38D/Y40H/V41R/L97bA/H99Q/C122S/Y149F/M157K/R
217E

<400> 189
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn

```
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Phe Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 190
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/V38D/Y40H/V41R/L97bA/H99Q/C122S/Y149F/M157K/R
217D

<400> 190

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
```

```
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Phe Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 191
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/V38D/Y40H/V41R/L97bA/H99Q/C122S/Y149L/M1
57K/R217E

<400> 191

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
```

```
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Leu Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 192
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35Q/V38D/Y40H/V41R/L97bA/H99Q/C122S/Y149L/M1
      57K/R217G

<400> 192
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
```

```
    130                 135                 140
Ser Thr Asp Leu Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Gly Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 193
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/H37D/V38D/Y40H/V41R/L97bA/H99Q/C122S/Y149L/M1
57K/R217E

<400> 193

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg Asp Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Leu Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
```

```
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 194
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/H37D/V38D/Y40H/V41R/L97bA/H99Q/C122S/Y149L/M157K/R217G

<400> 194

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg Asp Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Leu Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
```

```
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Gly Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 195
<211> 254
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/V38D/Y40H/V41R/L97bA/H99Q/C122S/Y149L/M157K

<400> 195
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His His
                85                  90                  95
Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala
            100                 105                 110
Gln Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn
        115                 120                 125
Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu
    130                 135                 140
Asn Ser Thr Asp Leu Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val
145                 150                 155                 160
Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser
                165                 170                 175
Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr
            180                 185                 190
```

```
Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln
        195                 200                 205
Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala
    210                 215                 220
Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro
225                 230                 235                 240
Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 196
<211> 254
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/V38D/Y40H/V41R/L97bA/H99Q/C122S/Y149F/M157K

<400> 196
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His His
                85                  90                  95
Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala
            100                 105                 110
Gln Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn
        115                 120                 125
Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu
    130                 135                 140
Asn Ser Thr Asp Phe Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val
145                 150                 155                 160
Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser
                165                 170                 175
Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr
            180                 185                 190
Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln
        195                 200                 205
Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala
```

```
    210                 215                 220
Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro
225                 230                 235                 240
Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 197
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
I17L/F30Y/V38D/Y40H/V41R/L97bA/H99Q/C122S/M157K

<400> 197

```
Ile Leu Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
```

Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 198
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
I17V/F30Y/V38D/Y40H/V41R/L97bA/H99Q/C122S/M157K

<400> 198
Ile Val Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 199
<211> 254
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/V38D/Y40H/V41R/L97bA/H99Q/C122S/Y149W/M157K

<400> 199
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His His
85 90 95
Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala
100 105 110
Gln Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn
115 120 125
Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu
130 135 140
Asn Ser Thr Asp Trp Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val
145 150 155 160
Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser
165 170 175
Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr
180 185 190
Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln
195 200 205
Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala
210 215 220
Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro
225 230 235 240
Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 200
<211> 254

<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/V38D/Y40H/V41R/L97bA/H99Q/C122S/Y149L/M157K

<400> 200

Ile	Ile	Gly	Gly	Glu	Phe	Thr	Thr	Ile	Glu	Asn	Gln	Pro	Trp	Tyr	Ala
1			5					10						15	
Ala	Ile	Tyr	Gln	Arg	His	Arg	Gly	Gly	Ser	Asp	Thr	His	Arg	Cys	Gly
		20					25					30			
Gly	Ser	Leu	Ile	Ser	Pro	Cys	Trp	Val	Ile	Ser	Ala	Thr	His	Cys	Phe
	35					40					45				
Ile	Asp	Tyr	Pro	Lys	Lys	Glu	Asp	Tyr	Ile	Val	Tyr	Leu	Gly	Arg	Ser
	50				55					60					
Arg	Leu	Asn	Ser	Asn	Thr	Gln	Gly	Glu	Met	Lys	Phe	Glu	Val	Glu	Asn
65				70					75					80	
Leu	Ile	Leu	His	Lys	Asp	Tyr	Ser	Ala	Asp	Thr	Ala	Ala	Gln	His	His
			85					90					95		
Asn	Asp	Ile	Ala	Leu	Leu	Lys	Ile	Arg	Ser	Lys	Glu	Gly	Arg	Cys	Ala
		100					105					110			
Gln	Pro	Ser	Arg	Thr	Ile	Gln	Thr	Ile	Ser	Leu	Pro	Ser	Met	Tyr	Asn
	115					120					125				
Asp	Pro	Gln	Phe	Gly	Thr	Ser	Cys	Glu	Ile	Thr	Gly	Phe	Gly	Lys	Glu
	130				135					140					
Asn	Ser	Thr	Asp	Leu	Leu	Tyr	Pro	Glu	Gln	Leu	Lys	Lys	Thr	Val	Val
145				150					155					160	
Lys	Leu	Ile	Ser	His	Arg	Glu	Cys	Gln	Gln	Pro	His	Tyr	Tyr	Gly	Ser
			165					170					175		
Glu	Val	Thr	Thr	Lys	Met	Leu	Cys	Ala	Ala	Asp	Pro	Gln	Trp	Lys	Thr
		180					185					190			
Asp	Ser	Cys	Gln	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Cys	Ser	Leu	Gln
	195					200					205				
Gly	Arg	Met	Thr	Leu	Thr	Gly	Ile	Val	Ser	Trp	Gly	Arg	Gly	Cys	Ala
	210				215					220					
Leu	Lys	Asp	Lys	Pro	Gly	Val	Tyr	Thr	Arg	Val	Ser	His	Phe	Leu	Pro
225				230					235					240	
Trp	Ile	Arg	Ser	His	Thr	Lys	Glu	Glu	Asn	Gly	Leu	Ala	Leu		
			245					250							

<210> 201
<211> 254
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/V38D/Y40H/V41R/L97bA/H99Q/C122S/Y149W/M1
57K

<400> 201
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Gln Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His His
85 90 95
Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala
100 105 110
Gln Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn
115 120 125
Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu
130 135 140
Asn Ser Thr Asp Trp Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val
145 150 155 160
Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser
165 170 175
Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr
180 185 190
Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln
195 200 205
Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala
210 215 220
Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro
225 230 235 240
Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 202
<211> 254
<212> PRT
<213> Artificial Sequence

<220>

<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/V38D/Y40H/V41R/L97bA/H99Q/C122S/Y149F/M157K

<400> 202
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Gln Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His His
85 90 95
Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala
100 105 110
Gln Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn
115 120 125
Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu
130 135 140
Asn Ser Thr Asp Phe Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val
145 150 155 160
Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser
165 170 175
Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr
180 185 190
Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln
195 200 205
Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala
210 215 220
Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro
225 230 235 240
Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 203
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain

F30Y/R35Q/V38D/Y40H/V41R/L97bA/H99Q/C122S/M157K

<400> 203
```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 204
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/H37T/V38D/Y40H/V41R/L97bA/H99Q/C122S/Y149L/M157K

<400> 204
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Arg Arg Thr Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Leu Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 205
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/H37T/V38D/Y40H/V41R/L97bA/H99Q/C122S/Y149F/M1
      57K

<400> 205
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala

```
 1               5                  10                  15
Ala Ile Tyr Arg Arg Thr Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Phe Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 206
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/H37T/V38D/Y40H/V41R/L97bA/H99Q/C122S/M157K

<400> 206

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg Thr Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
```

```
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 207
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/H37T/V38D/Y40H/V41R/L97bA/H99Q/C122S/Y14
9L/M157K

<400> 207

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Thr Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
```

```
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Leu Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 208
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/H37T/V38D/Y40H/V41R/L97bA/H99Q/C122S/Y14
9W/M157K

<400> 208

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Thr Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
```

```
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Trp Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 209
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35Q/H37T/V38D/Y40H/V41R/L97bA/H99Q/C122S/Y14
      9F/M157K

<400> 209
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Thr Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
```

```
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Phe Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 210
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/H37T/V38D/Y40H/V41R/L97bA/H99Q/C122S/M15
7K

<400> 210

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Thr Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
```

```
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 211
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/V38D/Y40H/V41R/T56A/L97bA/H99Q/C122S/M157K

<400> 211
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Ala His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
```

```
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 212
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/V38D/Y40H/V41R/L97bA/H99Q/C122S/Y151F/M157K

<400> 212
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
```

```
Ser Thr Asp Tyr Leu Phe Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 213
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain V38D/L97bA/H99Q/C122S/M157K/T158A

<400> 213
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Ala Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
```

```
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 214
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/V41R/L97bA/H99Q/C122S/M157K/T158A

<400> 214
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Ala Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
```

```
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 215
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R37aH/V38D/Y40Q/V41I/L97bA/H99Q/C122S/Y151L/M
157W/Q192Y

<400> 215

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His His Gly Gly Ser Asp Thr Gln Ile Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Trp Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Tyr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
```

```
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 216
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
I17V/F30Y/R35Q/H37W/V38D/Y40H/V41R/Y60bN/L97bA/H99
Q/C122S/Y149H/M157K

<400> 216

```
Ile Val Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Trp Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp His Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
```

225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 217
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/H37W/V38D/Y40H/V41R/Y60bN/L97bA/H99Q/C12
2S/Y149H/M157K/T158A

<400> 217
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Gln Arg Trp Arg Gly Gly Ser Asp Thr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp His Leu Tyr Pro Glu Gln Leu Lys Lys Ala Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu

245 250

<210> 218
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
I17V/F30Y/R35Q/H37W/V38D/Y40H/V41R/Y60bN/L97bA/H99
Q/C122S/Y149H/M157K/T158A

<400> 218
Ile Val Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Gln Arg Trp Arg Gly Gly Ser Asp Thr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp His Leu Tyr Pro Glu Gln Leu Lys Lys Ala Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 219
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
I17V/F30Y/V38D/Y40H/V41R/L97bA/H99Q/C122S/M157K/T1
58A

<400> 219
Ile Val Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Ala Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 220

<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38D/V41R/L97bA/H99Q/C122S

<400> 220
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 221
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/R36H/H37W/V38E/Y40H/V41R/T97aI/L97bA/H99
Q/C122S/M157K

<400> 221
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Gln His Trp Arg Gly Gly Ser Glu Thr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 222
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)

protease domain
I17V/F30Y/R36H/V38E/Y40H/V41R/T97aI/L97bA/H99Q/C12
2S/M157K

<400> 222
Ile Val Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Glu Thr His Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 223
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
I17V/F30Y/R35Q/R36H/H37W/V38E/Y40H/V41R/T97aI/L97b

A/H99Q/C122S/M157K

<400> 223
Ile Val Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Gln His Trp Arg Gly Gly Ser Glu Thr His Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 224
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R36H/V38E/Y40H/V41R/T97aI/L97bA/H99Q/C122S/M1
      57K/T158A

<400> 224
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Glu Thr His Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ala Ile Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Ala Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 225
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      I17V/F30Y/R35Q/R36H/H37W/V38E/Y40H/V41R/T97aI/L97b
      A/H99Q/C122S/M157K/T158A

<400> 225
Ile Val Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala

```
 1               5                  10                  15
Ala Ile Tyr Gln His Trp Arg Gly Gly Ser Glu Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Ala Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 226
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/V38E/Y40H/V41R/T97aI/L97bA/H99Q/C122S/Y1
49R/M157K

<400> 226

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Glu Thr His Arg Cys Gly
```

```
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ala Ile Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 227
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      I17V/F30Y/V38D/Y40H/V41R/L97bA/H99Q/C122S/Y149R/M1
      57K

<400> 227
Ile Val Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
```

```
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 228
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/H37W/V38D/Y40H/V41R/Y60bN/L97bA/H99Q/C12
2S/Y149R/M157K

<400> 228

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Trp Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
```

```
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 229
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/V38D/Y40H/V41R/L97bA/H99Q/C122S/Y149R/M157K

<400> 229

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
```

```
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 230
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/V38E/Y40H/V41R/K61E/T97aI/L97bA/H99Q/C12
2S/M157K

<400> 230

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Glu Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Glu Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
```

```
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 231
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/R37aH/V38E/Y40H/V41R/K61E/T97aI/L97bA/H99Q/C122S/M157K

<400> 231

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His His Gly Gly Ser Glu Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Glu Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
```

```
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 232
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/V38E/Y40H/V41R/K61E/T97aI/L97bA/H99Q/C12
2S/Y149R/M157K

<400> 232

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Glu Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Glu Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
```

```
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 233
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/R37aH/V38E/Y40H/V41R/K61E/T97aI/L97bA/H99Q/C122S/Y149R/M157K

<400> 233

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His His Gly Gly Ser Glu Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Glu Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
```

```
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 234
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35Q/H37D/V38D/Y40H/V41R/D60aE/Y60bN/L97bA/H9
      9Q/C122S/Y149S/M157K

<400> 234
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Asp Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Glu Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Ser Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
```

```
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 235
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35Q/H37T/V38D/Y40H/V41R/D60aE/Y60bN/L97bA/H9
      9Q/C122S/Y149L/M157K

<400> 235
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Thr Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Glu Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Leu Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
```

```
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 236
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35Q/V38D/Y40H/V41R/Y60bE/L97bA/H99Q/C122S/Y1
      49Q/M157K/R217S

<400> 236
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Gln Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
```

```
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Ser Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 237
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35Q/V38Y/Y40H/V41R/D60aE/Y60bE/L97bA/H99Q/C1
      22S/Y149V/M157K/R217M

<400> 237
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg His Arg Gly Gly Ser Tyr Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Glu Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Val Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
```

```
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Met Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 238
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/V38D/Y40H/V41R/D60aE/Y60bS/L97bA/H99Q/C1
22S/Y149T/M157K

<400> 238

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Glu Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Thr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
```

```
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 239
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/V38D/Y40H/V41R/D60aE/Y60bE/L97bA/H99Q/C1
22S/Y149L/M157K/R217S

<400> 239

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Glu Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Leu Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Ser Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
```

Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 240
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/H37Y/V38D/Y40H/V41R/Y60bE/L97bA/H99Q/C12
2S/Y149R/M157K

<400> 240
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Gln Arg Tyr Arg Gly Gly Ser Asp Thr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 241
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/V38D/Y40H/V41R/L97bA/H99Q/C122S/M157K/Q192H

<400> 241
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys His Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 242

<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/V38E/Y40H/V41R/I65T/T97aI/L97bA/H99Q/C12
2S/M157K

<400> 242

Ile	Ile	Gly	Gly	Glu	Phe	Thr	Thr	Ile	Glu	Asn	Gln	Pro	Trp	Tyr	Ala
1			5					10						15	
Ala	Ile	Tyr	Arg	His	His	Arg	Gly	Gly	Ser	Glu	Thr	His	Arg	Cys	Gly
		20					25					30			
Gly	Ser	Leu	Ile	Ser	Pro	Cys	Trp	Val	Ile	Ser	Ala	Thr	His	Cys	Phe
	35					40					45				
Ile	Asp	Tyr	Pro	Lys	Lys	Glu	Asp	Tyr	Thr	Val	Tyr	Leu	Gly	Arg	Ser
50					55					60					
Arg	Leu	Asn	Ser	Asn	Thr	Gln	Gly	Glu	Met	Lys	Phe	Glu	Val	Glu	Asn
65				70					75						80
Leu	Ile	Leu	His	Lys	Asp	Tyr	Ser	Ala	Asp	Ile	Ala	Ala	Gln	His	Asn
			85					90					95		
Asp	Ile	Ala	Leu	Leu	Lys	Ile	Arg	Ser	Lys	Glu	Gly	Arg	Cys	Ala	Gln
		100					105					110			
Pro	Ser	Arg	Thr	Ile	Gln	Thr	Ile	Ser	Leu	Pro	Ser	Met	Tyr	Asn	Asp
	115					120					125				
Pro	Gln	Phe	Gly	Thr	Ser	Cys	Glu	Ile	Thr	Gly	Phe	Gly	Lys	Glu	Asn
130					135					140					
Ser	Thr	Asp	Tyr	Leu	Tyr	Pro	Glu	Gln	Leu	Lys	Lys	Thr	Val	Val	Lys
145				150					155						160
Leu	Ile	Ser	His	Arg	Glu	Cys	Gln	Gln	Pro	His	Tyr	Tyr	Gly	Ser	Glu
			165					170					175		
Val	Thr	Thr	Lys	Met	Leu	Cys	Ala	Ala	Asp	Pro	Gln	Trp	Lys	Thr	Asp
		180					185					190			
Ser	Cys	Gln	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Cys	Ser	Leu	Gln	Gly
	195					200					205				
Arg	Met	Thr	Leu	Thr	Gly	Ile	Val	Ser	Trp	Gly	Arg	Gly	Cys	Ala	Leu
210					215					220					
Lys	Asp	Lys	Pro	Gly	Val	Tyr	Thr	Arg	Val	Ser	His	Phe	Leu	Pro	Trp
225				230					235						240
Ile	Arg	Ser	His	Thr	Lys	Glu	Glu	Asn	Gly	Leu	Ala	Leu			
			245					250							

<210> 243
<211> 253
<212> PRT

<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/V38E/Y40L/V41R/T97aI/L97bA/H99Q/C122S/M157K

<400> 243

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Glu Thr Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 244
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/V38E/Y40H/V41R/T97aI/L97bA/H99Q/C122S/M157K/Q192H

<400> 244
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Glu Thr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys His Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 245
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)

protease domain
N26D/F30Y/R36H/R37aH/V38E/Y40H/V41R/K61E/I65T/L97b
A/H99Q/C122S/M126I/M157K

<400> 245

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asp Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His His Gly Gly Ser Glu Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Glu Lys Glu Asp Tyr Thr Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Ile Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 246
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
N26D/F30Y/V38D/Y40H/V41R/I65T/L97bA/H99Q/C122S/M12

6I/M157K/Q192H

<400> 246
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asp Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Thr Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Ile Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys His Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 247
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      N26D/F30Y/V38D/Y40L/V41R/I65T/L97bA/H99Q/C122S/M12
      6I/M157K

<400> 247
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asp Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Leu Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Thr Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Ile Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 248
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      N26D/F30Y/V38D/Y40H/V41R/I65T/L97bA/H99Q/C122S/M12
      6I/Y149R/M157K

<400> 248
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asp Gln Pro Trp Tyr Ala

```
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Thr Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Ile Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 249
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/V38E/Y40H/V41R/I65T/T97aI/L97bA/H99Q/C12
2S/Y149R/M157K

<400> 249

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Glu Thr His Arg Cys Gly
```

```
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Thr Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 250
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/V38D/Y40L/V41R/L97bA/H99Q/C122S/M157K

<400> 250
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
```

```
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 251
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/V38D/Y40L/V41R/L97bA/H99Q/C122S/M157K/Q192H

<400> 251

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
```

65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys His Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 252
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/V38E/Y40L/V41R/T97aI/L97bA/H99Q/C122S/M1
57K/Q192H

<400> 252
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Glu Thr Leu Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn

```
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys His Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 253
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36H/H37E/V38E/T39S/Y40H/V41W/Y60bW/T97a
I/L97bA/H99Q/C122S/Y149R/M157K/Q192Y

<400> 253

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp His Glu Arg Gly Gly Ser Glu Ser His Trp Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Trp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
```

```
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Tyr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 254
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35W/R36H/H37E/V38E/T39W/Y40H/V41R/Y60bH/T97a
      I/L97bA/H99Q/C122S/Y149R/M157K/Q192A

<400> 254
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp His Glu Arg Gly Gly Ser Glu Trp His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp His Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
```

```
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Ala Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 255
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36H/H37E/V38E/T39Q/Y40H/V41W/Y60bW/T97a
I/L97bA/H99Q/C122S/Y149R/M157K/Q192F

<400> 255

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp His Glu Arg Gly Gly Ser Glu Gln His Trp Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Trp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
```

```
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Phe Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 256
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35W/R36H/H37E/V38E/T39R/Y40H/V41W/Y60bW/T97a
      I/L97bA/H99Q/C122S/Y149R/M157K/Q192Y

<400> 256
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp His Glu Arg Gly Gly Ser Glu Arg His Trp Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Trp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
```

```
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Tyr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 257
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35Y/R36H/H37E/V38E/T39S/Y40H/V41W/Y60bW/T97a
      I/L97bA/H99Q/C122S/Y149R/M157K/Q192F

<400> 257
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Tyr His Glu Arg Gly Gly Ser Glu Ser His Trp Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Trp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
```

```
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Phe Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 258
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Y/R36H/H37E/V38E/T39R/Y40H/V41W/Y60bW/T97a
I/L97bA/H99Q/C122S/Y149R/M157K/Q192H

<400> 258

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Tyr His Glu Arg Gly Gly Ser Glu Arg His Trp Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Trp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
```

```
            180                 185                 190
Ser Cys His Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 259
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Y/R36H/H37E/V38E/T39R/Y40H/V41W/Y60bW/T97a
I/L97bA/H99Q/C122S/Y149R/M157K/Q192F

<400> 259

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Tyr His Glu Arg Gly Gly Ser Glu Arg His Trp Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Trp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Phe Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
```

```
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 260
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      I17V/F30Y/R35W/R36H/H37E/V38E/T39W/Y40H/V41R/Y60bQ
      /T97aE/L97bA/H99Q/C122S/Y149K/M157K

<400> 260
Ile Val Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp His Glu Arg Gly Gly Ser Glu Trp His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Lys Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
```

```
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 261
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36Q/H37E/V38A/T39W/Y40H/V41R/Y60bQ/K61D
/I65V/T97aE/L97bA/H99Q/C122S/Y149K/M157K

<400> 261

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp Gln Glu Arg Gly Gly Ser Ala Trp His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Gln Pro Asp Lys Glu Asp Tyr Val Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Lys Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
```

225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 262
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36Q/H37E/V38E/T39W/Y40H/V41R/Y60bQ/K61L
/I65V/T97aE/L97bA/H99Q/C122S/Y149K/M157K

<400> 262
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Trp Gln Glu Arg Gly Gly Ser Glu Trp His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Gln Pro Leu Lys Glu Asp Tyr Val Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Lys Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu

245 250

<210> 263
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36A/H37E/V38E/T39W/Y40H/V41R/Y60bQ/K61D
/I65R/T97aE/L97bA/H99Q/C122S/Y149K/M157K

<400> 263
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Trp Ala Glu Arg Gly Gly Ser Glu Trp His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Gln Pro Asp Lys Glu Asp Tyr Arg Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Lys Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 264
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36K/H37E/V38E/T39W/Y40H/V41R/Y60bQ/K61E
/I65T/T97aE/L97bA/H99Q/C122S/Y149K/M157K

<400> 264
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Trp Lys Glu Arg Gly Gly Ser Glu Trp His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Gln Pro Glu Lys Glu Asp Tyr Thr Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Lys Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 265

<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36H/H37E/V38E/T39Y/Y40F/V41R/Y60bQ/T97a
E/L97bA/H99Q/C122S/Y149R/M157K

<400> 265
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Trp His Glu Arg Gly Gly Ser Glu Tyr Phe Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 266
<211> 253
<212> PRT

<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36H/H37E/V38E/T39W/Y40H/V41R/Y60bQ/T97a
E/L97bA/H99Q/C122S/Y149K/M157K/Q192P

<400> 266

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp His Glu Arg Gly Gly Ser Glu Trp His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Lys Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Pro Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 267
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38E/Y40Q/V41Q/D60aP/Y60bL/L97bA/H99Q/C122S/Y149W

<400> 267

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Thr Gln Gln Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Leu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Trp Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 268
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain

V38E/Y40Q/V41L/D60aP/Y60bL/L97bA/H99Q/C122S/Y149W

<400> 268
```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Leu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Trp Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 269
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36H/H37E/V38E/T39W/Y40H/V41R/Y60bQ/T97a
E/L97bA/H99L/C122S/Y149K/M157K

<400> 269
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Trp His Glu Arg Gly Gly Ser Glu Trp His Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Leu His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Lys Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 270
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R36H/V38E/Y40H/V41R/T97aE/L97bA/H99Q/C122S/M1
      57K

<400> 270
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala

```
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Glu Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 271
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Y/R36H/H37K/V38E/T39F/V41R/T97aI/L97bA/H99Q/C12
2S/Y149R/M157K

<400> 271

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Tyr His Lys Arg Gly Gly Ser Glu Phe Tyr Arg Cys Gly
```

```
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 272
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35Y/R36H/H37K/V38E/T39F/Y40F/V41R/T97aI/L97b
      A/H99Q/C122S/M157K

<400> 272
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Tyr His Lys Arg Gly Gly Ser Glu Phe Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
```

```
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 273
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/V38E/Y40H/V41R/T97aE/L97bA/H99Q/C122S/Y1
49R/M157K

<400> 273

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Glu Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
```

```
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 274
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain L97bA/H99Q/C122S

<400> 274

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
```

```
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 275
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Y/R36H/H37K/V38E/T39F/Y40F/V41R/T97aI/L97b
A/H99Q/Y149R/M157K

<400> 275

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Tyr His Lys Arg Gly Gly Ser Glu Phe Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
```

```
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 276
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Y/R36H/H37K/V38E/T39F/Y40F/V41R/K61R/K62R/
T97aI/L97bA/H99Q/C122S/Y149R/M157K

<400> 276

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Tyr His Lys Arg Gly Gly Ser Glu Phe Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Arg Arg Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
```

```
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 277
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Y/R36H/H37K/V38E/T39F/Y40F/V41R/K82R/T97aI
/L97bA/H99Q/K110aR/C122S/Y149R/M157K

<400> 277

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Tyr His Lys Arg Gly Gly Ser Glu Phe Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Arg Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Arg Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
```

```
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 278
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35Y/R36H/H37K/V38E/T39F/Y40F/V41R/K92R/T97aI
      /L97bA/H99Q/C122S/Y149R/M157K

<400> 278
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Tyr His Lys Arg Gly Gly Ser Glu Phe Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Arg Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
```

```
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 279
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35Y/R36H/H37K/V38E/T39F/Y40F/V41R/K92S/T97aI
      /L97bA/H99Q/C122S/Y149R/M157K

<400> 279
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Tyr His Lys Arg Gly Gly Ser Glu Phe Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Ser Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
```

```
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 280
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Y/R36H/H37K/V38E/T39F/Y40F/V41R/T97aI/L97b
A/H99Q/C122S/Y149R/M157K/K179R

<400> 280

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Tyr His Lys Arg Gly Gly Ser Glu Phe Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Arg Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
```

```
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 281
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Y/R36H/H37K/V38E/T39F/Y40F/V41R/T97aI/L97b
A/H99Q/C122S/Y149R/M157K/K179S

<400> 281

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Tyr His Lys Arg Gly Gly Ser Glu Phe Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Ser Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
```

```
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 282
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Y/R36H/H37K/V38E/T39F/Y40F/V41R/T97aI/L97b
A/H99Q/C122S/Y149R/M157K/K187S/K223S/K224Y

<400> 282

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Tyr His Lys Arg Gly Gly Ser Glu Phe Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Ser Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
```

```
    210                 215                 220
Ser Asp Tyr Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 283
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36H/H37S/V38E/T39Y/Y40H/V41R/Y60bN/T97a
E/L97bA/H99Q/C122S/M157K

<400> 283

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp His Ser Arg Gly Gly Ser Glu Tyr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
```

225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 284
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36H/H37S/V38E/T39Y/Y40H/V41R/Y60bN/T97a
E/L97bA/H99Q/C122S

<400> 284
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Trp His Ser Arg Gly Gly Ser Glu Tyr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu

245 250

<210> 285
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/H37S/V38E/T39Y/Y40H/V41R/Y60bN/T97aE/L97
bA/H99Q/C122S/Y149R

<400> 285
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Trp Arg Ser Arg Gly Gly Ser Glu Tyr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 286
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/H37S/V38E/T39Y/Y40H/V41R/Y60bN/T97aE/L97
bA/H99Q/C122S/M157K

<400> 286
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Trp Arg Ser Arg Gly Gly Ser Glu Tyr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 287

<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Y/R36H/H37K/V38E/T39F/Y40F/V41R/K61S/K62S/
T97aI/L97bA/H99Q/C122S/Y149R/M157K

<400> 287
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Tyr His Lys Arg Gly Gly Ser Glu Phe Phe Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Ser Ser Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 288
<211> 253
<212> PRT

<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Y/R36H/H37K/V38E/T39F/Y40F/V41R/K82S/T97aI
/L97bA/H99Q/K110aS/C122S/Y149R/M157K

<400> 288

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Tyr His Lys Arg Gly Gly Ser Glu Phe Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Ser Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Ser Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
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<210> 289
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Y/R36H/H37K/V38E/T39F/Y40F/V41R/T97aI/L97b
A/H99Q/C122S/Y149R/M157K/K187R/K223R/K224R

<400> 289
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Tyr His Lys Arg Gly Gly Ser Glu Phe Phe Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Arg Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Arg Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 290
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)

protease domain
F30Y/R35W/H37S/V38E/T39Y/Y40H/V41R/Y60bN/T97aE/L97
bA/H99Q/C122S

<400> 290

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp Arg Ser Arg Gly Gly Ser Glu Tyr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 291
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35W/H37P/R37aN/V38E/T39Y/V41R/D60aP/Y60bL/T97aI/L

97bA/H99Q/C122S

<400> 291

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Trp Arg Pro Asn Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Leu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 292
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36H/H37S/V38E/T39Y/Y40F/V41R/Y60bN/T97a
E/L97bA/H99Q/C122S/Y149R/M157K

<400> 292
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Trp His Ser Arg Gly Gly Ser Glu Tyr Phe Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 293
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain V38E/V41R/T97aI/L97bA/H99Q/C122S

<400> 293
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Thr Tyr Arg Cys Gly

```
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 294
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain V38E/T97aE/L97bA/H99Q/C122S

<400> 294
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
```

```
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 295
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38E/T97aI/L97bA/H99Q/C122S

<400> 295

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
```

```
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 296
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38D/L97bR/H99E/C122S/E175D

<400> 296

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
```

```
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 297
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain V38D/L97bR/H99E/C122S/E175D/R217E

<400> 297
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
```

```
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 298
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain V38D/L97bR/H99E/C122S/E175D/K224R

<400> 298
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
```

```
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 299
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37Y/R37aE/V38D/T39Y/V41R/D60aP/Y60bQ/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 299

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Asp Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
```

```
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 300
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37Y/V38E/T39Y/V41R/D60aP/T97aI/L97bA/H99Q/C1
22S/Y149R

<400> 300

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Tyr Arg Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
```

```
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 301
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38E/V41L/Y60bL/L97bA/H99Q/C122S

<400> 301

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Thr Tyr Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Leu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
```

245 250

<210> 302
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain L97bG/H99Q/C122S/R217Q

<400> 302
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Gln Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 303

<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38D/H99Q/C122S/R217Q

<400> 303
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Gln Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 304
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38D/L97bG/C122S/R217Q

<400> 304
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala His His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Gln Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 305
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38D/L97bG/H99Q/C122S

<400> 305
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 306
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain V38D/L97bG/H99Q/C122S/S195A/R217Q

<400> 306
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly

```
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ala Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Gln Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 307
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain Y40Q/Y60bL/L97bA/H99Q/C122S

<400> 307
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Gln Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Leu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
```

```
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 308
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38E/Y40Q/L97bA/H99Q/C122S

<400> 308

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Thr Gln Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
```

```
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 309
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38E/Y40Q/V41L/L97bA/C122S

<400> 309

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala His His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
```

```
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 310
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain Y40Q/L97bA/H99Q/C122S

<400> 310
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Gln Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
```

```
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 311
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      T39L/Y40L/V41R/T97aI/L97bA/H99Q/C122S

<400> 311
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Leu Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
```

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Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 312
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/Y40L/V41R/T97aI/L97bA/H99Q/C122S

<400> 312
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
```

```
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 313
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/T39L/V41R/T97aI/L97bA/H99Q/C122S

<400> 313
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Leu Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
```

Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 314
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/T39L/Y40L/T97aI/L97bA/H99Q/C122S

<400> 314
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Leu Leu Val Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu

245 250

<210> 315
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/T39L/Y40L/V41R/L97bA/H99Q/C122S

<400> 315
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Leu Leu Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 316
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/T39L/Y40L/V41R/T97aI/H99Q/C122S

<400> 316
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Leu Leu Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Leu Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 317
<211> 253
<212> PRT

<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38D/L97bR/H99Q/C122S/Y151L/R217V

<400> 317
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 318
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)

protease domain V38D/V41R/L97bR/H99Q/C122S/R217V

<400> 318
```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 319
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/Y40L/V41K/L97bR/H99L/C122S/E175D

<400> 319

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Leu Lys Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Leu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 320
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/T39L/Y40L/V41K/L97bR/H99L/C122S/E175D

<400> 320

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Leu Leu Lys Cys Gly
```

```
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Leu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 321
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/T39L/Y40L/V41R/T97aI/L97bA/C122S

<400> 321
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Leu Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
```

```
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala His His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 322
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38D/V41R/L97bR/H99Q/C122S/Y151L

<400> 322

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
```

```
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 323
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aD/G37bD/V38F/T39H/V41R/Y60bK/T97aS/L97bR/H99E/
C122S/Y151L/E175D/Q192T/R217E/K224R

<400> 323

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Asp Asp Gly Ser Phe His Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Lys Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ser Arg Ala Glu His Asn
                85                  90                  95
```

```
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 324
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      H37G/G37bD/V38F/T39H/V41R/Y60bK/T97aS/L97bR/H99E/C
      122S/Y151L/E175D/Q192T/R217E/K224R

<400> 324
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg Gly Arg Asp Gly Ser Phe His Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Lys Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ser Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
```

```
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 325
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
H37G/R37aD/V38F/T39H/V41R/Y60bK/T97aS/L97bR/H99E/C
122S/Y151L/E175D/Q192T/R217E/K224R

<400> 325

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg Gly Asp Gly Gly Ser Phe His Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Lys Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ser Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
```

```
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 326
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
H37G/R37aD/G37bD/T39H/V41R/Y60bK/T97aS/L97bR/H99E/
C122S/Y151L/E175D/Q192T/R217E/K224R

<400> 326

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg Gly Asp Asp Gly Ser Val His Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Lys Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ser Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
```

```
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 327
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      H37G/R37aD/G37bD/V38F/V41R/Y60bK/T97aS/L97bR/H99E/
      C122S/Y151L/E175D/Q192T/R217E/K224R

<400> 327
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg Gly Asp Asp Gly Ser Phe Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Lys Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ser Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
```

```
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 328
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      H37G/R37aD/G37bD/V38F/T39H/Y60bK/T97aS/L97bR/H99E/
      C122S/Y151L/E175D/Q192T/R217E/K224R

<400> 328
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg Gly Asp Asp Gly Ser Phe His Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Lys Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ser Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
```

```
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 329
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
H37G/R37aD/G37bD/V38F/T39H/V41R/T97aS/L97bR/H99E/C
122S/Y151L/E175D/Q192T/R217E/K224R

<400> 329

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg Gly Asp Asp Gly Ser Phe His Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ser Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
```

Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210   215   220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 330
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      H37G/R37aD/G37bD/V38F/T39H/V41R/Y60bK/L97bR/H99E/C
      122S/Y151L/E175D/Q192T/R217E/K224R

<400> 330
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg Gly Asp Asp Gly Ser Phe His Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Lys Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Glu His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205

```
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 331
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
H37G/R37aD/G37bD/V38F/T39H/V41R/Y60bK/T97aS/H99E/C
122S/Y151L/E175D/Q192T/R217E/K224R

<400> 331

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg Gly Asp Asp Gly Ser Phe His Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Lys Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ser Leu Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
```

```
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 332
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      H37G/R37aD/G37bD/V38F/T39H/V41R/Y60bK/T97aS/L97bR/
      C122S/Y151L/E175D/Q192T/R217E/K224R

<400> 332
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg Gly Asp Asp Gly Ser Phe His Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Lys Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ser Arg Ala His His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
```

Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 333
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
H37G/R37aD/G37bD/V38F/T39H/V41R/Y60bK/T97aS/L97bR/
H99E/C122S/E175D/Q192T/R217E/K224R

<400> 333
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg Gly Asp Asp Gly Ser Phe His Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Lys Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ser Arg Ala Glu His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
210 215 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 334
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
H37G/R37aD/G37bD/V38F/T39H/V41R/Y60bK/T97aS/L97bR/
H99E/C122S/Y151L/Q192T/R217E/K224R

<400> 334
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg Gly Asp Asp Gly Ser Phe His Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Lys Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ser Arg Ala Glu His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
210 215 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 335
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
H37G/R37aD/G37bD/V38F/T39H/V41R/Y60bK/T97aS/L97bR/
H99E/C122S/Y151L/E175D/R217E/K224R

<400> 335
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg Gly Asp Asp Gly Ser Phe His Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Lys Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ser Arg Ala Glu His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
210 215 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 336
<211> 253

<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
H37G/R37aD/G37bD/V38F/T39H/V41R/Y60bK/T97aS/L97bR/
H99E/C122S/Y151L/E175D/Q192T/K224R

<400> 336
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg Gly His His Gly Ser Phe His Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Lys Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ser Arg Ala Glu His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 337
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
H37G/R37aD/G37bD/V38F/T39H/V41R/Y60bK/T97aS/L97bR/
H99E/C122S/Y151L/E175D/Q192T/R217E

<400> 337
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Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg Gly His His Gly Ser Phe His Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Lys Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ser Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 338
<211> 253
<212> PRT
<213> Artificial Sequence

<220>

<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
H37G/R37aD/V38F/T39H/V41R/Y60bK/L97bR/H99E/C122S/Y
151L/E175D/Q192T/R217E/K224R

<400> 338
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg Gly Asp Gly Gly Ser Phe His Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Lys Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Glu His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210   215   220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 339
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain

H37G/R37aD/V38F/T39H/V41R/Y60bK/T97aS/L97bR/H99E/C
122S/Y151L/E175D/Q192T/R217E

<400> 339
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg Gly Asp Gly Gly Ser Phe His Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Lys Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ser Arg Ala Glu His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 340
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
H37G/R37aD/G37bD/V38F/T39H/V41R/Y60bK/L97bR/H99E/C
122S/Y151L/E175D/Q192T/R217E

<400> 340
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg Gly Asp Asp Gly Ser Phe His Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Lys Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Glu His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 341
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      H37G/R37aD/V38F/T39H/V41R/Y60bK/L97bR/H99E/C122S/Y
      151L/E175D/Q192T/R217E

<400> 341

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg Gly Asp Gly Gly Ser Phe His Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Lys Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 342
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38D/C122S/S190H/G216A

<400> 342

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
```

```
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala His His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
His Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Ala Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 343
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V41L/L97bA/H99Q/C122S

<400> 343

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
```

```
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 344
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain Y40Q/V41L/C122S

<400> 344
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala His His Asn
                85                  90                  95
```

```
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 345
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain Y40Q/V41L/H99Q/C122S

<400> 345
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
```

```
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 346
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain Y40Q/V41L/L97bA/H99Q/C122S/Y149R

<400> 346

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
```

```
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 347
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain R37aE/Y40Q/V41L/L97bA/H99Q/C122S

<400> 347
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Glu Gly Gly Ser Val Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
```

```
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 348
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R37aE/Y40Q/V41L/L97bA/H99Q/C122S/Y149R

<400> 348
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Glu Gly Gly Ser Val Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
```

```
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 349
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
Y40Q/V41L/Y60bE/L97bA/H99Q/C122S/Y149R

<400> 349

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
```

Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 350
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
Y40Q/V41L/Y60bT/T97aE/L97bA/H99Q/C122S/Y149R

<400> 350
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Gln Leu Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Thr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 351
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
Y40Q/V41L/Y60bS/T97aE/L97bA/H99Q/C122S/Y149R

<400> 351
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Gln Leu Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 352
<211> 253

<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain R37aE/Y40Q/V41L/L97bA/C122S

<400> 352
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Glu Gly Gly Ser Val Thr Gln Leu Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala His His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 353
<211> 253
<212> PRT
<213> Artificial Sequence

<220>

<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain Y40Q/V41L/L97bA/C122S/Y149R

<400> 353
```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala His His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 354
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain R37aE/Y40Q/V41L/L97bA/C122S/Y149R

<400> 354

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Glu Gly Gly Ser Val Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala His His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 355
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aE/Y40Q/V41L/Y60bE/L97bA/H99Q/C122S/Y149R

<400> 355

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Glu Gly Gly Ser Val Thr Gln Leu Cys Gly
```

```
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 356
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35K/Y40Q/V41L/Y60bE/L97bA/H99Q/C122S/Y149R

<400> 356
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Lys Arg His Arg Gly Gly Ser Val Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
```

```
Ile Asp Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 357
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aD/Y40Q/V41L/Y60bT/T97aE/L97bA/H99Q/C122S/Y149R

<400> 357

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Asp Gly Gly Ser Val Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Thr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
```

65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 358
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35S/Y40Q/V41L/Y60bT/T97aE/L97bA/H99Q/C122S/Y149R

<400> 358
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Ser Arg His Arg Gly Gly Ser Val Thr Gln Leu Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Thr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
85 90 95

```
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 359
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R37aE/Y40Q/V41L/Y60bS/T97aE/L97bA/H99Q/C122S/Y149R

<400> 359
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Glu Gly Gly Ser Val Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
```

```
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 360
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35V/Y40Q/V41L/Y60bS/T97aE/L97bA/H99Q/C122S/Y149R

<400> 360

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Val Arg His Arg Gly Gly Ser Val Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
```

```
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 361
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R37aD/Y40Q/V41L/Y60bE/L97bA/H99Q/C122S/Y149R

<400> 361
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Asp Gly Gly Ser Val Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
```

```
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 362
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35V/R37aE/V38E/V41L/Y60bS/T97aE/L97bA/H99Q/C122S/
Y149R

<400> 362

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Val Arg His Glu Gly Gly Ser Glu Thr Tyr Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
```

```
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 363
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35V/R37aE/Y40Q/Y60bS/T97aE/L97bA/H99Q/C122S/Y149R

<400> 363

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Val Arg His Glu Gly Gly Ser Val Thr Gln Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
```

```
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 364
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35V/R37aE/V38E/Y40Q/V41L/T97aE/L97bA/H99Q/C122S/Y
149R

<400> 364

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Val Arg His Glu Gly Gly Ser Glu Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
```

```
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 365
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35V/R37aE/V38E/Y40Q/V41L/Y60bS/L97bA/H99Q/C122S/Y
149R

<400> 365

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Val Arg His Glu Gly Gly Ser Glu Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
```

Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 366
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35V/R37aE/V38E/Y40Q/V41L/Y60bS/T97aE/H99Q/C122S/Y
149R

<400> 366
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Val Arg His Glu Gly Gly Ser Glu Thr Gln Leu Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Leu Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 367
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35V/R37aE/V38E/Y40Q/V41L/Y60bS/T97aE/L97bA/C122S/
Y149R

<400> 367
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Val Arg His Glu Gly Gly Ser Glu Thr Gln Leu Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala His His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 368
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35V/R37aE/V38E/Y40Q/V41L/Y60bS/T97aE/L97bA/H99Q/C
122S

<400> 368
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Val Arg His Glu Gly Gly Ser Glu Thr Gln Leu Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 369
<211> 253

<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V41R/L97bR/H99Q/C122S/Y151L/R217V

<400> 369
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 370
<211> 253
<212> PRT
<213> Artificial Sequence

<220>

<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38D/V41R/H99Q/C122S/Y151L/R217V

<400> 370
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 371
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38D/V41R/L97bR/C122S/Y151L/R217V

<400> 371

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala His His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 372
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aE/V38E/Y40Q/V41L/Y60bS/T97aE/L97bA/H99Q/C122S/
Y149R

<400> 372

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
```

```
Ala Ile Tyr Arg Arg His Glu Gly Gly Ser Glu Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 373
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35V/V38E/Y40Q/V41L/Y60bS/T97aE/L97bA/H99Q/C122S/Y
149R

<400> 373

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Val Arg His Arg Gly Gly Ser Glu Thr Gln Leu Cys Gly
            20                  25                  30
```

```
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 374
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35V/R37aE/Y40Q/V41L/Y60bS/T97aE/L97bA/H99Q/C122S/
Y149R

<400> 374

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Val Arg His Glu Gly Gly Ser Val Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
```

```
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 375
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35V/R37aE/V38E/Y40Q/Y60bS/T97aE/L97bA/H99Q/C122S/
Y149R

<400> 375

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Val Arg His Glu Gly Gly Ser Glu Thr Gln Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
```

```
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 376
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain L97bR/H99Q/C122S/Y151L/R217V

<400> 376

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Gln His Asn
                85                  90                  95
```

```
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 377
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38D/H99Q/C122S/Y151L/R217V

<400> 377

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
```

```
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 378
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain V38D/L97bR/C122S/Y151L/R217V

<400> 378
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala His His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
```

```
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 379
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain V38D/L97bR/H99Q/C122S/R217V

<400> 379
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
```

```
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 380
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain L97bR/H99Q/C122S/Y151L/R217V

<400> 380
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
    210                 215                 220
```

Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 381
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain H99Q/C122S/Y151L/R217V

<400> 381
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 382
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V41R/H99Q/C122S/Y151L/R217V

<400> 382
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 383
<211> 253

<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain L97bR/H99Q/C122S/Y151L

<400> 383
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 384
<211> 253
<212> PRT
<213> Artificial Sequence

<220>

<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain L97bR/C122S/Y151L/R217V

<400> 384
```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala His His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 385
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain R37aS/V41R/L97bG/H99Q/C122S/R217V

<400> 385

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Ser Gly Gly Ser Val Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 386
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain R37aS/V41R/L97bG/C122S/R217V

<400> 386
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Ser Gly Gly Ser Val Thr Tyr Arg Cys Gly
            20                  25                  30
```

```
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala His His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 387
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain Y40H/V41Q/L97bG/H99Q/C122S/R217T

<400> 387

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr His Gln Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
```

```
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 388
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain Y40H/V41Q/L97bG/C122S/R217T

<400> 388

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr His Gln Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala His His Asn
                85                  90                  95
```

```
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 389
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain Y40H/V41Q/L97bG/H99Q/C122S

<400> 389
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr His Gln Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
```

```
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 390
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain Y40H/V41T/L97bG/H99Q/C122S/R217T

<400> 390
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr His Thr Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
```

```
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Thr Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 391
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain Y40H/V41T/L97bG/C122S/R217T

<400> 391
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr His Thr Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala His His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
```

```
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Thr Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 392
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain Y40H/V41T/L97bG/H99Q/C122S

<400> 392

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr His Thr Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
```

Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 393
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V41R/L97bG/H99Q/C122S

<400> 393
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 394
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V41Q/L97bG/H99Q/C122S

<400> 394
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Gln Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 395
<211> 253

<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V41T/L97bG/H99Q/C122S

<400> 395
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr Tyr Thr Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 396
<211> 253
<212> PRT
<213> Artificial Sequence

<220>

<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain T39Y/V41R/L97bA/C122S

<400> 396
```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala His His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 397
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain T39Y/V41R/Y60bQ/L97bA/C122S

<400> 397

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala His His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 398
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
T39Y/V41R/D60aP/Y60bQ/L97bA/H99Q/C122S

<400> 398

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Tyr Tyr Arg Cys Gly
```

```
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 399
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain T39Y/V41R/L97bG/H99Q/C122S

<400> 399
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
```

```
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 400
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain T39H/V41R/L97bG/H99Q/C122S

<400> 400

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val His Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
```

```
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 401
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain T39W/V41R/L97bG/H99Q/C122S

<400> 401

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Trp Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
```

```
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 402
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain T39Y/V41R/Y60bQ/L97bG/H99Q/C122S

<400> 402
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
```

```
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 403
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain T39Y/V41R/Y60bP/L97bA/H99Q/C122S

<400> 403
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
```

```
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 404
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain T39Y/V41R/Y60bP/L97bG/H99Q/C122S

<400> 404

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
```

```
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 405
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41S/A96_T97adelinsERG/A98_H99del/C122S/E175A

<400> 405

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Ser Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Glu Arg Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Ala Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
```

Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 406
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41S/A96D/D97E/T97aG/A98_H99del/C122S/E175S

<400> 406
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Ser Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Asp Glu Gly Leu His Asn Asp Ile
85 90 95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
100 105 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
115 120 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
130 135 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145 150 155 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Ser Val Thr
165 170 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
180 185 190
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
195 200 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys Asp
210 215 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225 230 235 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 407
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41S/A96E/D97E/T97aG/A98_H99del/C122S/E175K

<400> 407
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Ser Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Glu Glu Gly Leu His Asn Asp Ile
85 90 95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
100 105 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
115 120 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
130 135 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145 150 155 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Lys Val Thr
165 170 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
180 185 190
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
195 200 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys Asp
210 215 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225 230 235 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 408
<211> 251

<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41A/A96_T97adelinsERG/A98_H99del/C122S/E175N

<400> 408

Ile	Ile	Gly	Gly	Glu	Phe	Thr	Thr	Ile	Glu	Asn	Gln	Pro	Trp	Phe	Ala
1				5				10						15	
Ala	Ile	Tyr	Arg	Arg	His	Arg	Gly	Gly	Ser	Asp	Thr	Tyr	Ala	Cys	Gly
			20					25					30		
Gly	Ser	Leu	Ile	Ser	Pro	Cys	Trp	Val	Ile	Ser	Ala	Thr	His	Cys	Phe
		35					40					45			
Ile	Asp	Tyr	Pro	Lys	Lys	Glu	Asp	Tyr	Ile	Val	Tyr	Leu	Gly	Arg	Ser
	50					55					60				
Arg	Leu	Asn	Ser	Asn	Thr	Gln	Gly	Glu	Met	Lys	Phe	Glu	Val	Glu	Asn
65					70					75					80
Leu	Ile	Leu	His	Lys	Asp	Tyr	Ser	Glu	Arg	Gly	Leu	His	Asn	Asp	Ile
				85					90					95	
Ala	Leu	Leu	Lys	Ile	Arg	Ser	Lys	Glu	Gly	Arg	Cys	Ala	Gln	Pro	Ser
			100					105					110		
Arg	Thr	Ile	Gln	Thr	Ile	Ser	Leu	Pro	Ser	Met	Tyr	Asn	Asp	Pro	Gln
		115					120					125			
Phe	Gly	Thr	Ser	Cys	Glu	Ile	Thr	Gly	Phe	Gly	Lys	Glu	Asn	Ser	Thr
	130					135					140				
Asp	Tyr	Leu	Tyr	Pro	Glu	Gln	Leu	Lys	Met	Thr	Val	Val	Lys	Leu	Ile
145					150					155					160
Ser	His	Arg	Glu	Cys	Gln	Gln	Pro	His	Tyr	Tyr	Gly	Ser	Asn	Val	Thr
				165					170					175	
Thr	Lys	Met	Leu	Cys	Ala	Ala	Asp	Pro	Gln	Trp	Lys	Thr	Asp	Ser	Cys
			180					185					190		
Gln	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Cys	Ser	Leu	Gln	Gly	Arg	Met
		195					200					205			
Thr	Leu	Thr	Gly	Ile	Val	Ser	Trp	Gly	Arg	Gly	Cys	Ala	Leu	Lys	Asp
	210					215					220				
Lys	Pro	Gly	Val	Tyr	Thr	Arg	Val	Ser	His	Phe	Leu	Pro	Trp	Ile	Arg
225					230					235					240
Ser	His	Thr	Lys	Glu	Glu	Asn	Gly	Leu	Ala	Leu					
				245					250						

<210> 409
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41T/A96E/D97E/T97aG/A98_H99del/C122S/E175K/R
217H

<400> 409
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Thr Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Glu Glu Gly Leu His Asn Asp Ile
85 90 95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
100 105 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
115 120 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
130 135 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145 150 155 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Lys Val Thr
165 170 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
180 185 190
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
195 200 205
Thr Leu Thr Gly Ile Val Ser Trp Gly His Gly Cys Ala Leu Lys Asp
210 215 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225 230 235 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 410
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)

protease domain
R35K/V38D/T39S/Y40F/V41M/D60aN/A96D/D97L/A98K/T97a
del/H99L/L97bdel/C122S/Y151L

<400> 410

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Lys Arg His Arg Gly Gly Ser Asp Ser Phe Met Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asn Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Asp Leu Lys Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 411
<211> 252
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41R/A96E/D97G/T97adelinsSG/A98_H99del/C122S

<400> 411
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Glu Gly Ser Gly Leu His Asn Asp
                85   90   95
Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro
            100   105   110
Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro
        115   120   125
Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser
    130   135   140
Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu
145   150   155   160
Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val
                165   170   175
Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser
            180   185   190
Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg
        195   200   205
Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys
    210   215   220
Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile
225   230   235   240
Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 412
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain V38D/L97bG/H99P/C122S/R217V/K224Q

<400> 412
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15

```
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Pro His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
    210                 215                 220
Lys Asp Gln Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 413
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/A96G/D97R/A98G/T97adel/H99I/L97bdel/C122S

<400> 413
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
```

```
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Gly Arg Gly Ile His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 414
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/A96E/D97E/T97aG/A98_H99del/L97bM/C122S

<400> 414

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
```

```
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Glu Glu Gly Met His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 415
<211> 252
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41R/A96D/D97G/T97aN/A98G/L97bdel/H99L/C122S/
R217F

<400> 415

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
```

```
Leu Ile Leu His Lys Asp Tyr Ser Asp Gly Asn Gly Leu His Asn Asp
                85                  90                  95
Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro
            100                 105                 110
Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro
        115                 120                 125
Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser
    130                 135                 140
Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu
145                 150                 155                 160
Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val
                165                 170                 175
Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser
            180                 185                 190
Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg
        195                 200                 205
Met Thr Leu Thr Gly Ile Val Ser Trp Gly Phe Gly Cys Ala Leu Lys
    210                 215                 220
Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile
225                 230                 235                 240
Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 416
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41Q/A96E/D97E/T97aG/A98_H99del/C122S/R217H

<400> 416

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Gln Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Glu Glu Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
```

```
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly His Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 417
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41R/A96D/D97G/A98G/T97adel/H99L/L97bdel/C122
S/R217D

<400> 417

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Asp Gly Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
```

```
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 418
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/V41K/A96D/D97E/T97aG/A98_H99del/C122S/R217K/K
      224N

<400> 418
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Lys Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Asp Glu Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
```

```
    130                 135                 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Lys Gly Cys Ala Leu Lys Asp
    210                 215                 220
Asn Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 419
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R36H/V38D/V41M/D97E/A98G/T97adel/H99L/L97bdel/C122
      S/R217D

<400> 419
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Tyr Met Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
```

```
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 420
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/V41H/A96D/D97E/T97aG/A98_H99del/C122S/R217del
      insF

<400> 420
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr His Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Asp Glu Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
```

```
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Phe Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 421
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/D97E/T97aG/A98_H99del/C122S/E175G/R217H

<400> 421
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Gly Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
```

```
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly His Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 422
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain A32S/V38D/H99E/C122S/K224A

<400> 422
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ser Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
```

Lys Asp Ala Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 423
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38D/L97bA/H99Q/C122S

<400> 423
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 424
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36S/V38D/L97bR/H99E/C122S/R217D/K224R

<400> 424
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Ser His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Glu His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu
210 215 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 425

<211> 252
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41Q/A96N/D97G/T97aI/A98G/L97bdel/H99L/C122S

<400> 425

Ile	Ile	Gly	Gly	Glu	Phe	Thr	Thr	Ile	Glu	Asn	Gln	Pro	Trp	Phe	Ala
1			5					10						15	
Ala	Ile	Tyr	Arg	Arg	His	Arg	Gly	Gly	Ser	Asp	Thr	Tyr	Gln	Cys	Gly
		20					25					30			
Gly	Ser	Leu	Ile	Ser	Pro	Cys	Trp	Val	Ile	Ser	Ala	Thr	His	Cys	Phe
	35					40					45				
Ile	Asp	Tyr	Pro	Lys	Lys	Glu	Asp	Tyr	Ile	Val	Tyr	Leu	Gly	Arg	Ser
	50				55					60					
Arg	Leu	Asn	Ser	Asn	Thr	Gln	Gly	Glu	Met	Lys	Phe	Glu	Val	Glu	Asn
65				70					75					80	
Leu	Ile	Leu	His	Lys	Asp	Tyr	Ser	Asn	Gly	Ile	Gly	Leu	His	Asn	Asp
			85					90					95		
Ile	Ala	Leu	Leu	Lys	Ile	Arg	Ser	Lys	Glu	Gly	Arg	Cys	Ala	Gln	Pro
		100					105					110			
Ser	Arg	Thr	Ile	Gln	Thr	Ile	Ser	Leu	Pro	Ser	Met	Tyr	Asn	Asp	Pro
	115					120					125				
Gln	Phe	Gly	Thr	Ser	Cys	Glu	Ile	Thr	Gly	Phe	Gly	Lys	Glu	Asn	Ser
	130				135					140					
Thr	Asp	Tyr	Leu	Tyr	Pro	Glu	Gln	Leu	Lys	Met	Thr	Val	Val	Lys	Leu
145				150					155					160	
Ile	Ser	His	Arg	Glu	Cys	Gln	Gln	Pro	His	Tyr	Tyr	Gly	Ser	Glu	Val
			165					170					175		
Thr	Thr	Lys	Met	Leu	Cys	Ala	Ala	Asp	Pro	Gln	Trp	Lys	Thr	Asp	Ser
		180					185					190			
Cys	Gln	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Cys	Ser	Leu	Gln	Gly	Arg
	195					200					205				
Met	Thr	Leu	Thr	Gly	Ile	Val	Ser	Trp	Gly	Arg	Gly	Cys	Ala	Leu	Lys
	210				215					220					
Asp	Lys	Pro	Gly	Val	Tyr	Thr	Arg	Val	Ser	His	Phe	Leu	Pro	Trp	Ile
225				230					235					240	
Arg	Ser	His	Thr	Lys	Glu	Glu	Asn	Gly	Leu	Ala	Leu				
			245					250							

<210> 426
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35S/V38D/V41T/A96D/D97G/A98G/T97adel/H99L/L97bdel
/C122S

<400> 426
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Ser Arg His Arg Gly Gly Ser Asp Thr Tyr Thr Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Asp Gly Gly Leu His Asn Asp Ile
85 90 95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
100 105 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
115 120 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
130 135 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145 150 155 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
165 170 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
180 185 190
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
195 200 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys Asp
210 215 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225 230 235 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 427
<211> 251
<212> PRT
<213> Artificial Sequence

<220>

<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41K/A96K/D97E/A98G/T97adel/H99L/L97bdel/C122
S

<400> 427
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Lys Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Lys Glu Gly Leu His Asn Asp Ile
                85   90   95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100   105   110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115   120   125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130   135   140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145   150   155   160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165   170   175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180   185   190
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195   200   205
Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys Asp
    210   215   220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225   230   235   240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 428
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain

R36H/V38D/V41S/A96E/D97R/A98G/T97adel/H99L/L97bdel
/C122S/K224R

<400> 428
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Tyr Ser Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Glu Arg Gly Leu His Asn Asp Ile
                85   90   95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100   105   110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115   120   125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130   135   140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145   150   155   160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165   170   175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180   185   190
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195   200   205
Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys Asp
    210   215   220
Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225   230   235   240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 429
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41R/A96D/D97G/A98G/T97adel/H99L/L97bdel/C122
S/Y151L/Q192D/R217D

<400> 429
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Asp Gly Gly Leu His Asn Asp Ile
                85   90   95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100   105   110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115   120   125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130   135   140
Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145   150   155   160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165   170   175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180   185   190
Asp Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195   200   205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210   215   220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225   230   235   240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 430
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/V41R/A96D/D97G/A98G/T97adel/H99L/L97bdel/C122
      S/Y151M/Q192E/R217D

<400> 430

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Asp Gly Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Met Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Glu Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 431
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41R/A96D/D97G/A98G/T97adel/H99L/L97bdel/C122
S/Y151K/Q192E/R217D

<400> 431

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
```

```
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Asp Gly Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Lys Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Glu Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 432
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36H/V38D/V41R/A96D/D97G/T97adel/A98G/L97bdel/H99L
/C122S/Y151F/Q192D/R217D

<400> 432

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
```

```
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Asp Gly Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Phe Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Asp Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 433
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41R/A96D/D97G/A98G/T97adel/H99L/L97bdel/C122
S/Y151W/Q192M/R217D

<400> 433

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
```

```
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Asp Gly Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Trp Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Met Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 434
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aH/V38D/V41R/A96D/D97G/A98G/T97adel/H99L/L97bde
l/C122S/Y151L/Q192G/R217D

<400> 434

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His His Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
```

```
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Asp Gly Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Gly Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 435
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/Y40P/V41R/A96D/D97G/A98G/T97adel/H99L/L97bdel
/C122S/Q192L/R217D

<400> 435

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Pro Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
```

```
Leu Ile Leu His Lys Asp Tyr Ser Asp Gly Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Leu Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 436
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41R/A96D/D97G/A98G/T97adel/H99L/L97bdel/C122
S/Y151L/Q192E/R217D

<400> 436

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Asp Gly Gly Leu His Asn Asp Ile
                85                  90                  95
```

```
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Glu Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 437
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/V41R/A96D/D97G/A98G/T97adel/H99L/L97bdel/C122
      S/Y151N/Q192M/R217D

<400> 437
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Asp Gly Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
```

```
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Asn Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Met Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 438
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36H/V38D/Y40F/V41R/D97E/A98G/T97adel/H99L/L97bdel
/C122S/Y151L/Q192D/R217D

<400> 438

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
```

```
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Asp Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 439
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R36H/V38D/Y40H/V41K/D97E/A98G/T97adel/H99L/L97bdel
      /C122S/Y151K/Q192V/R217D

<400> 439
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr His Lys Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
```

```
Asp Tyr Leu Lys Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Val Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 440
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R36H/V38D/Y40L/V41K/D97E/A98G/T97adel/H99L/L97bdel
      /C122S/Y151R/Q192L/R217D

<400> 440
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Leu Lys Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Arg Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
```

```
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Leu Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 441
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36H/V38D/Y40V/V41K/D97E/A98G/T97adel/H99L/L97bdel
/C122S/Y151F/Q192F/R217D

<400> 441

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Val Lys Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Phe Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
```

```
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Phe Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 442
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36H/V38D/D97E/A98G/T97adel/H99L/L97bdel/C122S/Y15
1K/Q192E/R217D

<400> 442

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Lys Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
```

Glu Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195   200   205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210   215   220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225   230   235   240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 443
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R36H/V38D/Y40L/V41K/D97E/A98G/T97adel/H99L/L97bdel
      /C122S/Y151K/Q192E/R217D

<400> 443
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Leu Lys Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
                85   90   95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100   105   110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115   120   125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130   135   140
Asp Tyr Leu Lys Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145   150   155   160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165   170   175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180   185   190
Glu Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195   200   205

Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210   215   220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225   230   235   240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 444
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R36H/V38D/Y40F/V41R/D97E/A98G/T97adel/H99L/L97bdel
      /C122S/Y151M/Q192D/R217D

<400> 444
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Phe Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
                85   90   95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100   105   110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115   120   125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130   135   140
Asp Tyr Leu Met Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145   150   155   160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165   170   175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180   185   190
Asp Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195   200   205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210   215   220

Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225   230   235   240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 445
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R36H/V38D/Y40L/V41K/D97E/A98G/T97adel/H99L/L97bdel
      /C122S/Y151L/Q192T/R217D

<400> 445
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Leu Lys Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
                85   90   95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100   105   110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115   120   125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130   135   140
Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145   150   155   160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165   170   175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180   185   190
Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195   200   205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210   215   220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225   230   235   240

Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 446
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36H/V38D/Y40F/V41R/D97E/A98G/T97adel/H99L/L97bdel
/C122S/Y151L/Q192E/R217D

<400> 446
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Phe Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
85 90 95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
100 105 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
115 120 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
130 135 140
Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145 150 155 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
165 170 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
180 185 190
Glu Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
195 200 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
210 215 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225 230 235 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 447
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36H/V38D/V41R/D97E/A98G/T97adel/H99L/L97bdel/C122
S/Y151L/Q192G/R217D

<400> 447
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
85 90 95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
100 105 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
115 120 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
130 135 140
Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145 150 155 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
165 170 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
180 185 190
Gly Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
195 200 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
210 215 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225 230 235 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 448
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36H/V38D/Y40I/V41K/D97E/A98G/T97adel/H99L/L97bdel
/C122S/Q192A/R217D

<400> 448
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Ile Lys Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
85 90 95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
100 105 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
115 120 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
130 135 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145 150 155 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
165 170 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
180 185 190
Ala Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
195 200 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
210 215 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225 230 235 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 449
<211> 251

<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36H/V38D/V41K/D97E/A98G/T97adel/H99L/L97bdel/C122
S/Y151K/Q192E/R217D

<400> 449
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Tyr Lys Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
85 90 95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
100 105 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
115 120 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
130 135 140
Asp Tyr Leu Lys Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145 150 155 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
165 170 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
180 185 190
Glu Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
195 200 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
210 215 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225 230 235 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 450
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36H/V38D/Y40L/V41R/D97E/A98G/T97adel/H99L/L97bdel
/C122S/Y151L/Q192D/R217D

<400> 450
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Leu Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
85 90 95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
100 105 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
115 120 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
130 135 140
Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145 150 155 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
165 170 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
180 185 190
Asp Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
195 200 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
210 215 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225 230 235 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 451
<211> 251
<212> PRT
<213> Artificial Sequence

<220>

<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36H/V38D/Y40L/V41R/D97E/A98G/T97adel/H99L/L97bdel
/C122S/Y151M/Q192T/R217D

<400> 451
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Leu Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
85 90 95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
100 105 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
115 120 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
130 135 140
Asp Tyr Leu Met Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145 150 155 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
165 170 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
180 185 190
Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
195 200 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
210 215 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225 230 235 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 452
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain

R36H/V38D/Y40L/V41R/D97E/A98G/T97adel/H99L/L97bdel
/C122S/Y151L/Q192R/R217D

<400> 452
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Leu Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
                85   90   95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100   105   110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115   120   125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130   135   140
Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145   150   155   160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165   170   175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180   185   190
Arg Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195   200   205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210   215   220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225   230   235   240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 453
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36H/V38D/Y40F/V41K/D97E/A98G/T97adel/H99L/L97bdel
/C122S/Y151R/Q192E/R217D

<400> 453
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Phe Lys Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
                85   90   95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100   105   110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115   120   125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130   135   140
Asp Tyr Leu Arg Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145   150   155   160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165   170   175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180   185   190
Glu Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195   200   205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210   215   220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225   230   235   240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 454
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R36H/V38D/Y40L/V41R/D97E/A98G/T97adel/H99L/L97bdel
      /C122S/Y151N/Q192V/R217D

<400> 454

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Asn Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Val Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 455
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36H/V38D/Y40L/V41R/D97E/A98G/T97adel/H99L/L97bdel
/C122S/Y151N/Q192D/R217D

<400> 455

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
```

```
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Asn Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Asp Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 456
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36H/V38D/V41R/D97E/A98G/T97adel/H99L/L97bdel/C122
S/Y151K/Q192E/R217D

<400> 456

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
```

```
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Lys Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Glu Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 457
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36H/V38D/Y40F/V41R/D97E/A98G/T97adel/H99L/L97bdel
/C122S/Y151K/Q192E/R217D

<400> 457

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
```

```
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Lys Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Glu Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 458
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36H/V38D/Y40I/V41A/D97E/A98G/T97adel/H99L/L97bdel
/C122S/Y151M/Q192L/R217D

<400> 458

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Ile Ala Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
```

```
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Met Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Leu Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 459
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36H/V38D/Y40H/V41M/D97E/A98G/T97adel/H99L/L97bdel
/C122S/R217D

<400> 459

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr His Met Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
```

```
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 460
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/V38D/V41K/D97E/T97adel/A98G/L97bdel/H99L
/C122S/R217D

<400> 460

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Tyr Lys Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
                85                  90                  95
```

```
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 461
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R36H/V38D/V41K/D97E/A98G/T97adel/H99L/L97bdel/C122
      S/V213A/R217D

<400> 461
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Tyr Lys Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
```

```
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Ala Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 462
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36H/V38D/V41M/F59I/D97E/T97adel/A98G/L97bdel/H99L
/C122S/R217D

<400> 462

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Tyr Met Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Ile
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
```

```
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 463
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R36H/V38D/V41M/A55S/D97E/A98G/T97adel/H99L/L97bdel
      /C122S/R217D

<400> 463
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Tyr Met Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ser Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Glu Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
```

```
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 464
<211> 252
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36H/V38D/V41R/A96D/D97G/T97aN/A98G/L97bdel/H99L/C
122S/G193R/R217F

<400> 464

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Asp Gly Asn Gly Leu His Asn Asp
                85                  90                  95
Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro
            100                 105                 110
Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro
        115                 120                 125
Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser
    130                 135                 140
Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu
145                 150                 155                 160
```

```
Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val
                165                 170                 175
Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser
            180                 185                 190
Cys Gln Arg Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg
        195                 200                 205
Met Thr Leu Thr Gly Ile Val Ser Trp Gly Phe Gly Cys Ala Leu Lys
    210                 215                 220
Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile
225                 230                 235                 240
Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 465
<211> 252
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R36H/V38D/V41R/A96D/D97G/T97aN/A98G/L97bdel/H99L/C
      122S/Q192R/R217F

<400> 465
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Asp Gly Asn Gly Leu His Asn Asp
                85                  90                  95
Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro
            100                 105                 110
Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro
        115                 120                 125
Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser
    130                 135                 140
Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu
145                 150                 155                 160
Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val
                165                 170                 175
```

```
Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser
            180                 185                 190
Cys Arg Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg
        195                 200                 205
Met Thr Leu Thr Gly Ile Val Ser Trp Gly Phe Gly Cys Ala Leu Lys
    210                 215                 220
Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile
225                 230                 235                 240
Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 466
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36H/G37cD/V38D/V41R/A96D/D97G/A98G/T97adel/H99L/L
97bdel/C122S/M157T/R217D

<400> 466

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Asp Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Asp Gly Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Thr Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
```

```
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 467
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/V41R/A96D/D97G/A98G/T97adel/H99L/L97bdel/C122
      S/Q192R/R217D

<400> 467
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Asp Gly Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Arg Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
```

Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
210 215 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225 230 235 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 468
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F21S/R36H/V38D/V41R/A96D/D97G/A98G/T97adel/H99L/L9
7bdel/C122S/E175D/R217D

<400> 468
Ile Ile Gly Gly Glu Ser Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Asp Gly Gly Leu His Asn Asp Ile
85 90 95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
100 105 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
115 120 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
130 135 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145 150 155 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp Val Thr
165 170 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
180 185 190
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
195 200 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
210 215 220

```
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 469
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R36H/V38D/V41R/A96D/D97E/A98G/T97adel/H99L/L97bdel
      /C122S/T178S/R217D

<400> 469
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Asp Glu Gly Leu His Asn Asp Ile
                85                  90                  95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            100                 105                 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
        115                 120                 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    130                 135                 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145                 150                 155                 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                165                 170                 175
Ser Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            180                 185                 190
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        195                 200                 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
    210                 215                 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225                 230                 235                 240
```

Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 470
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36H/V38D/V41R/A96D/D97E/A98G/T97adel/H99L/L97bdel
/C122S/G193R/R217D

<400> 470
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Asp Glu Gly Leu His Asn Asp Ile
85 90 95
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
100 105 110
Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln
115 120 125
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
130 135 140
Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
145 150 155 160
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
165 170 175
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
180 185 190
Gln Arg Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
195 200 205
Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu Lys Asp
210 215 220
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
225 230 235 240
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 471
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/V38D/V41R/L97bA/H99Q/C122S/M157E

<400> 471
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Glu Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 472

<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/V38D/V41R/L97bA/H99Q/C122S/Y151F/M157K/Q192W

<400> 472

Ile	Ile	Gly	Gly	Glu	Phe	Thr	Thr	Ile	Glu	Asn	Gln	Pro	Trp	His	Ala
1			5					10						15	
Ala	Ile	Tyr	Arg	Arg	His	Arg	Gly	Gly	Ser	Asp	Thr	Tyr	Arg	Cys	Gly
		20					25					30			
Gly	Ser	Leu	Ile	Ser	Pro	Cys	Trp	Val	Ile	Ser	Ala	Thr	His	Cys	Phe
	35					40					45				
Ile	Asp	Tyr	Pro	Lys	Lys	Glu	Asp	Tyr	Ile	Val	Tyr	Leu	Gly	Arg	Ser
	50				55					60					
Arg	Leu	Asn	Ser	Asn	Thr	Gln	Gly	Glu	Met	Lys	Phe	Glu	Val	Glu	Asn
65				70					75					80	
Leu	Ile	Leu	His	Lys	Asp	Tyr	Ser	Ala	Asp	Thr	Ala	Ala	Gln	His	Asn
			85					90					95		
Asp	Ile	Ala	Leu	Leu	Lys	Ile	Arg	Ser	Lys	Glu	Gly	Arg	Cys	Ala	Gln
		100					105					110			
Pro	Ser	Arg	Thr	Ile	Gln	Thr	Ile	Ser	Leu	Pro	Ser	Met	Tyr	Asn	Asp
	115					120					125				
Pro	Gln	Phe	Gly	Thr	Ser	Cys	Glu	Ile	Thr	Gly	Phe	Gly	Lys	Glu	Asn
	130				135					140					
Ser	Thr	Asp	Tyr	Leu	Phe	Pro	Glu	Gln	Leu	Lys	Lys	Thr	Val	Val	Lys
145				150					155					160	
Leu	Ile	Ser	His	Arg	Glu	Cys	Gln	Gln	Pro	His	Tyr	Tyr	Gly	Ser	Glu
			165					170					175		
Val	Thr	Thr	Lys	Met	Leu	Cys	Ala	Ala	Asp	Pro	Gln	Trp	Lys	Thr	Asp
		180					185					190			
Ser	Cys	Trp	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Cys	Ser	Leu	Gln	Gly
	195					200					205				
Arg	Met	Thr	Leu	Thr	Gly	Ile	Val	Ser	Trp	Gly	Arg	Gly	Cys	Ala	Leu
	210				215					220					
Lys	Asp	Lys	Pro	Gly	Val	Tyr	Thr	Arg	Val	Ser	His	Phe	Leu	Pro	Trp
225				230					235					240	
Ile	Arg	Ser	His	Thr	Lys	Glu	Glu	Asn	Gly	Leu	Ala	Leu			
			245					250							

<210> 473
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/V38D/Y40H/V41A/L97bA/H99Q/C122S/M157R

<400> 473
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Ala Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Arg Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 474
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)

protease domain
F30H/V38D/Y40F/V41R/L97bA/H99Q/C122S/Y151R/M157K

<400> 474
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Phe Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Arg Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 475
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/V38D/Y40F/V41R/L97bA/H99Q/C122S/Y151L/M157F

<400> 475
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Phe Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Phe Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 476
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/V38D/Y40H/V41N/L97bA/H99Q/C122S

<400> 476
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15

```
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Asn Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 477
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30S/V38D/V41R/L97bA/H99Q/C122S/Y151L/M157K

<400> 477
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Ser Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
```

```
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 478
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/V38D/Y40L/V41R/L97bA/H99Q/C122S/M157R

<400> 478

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
```

```
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Arg Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 479
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/V38D/Y40F/V41R/L97bA/H99Q/C122S/Y151M/M157Y/Q192A

<400> 479

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
```

```
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Met Pro Glu Gln Leu Lys Tyr Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Ala Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 480
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/V38D/Y40L/V41R/L97bA/H99Q/C122S/Y151L/M157T/Q
192L

<400> 480

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
```

```
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Thr Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Leu Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 481
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30H/V38D/V41R/L97bA/H99Q/C122S/Y151L/M157S

<400> 481
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
```

```
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Ser Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 482
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/V38D/Y40H/V41K/L97bA/H99Q/C122S/Y151R/M157R

<400> 482

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Lys Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
```

```
Ser Thr Asp Tyr Leu Arg Pro Glu Gln Leu Lys Arg Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 483
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/V38D/Y40M/V41R/L97bA/H99Q/C122S

<400> 483
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Met Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
```

```
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 484
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30H/V38D/V41R/L97bA/H99Q/C122S/Y151L/M157K

<400> 484
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
```

```
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 485
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/V38D/Y40H/V41R/L97bA/H99Q/C122S

<400> 485
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
```

```
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 486
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/V38D/V41R/A96G/L97bA/H99Q/C122S/Y151L/M157K

<400> 486

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Gly Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
```

Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 487
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/G37bD/V38D/T39H/V41R/L97bA/H99Q/R110dH/C122S/
Y151L/M157K/S240I

<400> 487
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Asp Gly Ser Asp His Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly His Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ile His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 488
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/V38D/V41R/L97bA/H99Q/C122S/Y149N/Y151L/M157K/
R239H

<400> 488
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Asn Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile His Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 489
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/A32E/V38D/Y40H/V41R/L97bA/H99Q/C122S/M157K

<400> 489
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Glu Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 490
<211> 253
<212> PRT

<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R37aH/V38D/Y40L/V41R/L97bA/H99Q/R110dH/C122S/
M157K/V160I

<400> 490

Ile	Ile	Gly	Gly	Glu	Phe	Thr	Thr	Ile	Glu	Asn	Gln	Pro	Trp	Tyr	Ala
1			5					10						15	
Ala	Ile	Tyr	Arg	Arg	His	His	Gly	Gly	Ser	Asp	Thr	Leu	Arg	Cys	Gly
		20					25					30			
Gly	Ser	Leu	Ile	Ser	Pro	Cys	Trp	Val	Ile	Ser	Ala	Thr	His	Cys	Phe
	35					40					45				
Ile	Asp	Tyr	Pro	Lys	Lys	Glu	Asp	Tyr	Ile	Val	Tyr	Leu	Gly	Arg	Ser
50					55					60					
Arg	Leu	Asn	Ser	Asn	Thr	Gln	Gly	Glu	Met	Lys	Phe	Glu	Val	Glu	Asn
65				70					75					80	
Leu	Ile	Leu	His	Lys	Asp	Tyr	Ser	Ala	Asp	Thr	Ala	Ala	Gln	His	Asn
			85					90					95		
Asp	Ile	Ala	Leu	Leu	Lys	Ile	Arg	Ser	Lys	Glu	Gly	His	Cys	Ala	Gln
		100					105					110			
Pro	Ser	Arg	Thr	Ile	Gln	Thr	Ile	Ser	Leu	Pro	Ser	Met	Tyr	Asn	Asp
	115					120					125				
Pro	Gln	Phe	Gly	Thr	Ser	Cys	Glu	Ile	Thr	Gly	Phe	Gly	Lys	Glu	Asn
130					135					140					
Ser	Thr	Asp	Tyr	Leu	Tyr	Pro	Glu	Gln	Leu	Lys	Lys	Thr	Val	Ile	Lys
145				150					155					160	
Leu	Ile	Ser	His	Arg	Glu	Cys	Gln	Gln	Pro	His	Tyr	Tyr	Gly	Ser	Glu
			165					170					175		
Val	Thr	Thr	Lys	Met	Leu	Cys	Ala	Ala	Asp	Pro	Gln	Trp	Lys	Thr	Asp
		180					185					190			
Ser	Cys	Gln	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Cys	Ser	Leu	Gln	Gly
	195					200					205				
Arg	Met	Thr	Leu	Thr	Gly	Ile	Val	Ser	Trp	Gly	Arg	Gly	Cys	Ala	Leu
210					215					220					
Lys	Asp	Lys	Pro	Gly	Val	Tyr	Thr	Arg	Val	Ser	His	Phe	Leu	Pro	Trp
225				230					235					240	
Ile	Arg	Ser	His	Thr	Lys	Glu	Glu	Asn	Gly	Leu	Ala	Leu			
			245					250							

<210> 491
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/A32E/Y34N/V38D/Y40H/V41R/L97bA/H99Q/C122S/M15
7K

<400> 491
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Glu Ile Asn Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 492
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)

protease domain
F30Y/R37aH/V38D/Y40L/V41R/L97bA/H99Q/C122S/M157K

<400> 492
```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His His Gly Gly Ser Asp Thr Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 493
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/V38D/V41R/L97bA/H99Q/C122S/M157K

<400> 493
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 494
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35H/V38D/Y40H/V41R/T56A/L97bA/H99Q/C122S/M15
      7K

<400> 494
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala

```
 1               5                  10                  15
Ala Ile Tyr His Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Ala His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 495
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/V38D/Y40H/V41R/L97bA/H99Q/C122S/M157K/T158A

<400> 495

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
```

```
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Ala Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 496
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/V38E/Y40H/V41R/T56A/L97bA/H99Q/C122S/M157K/K2
43M

<400> 496

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Ala His Cys Phe
        35                  40                  45
```

```
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Met Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 497
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/Y34N/V38D/Y40H/V41R/Y94F/S95R/L97bA/H99Q/C122
S/M157K/T242I

<400> 497

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Asn Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
```

```
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Phe Arg Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Ile Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 498
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/V38E/Y40H/V41R/T97aI/L97bA/H99Q/C122S/M1
57K

<400> 498

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Glu Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
```

```
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 499
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35H/V38D/T39S/Y40H/V41R/S75P/L97bA/H99Q/C122
S/M157K/I163M/Q204H/K243E

<400> 499

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr His Arg His Arg Gly Gly Ser Asp Ser His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Pro Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
```

```
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Met Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu His Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Glu Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 500
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35H/V38D/T39S/Y40L/V41R/L97bA/H99Q/C122S/T14
      7S/M157K

<400> 500
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr His Arg His Arg Gly Gly Ser Asp Ser Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
```

```
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Ser Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 501
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R36S/V38H/Y40L/V41R/N76K/L97bA/H99Q/C122S/M15
      7K

<400> 501
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Ser His Arg Gly Gly Ser His Thr Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Lys Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
```

```
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 502
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30H/V38D/V41R/L73Q/L97bA/H99Q/E110bD/C122S/Y149N/
      Y151L/M157K

<400> 502
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Gln Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Asp Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
```

Ser Thr Asp Asn Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 503
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/R36L/V38E/V41R/K82R/L97bA/H99Q/C122S/Y151L/M1
57K

<400> 503
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
1 5 10 15
Ala Ile Tyr Arg Leu His Arg Gly Gly Ser Glu Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Arg Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160

```
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 504
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30H/R35H/V38D/V41R/K61E/L97bA/H99Q/C122S/Y151L/M1
      57K/R206H

<400> 504
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr His Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Glu Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
```

```
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
His Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 505
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      I17V/F30H/V38D/V41R/L97bA/H99Q/C122S/Y151L/M157K

<400> 505
Ile Val Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
```

```
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 506
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/R35S/V38E/V41R/Y60bH/L97bA/H99Q/C122S/Y151L/M
157K

<400> 506

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Ser Arg His Arg Gly Gly Ser Glu Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp His Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
```

```
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 507
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/R36H/V38D/V41R/T56A/L97bA/H99Q/C122S/Y151L/M1
57K

<400> 507

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Ala His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
```

225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 508
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/R35Q/H37T/V38D/V41R/L97bA/H99Q/C122S/Y149I/Y1
51L/M157K/R217D

<400> 508
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
1 5 10 15
Ala Ile Tyr Gln Arg Thr Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Ile Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu

245 250

<210> 509
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/R35Q/H37W/V38D/V41R/D60aE/Y60bS/L97bA/H99Q/C1
22S/Y149L/Y151L/M157K

<400> 509
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
1 5 10 15
Ala Ile Tyr Gln Arg Trp Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Glu Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Leu Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 510
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/R35Q/H37Q/V38D/V41R/A96D/L97bA/H99Q/C122S/Y14
9L/Y151L/M157K/R217D

<400> 510
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
1 5 10 15
Ala Ile Tyr Gln Arg Gln Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Asp Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Leu Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 511

<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/R35H/H37I/V38D/V41R/L97bA/H99Q/C122S/Y149W/Y1
51L/M157K/R217S

<400> 511
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
1 5 10 15
Ala Ile Tyr His Arg Ile Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Trp Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Ser Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 512
<211> 253
<212> PRT

<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/R35T/H37M/V38D/V41R/D60aS/Y60bT/L97bA/H99Q/A1
12V/C122S/Y151L/M157K/R217T

<400> 512

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Thr Arg Met Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Ser Thr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Val Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Thr Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 513
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/R35Q/H37W/V38D/V41R/L97bA/H99Q/C122S/Y151L/M157K

<400> 513
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
1 5 10 15
Ala Ile Tyr Gln Arg Trp Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 514
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)

protease domain
F30H/R35L/H37D/V38D/V41R/L97bA/H99Q/C122S/Y151L/M1
57K/R217E

<400> 514

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Leu Arg Asp Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
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<210> 515
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/R35Q/H37T/V38D/V41R/L97bA/H99Q/C122S/Y151L/M1

57K

<400> 515
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1   5   10   15
Ala Ile Tyr Gln Arg Thr Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 516
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30H/R35Q/V38D/V41R/L97bA/H99Q/C122S/Y151L/M157K

<400> 516

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 517
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/R35Q/H37W/V38D/V41R/D60aE/L97bA/H99Q/C122S/Y1
49L/Y151L/M157K/R217D

<400> 517

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
```

```
Ala Ile Tyr Gln Arg Trp Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Glu Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Leu Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 518
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30H/R35Q/V38D/V41R/Y60bE/L97bA/H99Q/C122S/Y149N/Y
      151L/M157K

<400> 518
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
```

```
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Asn Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 519
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/V38D/Y40H/V41R/L97bA/H99Q/C122S/Y149W/M1
57K/R217D

<400> 519

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
```

```
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Trp Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Asp Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 520
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/H37W/V38D/Y40H/V41R/Y60bN/L97bA/H99Q/C12
2S/Y149H/M157K

<400> 520

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Trp Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
```

```
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp His Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 521
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/H37T/V38D/Y40H/V41R/L97bA/H99Q/C122S/Y14
9I/M157K

<400> 521

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Thr Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
```

Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Ile Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 522
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35Q/H37T/V38D/Y40H/V41R/D60aE/Y60bN/L97bA/H9
      9Q/C122S/Y149H/M157K

<400> 522
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Gln Arg Thr Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Glu Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85   90   95

```
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp His Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 523
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35H/V38D/Y40H/V41R/L97bA/H99Q/C122S/M157K

<400> 523

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr His Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
```

```
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 524
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35H/V38D/Y40H/V41R/T56A/L97bV/H99Q/R116S/C12
      2S/M157K/T210N

<400> 524
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr His Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Ala His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Val Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Ser Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
```

```
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Asn Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 525
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/V38D/Y40H/V41R/L97bA/H99Q/C122S/E153D/M1
57K

<400> 525

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Asp Gln Leu Lys Lys Thr Val Val Lys
```

```
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 526
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/V38D/Y40H/V41R/L97bA/H99Q/C122S/D148N/M157K/T
      188S

<400> 526
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asn Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
```

```
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Ser Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 527
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/V38D/Y40H/V41R/L97bA/H99Q/C122S/M157K/K223N/P
      236S

<400> 527
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
```

```
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Asn Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Ser Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 528
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/V38D/Y40M/V41R/L97bA/H99Q/C122S/Y151L/M157R/Q
192M

<400> 528

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Met Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Arg Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Met Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
```

```
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 529
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30H/V38D/L97bA/H99Q/C122S/Y151L/M157L/Q192H

<400> 529
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Leu Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys His Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
```

Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 530
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/V38D/L97bA/H99Q/C122S/Y151L/M157S/Q192L

<400> 530
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Ser Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Leu Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu

245 250

<210> 531
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30N/V38D/Y40F/V41R/L97bA/H99Q/C122S/Y151L/M157S/Q
192H

<400> 531
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Asn Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Phe Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Ser Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys His Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 532
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/V38D/Y40H/V41Q/L97bA/H99Q/C122S/Q192H

<400> 532
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Gln Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys His Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 533
<211> 253

<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Q/V38D/Y40L/V41R/L97bA/H99Q/C122S/Y151H/M157R/Q
192Y

<400> 533

Ile	Ile	Gly	Gly	Glu	Phe	Thr	Thr	Ile	Glu	Asn	Gln	Pro	Trp	Gln	Ala
1			5					10						15	
Ala	Ile	Tyr	Arg	Arg	His	Arg	Gly	Gly	Ser	Asp	Thr	Leu	Arg	Cys	Gly
		20					25					30			
Gly	Ser	Leu	Ile	Ser	Pro	Cys	Trp	Val	Ile	Ser	Ala	Thr	His	Cys	Phe
	35					40					45				
Ile	Asp	Tyr	Pro	Lys	Lys	Glu	Asp	Tyr	Ile	Val	Tyr	Leu	Gly	Arg	Ser
	50				55					60					
Arg	Leu	Asn	Ser	Asn	Thr	Gln	Gly	Glu	Met	Lys	Phe	Glu	Val	Glu	Asn
65				70					75					80	
Leu	Ile	Leu	His	Lys	Asp	Tyr	Ser	Ala	Asp	Thr	Ala	Ala	Gln	His	Asn
			85					90					95		
Asp	Ile	Ala	Leu	Leu	Lys	Ile	Arg	Ser	Lys	Glu	Gly	Arg	Cys	Ala	Gln
		100					105					110			
Pro	Ser	Arg	Thr	Ile	Gln	Thr	Ile	Ser	Leu	Pro	Ser	Met	Tyr	Asn	Asp
	115					120					125				
Pro	Gln	Phe	Gly	Thr	Ser	Cys	Glu	Ile	Thr	Gly	Phe	Gly	Lys	Glu	Asn
	130				135					140					
Ser	Thr	Asp	Tyr	Leu	His	Pro	Glu	Gln	Leu	Lys	Arg	Thr	Val	Val	Lys
145				150					155					160	
Leu	Ile	Ser	His	Arg	Glu	Cys	Gln	Gln	Pro	His	Tyr	Tyr	Gly	Ser	Glu
			165					170					175		
Val	Thr	Thr	Lys	Met	Leu	Cys	Ala	Ala	Asp	Pro	Gln	Trp	Lys	Thr	Asp
		180					185					190			
Ser	Cys	Tyr	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Cys	Ser	Leu	Gln	Gly
	195					200					205				
Arg	Met	Thr	Leu	Thr	Gly	Ile	Val	Ser	Trp	Gly	Arg	Gly	Cys	Ala	Leu
	210				215					220					
Lys	Asp	Lys	Pro	Gly	Val	Tyr	Thr	Arg	Val	Ser	His	Phe	Leu	Pro	Trp
225				230					235					240	
Ile	Arg	Ser	His	Thr	Lys	Glu	Glu	Asn	Gly	Leu	Ala	Leu			
			245					250							

<210> 534
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35S/V38D/L97bA/H99Q/C122S/Y151L/M157Y

<400> 534
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Ser Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Tyr Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 535
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)

protease domain
F30H/V38D/V41R/L97bA/H99Q/C122S/Y151L/M157T

<400> 535

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Thr Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 536
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aL/V38D/L97bA/H99Q/C122S/Y151L/M157S

<400> 536
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Leu Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Ser Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 537
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30N/V38D/V41L/L97bA/H99Q/C122S/Y151L/M157R

<400> 537
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Asn Ala
 1   5   10   15

```
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Arg Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 538
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/V38D/Y40F/V41L/L97bA/H99Q/C122S/Y151L/M157R

<400> 538
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Phe Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
```

```
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Arg Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 539
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/V38D/Y40F/V41R/L97bA/H99Q/C122S/Y151L/M157R/Q
192H

<400> 539

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
```

```
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Arg Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys His Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 540
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/V38D/Y40H/V41R/L97bA/H99Q/C122S/M157K/T2
10S

<400> 540

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
```

```
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Ser Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 541
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/V38D/L97bA/H99Q/C122S/Y151L/M157K

<400> 541

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
```

```
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 542
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
N26D/F30Y/V38D/Y40H/V41R/I65T/L97bA/H99Q/C122S/M12
6I/M157K

<400> 542

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asp Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Thr Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
```

```
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Ile Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 543
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/V38D/Y40L/V41R/L97bA/H99Q/C122S/Y151L/M157K/Q
192H

<400> 543

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
```

```
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys His Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 544
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/V38D/Y40L/V41Q/L97bA/H99Q/C122S/Y151L/M157R/Q
      192Y

<400> 544
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Leu Gln Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
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Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Arg Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Tyr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 545
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/V38D/Y40L/V41R/L97bA/H99Q/C122S/Y151L/M157A/Q
      192Y

<400> 545
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Ala Thr Val Val Lys
145                 150                 155                 160
```

Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Tyr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 546
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R36S/V38D/Y40H/V41R/L97bA/H99Q/C122S/M157K

<400> 546
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Arg Ser His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp

```
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 547
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30H/V38D/V41Q/L97bA/H99Q/C122S/Y151L/M157R

<400> 547
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Gln Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Arg Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
```

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Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 548
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/V38D/L97bA/H99Q/C122S/Y151F/M157K

<400> 548

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Phe Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
```

225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 549
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R37aH/V38D/Y40H/V41R/K61E/L97bA/H99Q/C122S/M1
57K

<400> 549
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Arg Arg His His Gly Gly Ser Asp Thr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Glu Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu

245 250

<210> 550
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/V38D/Y40H/V41R/L97bA/H99L/C122S/F141L/M1
57K/T158A

<400> 550
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Leu His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Leu Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Ala Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 551
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35H/V38D/Y40H/V41R/L97bA/H99Q/C122S/I138V/M1
57K

<400> 551
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr His Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Val Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 552

<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
T22I/F30Y/R35S/V38D/Y40H/V41R/L97bA/H99Q/C122S/I13
8V/M157K

<400> 552
Ile Ile Gly Gly Glu Phe Ile Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Ser Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Val Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 553
<211> 253
<212> PRT

<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36S/V38D/T39I/Y40H/V41R/L97bA/H99Q/C122S/S14
6P/M157K/T158S

<400> 553

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Ser His Arg Gly Gly Ser Asp Ile His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Pro Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Ser Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
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<210> 554
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/Y34S/R37aH/V38D/Y40H/V41R/L97bA/H99Q/C122S/Y1
49F/M157K

<400> 554
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Ser Arg Arg His His Gly Gly Ser Asp Thr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Phe Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 555
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)

protease domain
F30Y/R35L/V38D/Y40H/V41R/L97bA/H99Q/C122S/M157K

<400> 555
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Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Leu Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
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<210> 556
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/S37dP/V38D/Y40H/V41R/L97bA/H99Q/C122S/M157K

<400> 556
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Pro Asp Thr His Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 557
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35L/V38D/Y40H/V41R/L97bA/H99Q/C122S/M157K/T1
      58A

<400> 557
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala

```
 1               5                  10                  15
Ala Ile Tyr Leu Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Ala Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 558
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R37aS/V38D/Y40H/V41R/E86D/L97bA/H99Q/C122S/M157K/F234Y

<400> 558

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Ser Gly Gly Ser Asp Thr His Arg Cys Gly
```

```
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Asp Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Tyr Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 559
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R37aH/V38D/Y40H/V41R/L97bA/H99Q/C122S/M157K/S
      174P

<400> 559
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His His Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
```

```
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Pro Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 560
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R37aS/V38D/Y40H/V41R/L97bA/H99Q/C122S/M157K

<400> 560

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Ser Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
```

```
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 561
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35L/V38D/Y40H/V41R/N76S/L97bA/H99Q/C122S/M15
7K/K187E

<400> 561

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Leu Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Ser Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
```

```
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Glu Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 562
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35H/V38D/Y40H/V41R/L97bA/H99Q/C122S/M157K/T1
58S

<400> 562

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr His Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
```

```
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Ser Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 563
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R37aS/V38D/Y40H/V41R/L97bA/H99Q/C122S/M157K/K
187Q/T208S

<400> 563

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Ser Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
```

```
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Gln Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Ser Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 564
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30H/V38D/V41R/L97bA/H99Q/C122S/Y151L/M157K/Q192H/
      R239H

<400> 564
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
```

```
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys His Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile His Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 565
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30H/R35Q/H37Y/V38D/V41R/D60aE/Y60bN/L97bA/H99Q/C1
      22S/Y149R/Y151L/M157K

<400> 565
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Tyr Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Glu Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
```

```
Ser Thr Asp Arg Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 566
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35T/H37Q/V38D/Y40H/V41R/D60aE/Y60bN/L97bA/H9
      9Q/C122S/Y149R/M157K

<400> 566
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Thr Arg Gln Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Glu Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
```

```
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 567
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35T/V38D/Y40H/V41R/D60aE/Y60bQ/L97bA/H99Q/C1
      22S/Y149R/M157K/R217K

<400> 567
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Thr Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Glu Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
```

```
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Lys Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 568
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35K/H37E/V38D/Y40H/V41R/D60aP/Y60bD/L97bA/H9
      9Q/C122S/Y149N/M157K

<400> 568
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Lys Arg Glu Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Asn Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
```

Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 569
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35L/H37D/V38D/Y40H/V41R/Y60bD/L97bA/H99Q/C12
      2S/Y149R/M157K

<400> 569
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Leu Arg Asp Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205

Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 570
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35H/H37T/V38D/Y40H/V41R/D60aE/Y60bD/L97bA/H9
      9Q/C122S/Y149K/M157K/R217K

<400> 570
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr His Arg Thr Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Glu Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Lys Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Lys Gly Cys Ala Leu
    210   215   220

Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 571
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35S/H37G/V38D/Y40H/V41R/D60aP/Y60bE/L97bA/H9
9Q/C122S/Y149K/M157K

<400> 571
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Ser Arg Gly Arg Gly Gly Ser Asp Thr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Pro Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Lys Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240

Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 572
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/V38D/Y40H/V41R/D60aE/Y60bE/L97bA/H99Q/C1
22S/Y149N/M157K

<400> 572
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Gln Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Glu Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Asn Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 573
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35T/H37A/V38D/Y40H/V41R/D60aP/Y60bE/L97bA/H99Q/C122S/Y149K/M157K/R217Y

<400> 573

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Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Thr Arg Ala Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Lys Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Tyr Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
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<210> 574
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/V38D/Y40H/V41R/Y60bS/L97bA/H99Q/C122S/Y1
49R/M157K/R217E

<400> 574
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Gln Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 575
<211> 253

<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R37aD/V38D/Y40L/V41R/L97bA/H99Q/C122S/M126K/M
157K

<400> 575

Ile	Ile	Gly	Gly	Glu	Phe	Thr	Thr	Ile	Glu	Asn	Gln	Pro	Trp	Tyr	Ala
1			5					10						15	
Ala	Ile	Tyr	Arg	Arg	His	Asp	Gly	Gly	Ser	Asp	Thr	Leu	Arg	Cys	Gly
		20					25					30			
Gly	Ser	Leu	Ile	Ser	Pro	Cys	Trp	Val	Ile	Ser	Ala	Thr	His	Cys	Phe
	35					40					45				
Ile	Asp	Tyr	Pro	Lys	Lys	Glu	Asp	Tyr	Ile	Val	Tyr	Leu	Gly	Arg	Ser
	50				55					60					
Arg	Leu	Asn	Ser	Asn	Thr	Gln	Gly	Glu	Met	Lys	Phe	Glu	Val	Glu	Asn
65				70					75					80	
Leu	Ile	Leu	His	Lys	Asp	Tyr	Ser	Ala	Asp	Thr	Ala	Ala	Gln	His	Asn
			85					90					95		
Asp	Ile	Ala	Leu	Leu	Lys	Ile	Arg	Ser	Lys	Glu	Gly	Arg	Cys	Ala	Gln
		100					105					110			
Pro	Ser	Arg	Thr	Ile	Gln	Thr	Ile	Ser	Leu	Pro	Ser	Lys	Tyr	Asn	Asp
	115					120					125				
Pro	Gln	Phe	Gly	Thr	Ser	Cys	Glu	Ile	Thr	Gly	Phe	Gly	Lys	Glu	Asn
	130				135					140					
Ser	Thr	Asp	Tyr	Leu	Tyr	Pro	Glu	Gln	Leu	Lys	Lys	Thr	Val	Val	Lys
145				150					155					160	
Leu	Ile	Ser	His	Arg	Glu	Cys	Gln	Gln	Pro	His	Tyr	Tyr	Gly	Ser	Glu
			165					170					175		
Val	Thr	Thr	Lys	Met	Leu	Cys	Ala	Ala	Asp	Pro	Gln	Trp	Lys	Thr	Asp
		180					185					190			
Ser	Cys	Gln	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Cys	Ser	Leu	Gln	Gly
	195					200					205				
Arg	Met	Thr	Leu	Thr	Gly	Ile	Val	Ser	Trp	Gly	Arg	Gly	Cys	Ala	Leu
	210				215					220					
Lys	Asp	Lys	Pro	Gly	Val	Tyr	Thr	Arg	Val	Ser	His	Phe	Leu	Pro	Trp
225				230					235					240	
Ile	Arg	Ser	His	Thr	Lys	Glu	Glu	Asn	Gly	Leu	Ala	Leu			
			245					250							

<210> 576
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35T/H37T/V38D/Y40H/V41R/D60aP/Y60bD/L97bA/H9
9Q/C122S/Y149T/M157K

<400> 576
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Thr Arg Thr Arg Gly Gly Ser Asp Thr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Pro Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Thr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 577
<211> 253
<212> PRT
<213> Artificial Sequence

<220>

<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35H/H37D/V38D/Y40H/V41R/D60aK/Y60bS/L97bA/H9
9Q/C122S/Y149R/M157K

<400> 577
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr His Arg Asp Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Lys Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 578
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain

F30Y/R35S/V38D/Y40H/V41R/D60aE/Y60bS/L97bA/H99Q/C1
22S/Y149R/M157K

<400> 578
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Ser Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Glu Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 579
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35H/H37T/V38D/Y40H/V41R/D60aR/Y60bD/L97bA/H9
9Q/C122S/Y149R/M157K

<400> 579
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr His Arg Thr Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Arg Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 580
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35Q/V38D/Y40H/V41R/D60aE/Y60bK/L97bA/H99Q/C1
      22S/Y149R/M157K/R217I

<400> 580

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Glu Lys Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Ile Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 581
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35Q/V38D/Y40H/V41R/D60aP/Y60bE/L97bA/H99Q/C1
      22S/Y149R/M157K/R217K

<400> 581
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
```

```
Ala Ile Tyr Gln Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Lys Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 582
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35Q/V38D/Y40H/V41R/D60aE/Y60bN/L97bA/H99Q/C1
      22S/Y149R/M157K

<400> 582
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
```

```
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Glu Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 583
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35T/H37T/V38D/Y40H/V41R/D60aT/Y60bS/L97bA/H99Q/C122S/Y149K/M157K

<400> 583

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Thr Arg Thr Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
```

```
Ile Thr Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Lys Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 584
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/V38E/Y40H/V41R/T97aI/L97bA/H99Q/C122S/Y1
49N/L150V/M157K

<400> 584

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Glu Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
```

```
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Asn Val Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 585
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/V38E/Y40H/V41R/Y60bN/N87D/A96T/T97aI/L97
bA/H99Q/C122S/N145S/M157K/M207K

<400> 585

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Glu Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asp
65                  70                  75                  80
```

```
Leu Ile Leu His Lys Asp Tyr Ser Thr Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Ser
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Lys Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 586
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/V38E/Y40H/V41R/T97aI/L97bA/H99Q/C122S/S1
46F/M157K/Q192H/K243Q

<400> 586

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Glu Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
```

```
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Phe Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys His Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Gln Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 587
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/V38E/Y40H/V41R/K61E/T97aI/L97bA/H99Q/C12
2S/Y149H/M157K/K187R

<400> 587

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Glu Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Glu Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
```

```
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp His Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Arg Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 588
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R37aP/V38D/Y40H/V41R/Y60bN/E84D/L97bA/H99Q/C1
22S/M157K/T242I

<400> 588

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Pro Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Asp Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
```

```
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Ile Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 589
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R37aP/G37bD/V38D/Y40H/V41R/Y60bN/L97bA/H99Q/C
122S/M157K

<400> 589

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Pro Asp Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
```

```
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 590
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35L/R36H/H37P/V38E/Y40H/V41R/Y60bG/T97aD/L97
      bA/H99Q/C122S/Y149R/M157K

<400> 590
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Leu His Pro Arg Gly Gly Ser Glu Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Gly Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Asp Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
```

```
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 591
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R36H/H37S/V38E/T39L/Y40H/V41R/Y60bH/T97aI/L97
      bA/H99Q/C122S/Y149R/M157K

<400> 591
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg His Ser Arg Gly Gly Ser Glu Leu His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp His Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
```

```
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 592
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35L/R36H/H37D/V38E/T39W/Y40H/V41R/Y60bA/T97a
      D/L97bA/H99Q/C122S/Y149R/M157K

<400> 592
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Leu His Asp Arg Gly Gly Ser Glu Trp His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Ala Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Asp Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
```

```
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 593
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/H37P/V38E/T39Y/Y40H/V41R/Y60bN/L97bA/H99
Q/C122S/Y149R/M157K

<400> 593

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg His Pro Arg Gly Gly Ser Glu Tyr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
```

Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 594
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R36H/H37E/V38E/T39Y/Y40H/V41R/Y60bN/T97aV/L97
      bA/H99Q/C122S/Y149K/M157K

<400> 594
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Arg His Glu Arg Gly Gly Ser Glu Tyr His Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Val Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Lys Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220

```
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 595
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/H37G/V38E/T39W/Y40H/V41R/Y60bA/T97aE/L97
bA/H99Q/C122S/Y149Q/M157K

<400> 595

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg His Gly Arg Gly Gly Ser Glu Trp His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Ala Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Gln Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
```

Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 596
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/H37E/V38E/T39W/Y40H/V41R/Y60bD/T97aD/L97
bA/H99Q/C122S/Y149R/M157K

<400> 596
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Arg His Glu Arg Gly Gly Ser Glu Trp His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Asp Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 597
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/H37F/V38E/T39Y/Y40H/V41R/Y60bD/T97aV/L97
bA/H99Q/C122S/Y149L/M157K

<400> 597
```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg His Phe Arg Gly Gly Ser Glu Tyr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Val Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Leu Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 598
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/H37N/V38E/T39Y/Y40H/V41R/Y60bQ/T97aV/L97
bA/H99Q/C122S/Y149L/M157K

<400> 598
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Arg His Asn Arg Gly Gly Ser Glu Tyr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Val Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Leu Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 599
<211> 253

<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35L/R36H/H37E/V38E/T39L/Y40H/V41R/Y60bS/T97a
D/L97bA/H99Q/C122S/Y149R/M157K

<400> 599
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Leu His Glu Arg Gly Gly Ser Glu Leu His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Asp Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 600
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/H37D/V38E/T39W/Y40H/V41R/Y60bV/T97aE/L97
bA/H99Q/C122S/Y149R/M157K

<400> 600
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Arg His Asp Arg Gly Gly Ser Glu Trp His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Val Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 601
<211> 253
<212> PRT
<213> Artificial Sequence

<220>

<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/H37A/V38E/T39Y/Y40H/V41R/Y60bQ/T97aV/L97
bA/H99Q/C122S/Y149R/M157K

<400> 601
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Arg His Ala Arg Gly Gly Ser Glu Tyr His Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Val Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 602
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain

F30Y/R36H/H37D/V38E/T39Y/Y40H/V41R/Y60bM/T97aD/L97
bA/H99Q/C122S/Y149R/M157K

<400> 602
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Arg His Asp Arg Gly Gly Ser Glu Tyr His Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Met Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Asp Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 603
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/H37D/V38E/T39W/Y40H/V41R/Y60bN/T97aV/L97
bA/H99Q/C122S/Y149R/M157K

<400> 603
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Arg His Asp Arg Gly Gly Ser Glu Trp His Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Val Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 604
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35W/R36H/H37D/V38E/T39Y/Y40H/V41R/Y60bS/T97a
      L/L97bA/H99Q/C122S/Y149L/M157K

<400> 604

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp His Asp Arg Gly Gly Ser Glu Tyr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Leu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Leu Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 605
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/V38E/T39V/Y40H/V41R/Y60bH/T97aE/L97bA/H99Q/C122S/Y149S/M157K

<400> 605

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
```

```
Ala Ile Tyr Arg His His Arg Gly Gly Ser Glu Val His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp His Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Ser Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 606
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/H37E/V38E/T39F/Y40H/V41R/Y60bN/T97aV/L97
bA/H99Q/C122S/Y149R/M157K

<400> 606

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg His Glu Arg Gly Gly Ser Glu Phe His Arg Cys Gly
            20                  25                  30
```

```
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Val Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 607
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/H37G/V38E/T39Y/Y40H/V41R/Y60bN/T97aA/L97
bA/H99Q/C122S/Y149R/M157K

<400> 607

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg His Gly Arg Gly Gly Ser Glu Tyr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
```

```
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ala Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 608
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35I/R36H/H37E/V38E/T39Y/Y40H/V41R/Y60bS/T97a
V/L97bA/H99Q/C122S/Y149L/M157K

<400> 608

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Ile His Glu Arg Gly Gly Ser Glu Tyr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
```

```
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Val Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Leu Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 609
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35L/H37D/V38D/Y40H/V41R/D60aE/Y60bT/L97bA/H9
9Q/C122S/Y149R/M157K

<400> 609

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Leu Arg Asp Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Glu Thr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
```

```
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 610
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/V38D/Y40H/V41R/D60aK/Y60bV/L97bA/H99Q/C1
22S/Y149R/M157K

<400> 610

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Lys Val Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
```

```
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 611
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36H/H37S/V38E/T39Y/Y40H/V41R/Y60bN/T97a
E/L97bA/H99Q/C122S/Y149R/M157K

<400> 611

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp His Ser Arg Gly Gly Ser Glu Tyr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
```

```
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 612
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36H/H37Q/V38E/T39H/Y40H/V41R/T97aE/L97b
A/H99Q/C122S/Y149L/M157K

<400> 612

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp His Gln Arg Gly Gly Ser Glu His His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
```

```
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Leu Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 613
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36H/H37D/V38E/T39Y/Y40H/V41R/Y60bD/T97a
I/L97bA/H99Q/C122S/M157K

<400> 613

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp His Asp Arg Gly Gly Ser Glu Tyr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
```

```
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 614
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35V/R36H/H37G/V38E/T39W/Y40H/V41R/Y60bW/T97a
      I/L97bA/H99Q/C122S/Y149E/M157K

<400> 614
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Val His Gly Arg Gly Gly Ser Glu Trp His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Trp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Glu Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
```

```
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 615
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35M/R36H/H37G/V38E/T39F/Y40H/V41R/Y60bP/T97a
      F/L97bA/H99Q/C122S/Y149R/M157K

<400> 615
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Met His Gly Arg Gly Gly Ser Glu Phe His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Phe Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
```

```
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 616
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35V/R36H/H37G/V38E/T39W/Y40H/V41R/Y60bA/T97a
      I/L97bA/H99Q/C122S/Y149R/M157K

<400> 616
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Val His Gly Arg Gly Gly Ser Glu Trp His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Ala Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
```

Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 617
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35V/R36H/H37S/V38E/T39F/Y40H/V41R/Y60bS/T97a
      M/L97bA/H99Q/C122S/Y149W/M157K

<400> 617
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Val His Ser Arg Gly Gly Ser Glu Phe His Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Met Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Trp Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205

Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 618
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35W/R36H/H37D/V38E/T39Y/Y40H/V41R/Y60bT/T97a
      D/L97bA/H99Q/C122S/Y149R/M157K

<400> 618
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Trp His Asp Arg Gly Gly Ser Glu Tyr His Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Thr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Asp Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220

Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 619
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35L/R36H/H37G/V38E/T39Y/Y40H/V41R/Y60bP/T97a
E/L97bA/H99Q/C122S/Y149M/M157K

<400> 619
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Leu His Gly Arg Gly Gly Ser Glu Tyr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Met Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240

Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 620
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35F/R36H/H37G/V38E/T39Y/Y40H/V41R/Y60bS/T97a
D/L97bA/H99Q/C122S/Y149R/M157K

<400> 620
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Phe His Gly Arg Gly Gly Ser Glu Tyr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Asp Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 621
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35V/R36H/H37S/V38E/T39Y/Y40H/V41R/Y60bP/T97a
E/L97bA/H99Q/C122S/Y149E/M157K

<400> 621
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Val His Ser Arg Gly Gly Ser Glu Tyr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Glu Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 622
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35V/R36H/H37S/V38E/T39F/Y40H/V41R/Y60bS/T97a
I/L97bA/H99Q/C122S/Y149R/M157K/Q192T

<400> 622
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Val His Ser Arg Gly Gly Ser Glu Phe His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 623
<211> 253

<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35V/R36H/H37K/V38E/T39F/Y40H/V41R/Y60bN/T97a
I/L97bA/H99Q/C122S/Y149R/M157K

<400> 623
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Val His Lys Arg Gly Gly Ser Glu Phe His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 624
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35V/R36H/H37D/V38E/T39W/Y40H/V41R/Y60bP/T97a
I/L97bA/H99Q/C122S/Y149R/M157K

<400> 624
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Val His Asp Arg Gly Gly Ser Glu Trp His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 625
<211> 253
<212> PRT
<213> Artificial Sequence

<220>

<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35V/R36H/H37G/V38E/T39L/Y40H/V41R/Y60bT/T97a
I/L97bA/H99Q/C122S/Y149R/M157K/Q192T/R239H

<400> 625
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Val His Gly Arg Gly Gly Ser Glu Leu His Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Thr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile His Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 626
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain

F30Y/R35Y/R36H/H37E/V38E/T39L/Y40H/V41W/Y60bE/T97a
I/L97bA/H99Q/C122S/Y149R/M157K/Q192F

<400> 626
```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Tyr His Glu Arg Gly Gly Ser Glu Leu His Trp Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Phe Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 627
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36H/H37D/V38E/T39F/Y40H/V41R/Y60bE/T97a
I/L97bA/H99Q/C122S/Y149R/M157K

<400> 627
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Trp His Asp Arg Gly Gly Ser Glu Phe His Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 628
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35W/R36H/H37D/V38E/T39Y/Y40H/V41R/Y60bA/T97a
      I/L97bA/H99Q/C122S/Y149R/M157K

<400> 628

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp His Asp Arg Gly Gly Ser Glu Tyr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Ala Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 629
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36H/H37E/V38E/T39Y/Y40H/V41R/Y60bD/T97a
I/L97bA/H99Q/C122S/Y149R/M157K/Q192M

<400> 629

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
```

```
Ala Ile Tyr Trp His Glu Arg Gly Gly Ser Glu Tyr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Met Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 630
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36H/H37E/V38E/T39V/Y40H/V41W/Y60bS/T97a
I/L97bA/H99Q/C122S/Y149R/M157K/Q192H

<400> 630

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp His Glu Arg Gly Gly Ser Glu Val His Trp Cys Gly
            20                  25                  30
```

```
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys His Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 631
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Y/R36H/H37E/V38E/T39A/Y40H/V41W/Y60bV/T97a
I/L97bA/H99Q/C122S/Y149R/M157K/Q192H

<400> 631

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Tyr His Glu Arg Gly Gly Ser Glu Ala His Trp Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
```

```
Ile Asp Val Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys His Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 632
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Y/R36H/H37P/V38E/T39R/Y40H/V41W/Y60bE/T97a
I/L97bA/H99Q/C122S/M157K/Q192F

<400> 632

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Tyr His Pro Arg Gly Gly Ser Glu Arg His Trp Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
```

```
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Phe Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 633
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Y/R36H/H37D/V38E/T39W/Y40H/V41R/Y60bE/T97a
I/L97bA/H99Q/C122S/Y149R/M157K

<400> 633

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Tyr His Asp Arg Gly Gly Ser Glu Trp His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
```

Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 634
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35W/R36H/H37E/V38E/T39V/Y40H/V41W/Y60bA/T97a
      I/L97bA/H99Q/C122S/Y149R/M157K/Q192A

<400> 634
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Trp His Glu Arg Gly Gly Ser Glu Val His Trp Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Ala Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85   90   95

```
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Ala Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 635
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37D/V38D/T39H/V41R/Y60bP/L97bA/H99Q/C122S/Y1
49R/Q192T

<400> 635

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Asp Arg Gly Gly Ser Asp His Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
```

```
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 636
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35F/H37G/V38D/T39H/V41A/Y60bD/L97bA/H99Q/C122S/Y1
      49R

<400> 636
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Phe Arg Gly Arg Gly Gly Ser Asp His Tyr Ala Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
```

```
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 637
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35E/H37D/V38D/T39N/V41R/Y60bN/L97bA/H99Q/C122S/Y1
      49R

<400> 637
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Glu Arg Asp Arg Gly Gly Ser Asp Asn Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
```

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Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 638
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35Q/H37Y/V38D/T39A/V41R/Y60bP/L97bA/H99Q/C122S/Y1
      49R/Q192S

<400> 638
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Tyr Arg Gly Gly Ser Asp Ala Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
```

Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Ser Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 639
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35Q/H37Y/V38D/T39F/V41R/Y60bP/L97bA/H99Q/C122S/Y1
      49R/Q192G

<400> 639
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Gln Arg Tyr Arg Gly Gly Ser Asp Phe Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175

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Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gly Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 640
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35F/H37E/V38D/T39S/V41A/Y60bD/L97bA/H99Q/C122S

<400> 640
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Phe Arg Glu Arg Gly Gly Ser Asp Ser Tyr Ala Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
```

```
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 641
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35D/H37R/V38D/T39V/V41T/Y60bT/L97bA/H99Q/C122S/Q1
92A

<400> 641

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Asp Arg Arg Arg Gly Gly Ser Asp Val Tyr Thr Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Thr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Ala Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
```

```
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 642
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37G/V38D/T39W/V41R/Y60bP/L97bA/H99Q/C122S/Y1
49R/Q192G

<400> 642

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Gly Arg Gly Gly Ser Asp Trp Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gly Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
```

225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 643
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37M/V38D/T39V/V41R/Y60bP/L97bA/H99Q/C122S/Y1
49R

<400> 643
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Gln Arg Met Arg Gly Gly Ser Asp Val Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu

245 250

<210> 644
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35L/H37E/V38D/T39Y/V41R/L97bA/H99Q/C122S/Y149R

<400> 644
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Leu Arg Glu Arg Gly Gly Ser Asp Tyr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 645
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35W/H37D/V38D/T39Y/V41R/Y60bS/L97bA/H99Q/C122S/Y1
49R

<400> 645
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Trp Arg Asp Arg Gly Gly Ser Asp Tyr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 646
<211> 253

<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35G/H37G/V38D/T39W/V41A/Y60bN/L97bA/H99Q/C122S

<400> 646
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Gly Arg Gly Arg Gly Gly Ser Asp Trp Tyr Ala Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 647
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37N/V38D/T39Y/V41R/Y60bP/L97bA/H99Q/C122S

<400> 647
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Gln Arg Asn Arg Gly Gly Ser Asp Tyr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 648
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain

R35W/H37D/V38D/T39Y/V41R/Y60bH/L97bA/H99Q/C122S/Y1
49R

<400> 648
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Trp Arg Asp Arg Gly Gly Ser Asp Tyr Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp His Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 649
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/R36H/H37G/V38E/T39H/Y40F/V41R/T97aI/L97b
A/H99Q/C122S/Y149R/M157K/Q192M

<400> 649
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Gln His Gly Arg Gly Gly Ser Glu His Phe Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Met Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 650
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35V/R36H/H37D/V38E/T39W/Y40M/V41R/T97aI/L97bA/H99
      Q/C122S/Y149R/M157K

<400> 650

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Val His Asp Arg Gly Gly Ser Glu Trp Met Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 651
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35L/R36H/H37D/V38E/T39Y/Y40F/V41R/T97aI/L97b
A/H99Q/C122S/Y149R/M157K/Q192N

<400> 651

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
```

```
Ala Ile Tyr Leu His Asp Arg Gly Gly Ser Glu Tyr Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Asn Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 652
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35L/R36H/H37E/V38E/T39L/Y40F/V41R/T97aI/L97b
A/H99Q/C122S/Y149R/M157K/Q192H

<400> 652

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Leu His Glu Arg Gly Gly Ser Glu Leu Phe Arg Cys Gly
            20                  25                  30
```

```
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys His Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 653
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/R35Q/R36H/H37Y/V38E/T39Y/Y40L/V41R/T97aI/L97b
A/H99Q/C122S/Y149R/M157K

<400> 653

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Gln His Tyr Arg Gly Gly Ser Glu Tyr Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
```

```
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 654
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/V38E/Y40H/V41R/T97aI/L97bA/H99Q/C122S/Y1
49R/M157K/Q192Y

<400> 654

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Glu Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
```

```
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Tyr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 655
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30L/R35L/R36H/H37D/V38E/T39Y/V41K/T97aI/L97bA/H99
Q/C122S/Y149R/M157K

<400> 655

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Leu Ala
 1               5                  10                  15
Ala Ile Tyr Leu His Asp Arg Gly Gly Ser Glu Tyr Tyr Lys Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
```

```
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 656
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/R36H/H37Y/V38E/T39Y/Y40L/V41R/T97aI/L97bA/H99
Q/C122S/Y149R/M157K

<400> 656

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln His Tyr Arg Gly Gly Ser Glu Tyr Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
```

```
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 657
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35L/R36H/H37E/V38E/T39N/Y40F/V41R/T97aI/L97b
      A/H99Q/C122S/Y149R/M157K

<400> 657
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Leu His Glu Arg Gly Gly Ser Glu Asn Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
```

```
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 658
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35I/R36H/H37D/V38E/T39F/Y40F/V41R/T97aI/L97b
A/H99Q/C122S/Y149R/M157K

<400> 658

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Ile His Asp Arg Gly Gly Ser Glu Phe Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
```

```
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 659
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36H/H37E/V38E/T39S/Y40L/V41R/T97aI/L97b
A/H99Q/C122S/Y149R/M157K/Q192A

<400> 659

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp His Glu Arg Gly Gly Ser Glu Ser Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
```

```
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Ala Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 660
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35E/R36H/H37D/V38E/T39W/Y40F/V41R/T97aI/L97bA/H99
      Q/C122S/Y149R/M157K/Q192T

<400> 660
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Glu His Asp Arg Gly Gly Ser Glu Trp Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
```

```
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 661
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30H/R35L/R36H/H37E/V38E/T39F/Y40F/V41R/T97aI/L97b
      A/H99Q/C122S/Y149R/M157K

<400> 661
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Leu His Glu Arg Gly Gly Ser Glu Phe Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
```

```
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 662
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30H/R35L/R36H/H37D/V38E/T39Y/Y40F/V41Q/T97aI/L97b
      A/H99Q/C122S/Y149R/M157K

<400> 662
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Leu His Asp Arg Gly Gly Ser Glu Tyr Phe Gln Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
```

```
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 663
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35W/R36H/H37D/V38E/T39Y/Y40F/V41R/Y60bS/T97a
      E/L97bA/H99Q/C122S/Y149K/M157K

<400> 663
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp His Asp Arg Gly Gly Ser Glu Tyr Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Lys Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
```

Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 664
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35W/R36H/H37E/S37dP/V38E/T39W/Y40H/V41R/Y60b
      Q/T97aE/L97bA/H99Q/C122S/Y149K/M157K

<400> 664
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Trp His Glu Arg Gly Gly Pro Glu Trp His Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Lys Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220

Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 665
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
I24T/F30Y/R35W/R36H/H37E/V38E/T39W/Y40H/V41R/Y60bQ
/T97aE/L97bA/H99Q/C122S/Y149K/M157K

<400> 665
Ile Ile Gly Gly Glu Phe Thr Thr Thr Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Trp His Glu Arg Gly Gly Ser Glu Trp His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Lys Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240

Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 666
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
I24N/F30Y/R35W/R36H/H37E/V38E/T39W/Y40L/V41R/Y60bQ
/N87D/T97aE/L97bA/H99Q/C122S/Y149K/M157K

<400> 666
Ile Ile Gly Gly Glu Phe Thr Thr Asn Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Trp His Glu Arg Gly Gly Ser Glu Trp Leu Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asp
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Lys Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 667
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36H/H37S/V38E/Y40H/Y60bN/T97aE/L97bA/H99Q/C122S/Y149R/M157K

<400> 667

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp His Ser Arg Gly Gly Ser Glu Thr His Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 668
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/H37Y/V38E/T39Y/Y40H/V41R/Y60bN/T97aE/L97
bA/H99Q/C122S/Y149R

<400> 668
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Trp Arg Tyr Arg Gly Gly Ser Glu Tyr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 669
<211> 253

<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/H37S/V38E/T39Y/Y40H/V41R/Y60bN/T97aI/L97
bA/H99Q/C122S/Y149R/M157K

<400> 669
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Trp Arg Ser Arg Gly Gly Ser Glu Tyr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 670
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36H/H37S/V38E/T39Y/Y40H/V41R/Y60bN/T97a
E/L97bA/H99Q/C122S/Y149R

<400> 670
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Trp His Ser Arg Gly Gly Ser Glu Tyr His Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 671
<211> 253
<212> PRT
<213> Artificial Sequence

<220>

<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Y/R36H/H37S/V38D/T39Y/V41R/Y60bN/T97aI/L97bA/H9
9Q/C122S/Y149R

<400> 671
```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Tyr His Ser Arg Gly Gly Ser Asp Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 672
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain

R36H/H37S/V38E/T39W/V41R/Y60bN/T97aI/L97bA/H99Q/C1
22S/Y149R

<400> 672

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg His Ser Arg Gly Gly Ser Glu Trp Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 673
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35W/R36H/H37S/V38E/T39Y/V41R/Y60bN/T97aE/L97bA/H9
9Q/C122S/Y149R/M157K

<400> 673
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Trp His Ser Arg Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 674
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35W/R36H/H37S/V38E/Y40H/Y60bN/T97aI/L97bA/H9
      9Q/C122S/Y149R

<400> 674

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp His Ser Arg Gly Gly Ser Glu Thr His Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 675
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35W/R36N/H37S/V38E/T39Y/Y40M/V41R/Y60bN/T97aE/L97
bA/H99Q/C122S/Y149R/M157S

<400> 675

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
```

```
Ala Ile Tyr Trp Asn Ser Arg Gly Gly Ser Glu Tyr Met Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Ser Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 676
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35W/R36Q/H37S/V38T/T39Y/Y40H/V41R/Y60bN/T97aE/L97
bA/H99Q/C122S/Y149R/Y151P/M157R

<400> 676

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Trp Gln Ser Arg Gly Gly Ser Thr Tyr His Arg Cys Gly
            20                  25                  30
```

```
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Pro Pro Glu Gln Leu Lys Arg Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 677
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36Q/H37S/V38P/T39Y/Y40L/V41R/Y60bN/T97a
E/L97bA/H99Q/C122S/Y149R/M157R

<400> 677

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp Gln Ser Arg Gly Gly Ser Pro Tyr Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
```

```
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Arg Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 678
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35W/R36Q/H37S/V38P/T39Y/V41R/Y60bN/T97aE/L97bA/H99Q/C122S/Y149R/Y151L

<400> 678

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Trp Gln Ser Arg Gly Gly Ser Pro Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
```

```
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 679
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/R35W/R36T/H37S/V38P/T39Y/V41R/Y60bN/T97aE/L97
bA/H99Q/C122S/Y149R/Y151L/M157S

<400> 679

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Trp Thr Ser Arg Gly Gly Ser Pro Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
```

```
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Leu Pro Glu Gln Leu Lys Ser Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 680
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36Q/H37S/V38E/T39Y/Y40L/V41R/Y60bN/T97a
E/L97bA/H99Q/C122S/Y149R/Y151L/M157T/Q192H

<400> 680

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp Gln Ser Arg Gly Gly Ser Glu Tyr Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
```

```
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Leu Pro Glu Gln Leu Lys Thr Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys His Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 681
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35W/R36K/H37S/V38D/T39Y/Y40L/V41R/Y60bN/T97a
      E/L97bA/H99Q/C122S/Y149R/Y151L/M157R/Q192T

<400> 681
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp Lys Ser Arg Gly Gly Ser Asp Tyr Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
```

```
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Leu Pro Glu Gln Leu Lys Arg Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 682
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35W/R36K/H37S/V38E/T39Y/Y40L/V41R/Y60bN/T97aE/L97
bA/H99Q/C122S/Y149R/Y151L/M157S/Q192H

<400> 682

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Trp Lys Ser Arg Gly Gly Ser Glu Tyr Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
```

```
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Leu Pro Glu Gln Leu Lys Ser Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys His Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 683
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36S/H37S/V38Q/T39Y/Y40L/V41R/Y60bN/T97a
E/L97bA/H99Q/C122S/Y149R/Y151L/M157S/Q192N

<400> 683

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp Ser Ser Arg Gly Gly Ser Gln Tyr Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
```

```
Ser Thr Asp Arg Leu Leu Pro Glu Gln Leu Lys Ser Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Asn Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 684
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35W/R36Q/H37S/V38T/T39Y/Y40L/V41R/Y60bN/T97a
      E/L97bA/H99Q/C122S/Y149R/Y151L/M157K/Q192T

<400> 684
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp Gln Ser Arg Gly Gly Ser Thr Tyr Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Leu Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
```

Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 685
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35W/R36K/H37S/V38A/T39Y/V41R/Y60bN/T97aE/L97bA/H9
      9Q/C122S/Y149R/Y151L/M157R/Q192T

<400> 685
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Trp Lys Ser Arg Gly Gly Ser Ala Tyr Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Leu Pro Glu Gln Leu Lys Arg Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175

Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 686
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35W/R36H/H37S/V38E/T39Y/Y40H/V41R/Y60bN/T97a
      E/L97bA/H99Q/C122S/Y149R/Y151P/M157K/Q192H

<400> 686
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Trp His Ser Arg Gly Gly Ser Glu Tyr His Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Pro Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190

Ser Cys His Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 687
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35W/R36Q/H37S/V38E/T39Y/Y40L/V41R/Y60bN/T97aE/L97
      bA/H99Q/C122S/Y149R/Y151L/M157S/Q192T

<400> 687
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Trp Gln Ser Arg Gly Gly Ser Glu Tyr Leu Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Leu Pro Glu Gln Leu Lys Ser Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205

Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 688
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35W/R36Q/H37S/V38S/T39Y/V41R/Y60bN/T97aE/L97bA/H9
      9Q/C122S/Y149R/Y151L/M157S/Q192H

<400> 688
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Trp Gln Ser Arg Gly Gly Ser Ser Tyr Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Leu Pro Glu Gln Leu Lys Ser Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys His Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220

```
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 689
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/R35W/R36H/H37S/V38E/T39Y/Y40M/V41R/Y60bN/T97a
E/L97bA/H99Q/C122S/Y149R/M157K

<400> 689

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Trp His Ser Arg Gly Gly Ser Glu Tyr Met Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
```

Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 690
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36T/H37S/V38S/T39Y/Y40L/V41R/Y60bN/T97a
E/L97bA/H99Q/C122S/Y149R/Y151L/M157R/Q192Y

<400> 690
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Trp Thr Ser Arg Gly Gly Ser Ser Tyr Leu Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Leu Pro Glu Gln Leu Lys Arg Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Tyr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 691
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35L/R36H/H37E/V38E/T39S/Y40F/V41R/T97aI/L97b
A/H99Q/C122S/Y149R/M157K

<400> 691
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Leu His Glu Arg Gly Gly Ser Glu Ser Phe Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 692
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35V/R36H/H37T/V38E/T39A/Y40L/V41Q/T97aI/L97b
A/H99Q/C122S/Y149R/M157K

<400> 692
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Val His Thr Arg Gly Gly Ser Glu Ala Leu Gln Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 693
<211> 253

<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35K/R36H/H37E/R37aK/V38E/T39F/Y40F/V41R/D60a
P/Y60bS/T97aI/L97bA/H99Q/C122S/Y149R/M157K

<400> 693
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Lys His Glu Lys Gly Gly Ser Glu Phe Phe Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Pro Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 694
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/R36H/H37G/R37aE/V38E/T39Y/Y40F/V41R/D60a
P/Y60bG/T97aI/L97bA/H99Q/C122S/Y149R/M157K

<400> 694
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Gln His Gly Glu Gly Gly Ser Glu Tyr Phe Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Pro Gly Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 695
<211> 253
<212> PRT
<213> Artificial Sequence

<220>

<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/R36H/H37G/R37aE/V38E/T39I/Y40F/V41R/D60a
P/Y60bD/T97aI/L97bA/H99Q/C122S/Y149M/M157K

<400> 695
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Gln His Gly Glu Gly Gly Ser Glu Ile Phe Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Pro Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Met Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 696
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain

F30Y/R35H/R36H/H37D/R37aE/V38E/T39Y/Y40F/V41R/D60a
P/Y60bD/T97aI/L97bA/H99Q/C122S/Y149R/M157K

<400> 696
```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr His His Asp Glu Gly Gly Ser Glu Tyr Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 697
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
H37M/R37aD/V38E/T39A/V41R/D60aP/Y60bS/T97aI/L97bA/
H99Q/C122S/Y149R

<400> 697
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg Met Asp Gly Gly Ser Glu Ala Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Pro Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 698
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35F/H37D/R37aS/V38E/T39Y/V41R/D60aE/Y60bD/T97aI/L
      97bA/H99Q/C122S/Y149R

<400> 698

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Phe Arg Asp Ser Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Glu Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 699
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35A/H37D/R37aN/V38E/T39F/V41R/D60aP/Y60bD/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 699

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
```

```
Ala Ile Tyr Ala Arg Asp Asn Gly Gly Ser Glu Phe Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 700
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37D/R37aA/V38E/T39F/V41R/D60aP/Y60bE/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 700

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Asp Ala Gly Gly Ser Glu Phe Tyr Arg Cys Gly
            20                  25                  30
```

```
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 701
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35W/H37D/R37aP/V38E/T39W/V41R/D60aR/Y60bS/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 701

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Trp Arg Asp Pro Gly Gly Ser Glu Trp Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
```

```
Ile Arg Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 702
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35F/H37D/R37aN/V38E/T39Y/V41R/Y60bS/T97aI/L97bA/H
99Q/C122S/Y149R

<400> 702

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Phe Arg Asp Asn Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
```

```
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 703
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Y/H37S/R37aP/V38E/T39Y/V41R/D60aP/Y60bD/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 703

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Tyr Arg Ser Pro Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
```

```
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 704
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37Y/R37aD/V38E/T39L/V41R/D60aE/Y60bT/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 704

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Tyr Asp Gly Gly Ser Glu Leu Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Glu Thr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
```

```
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 705
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35W/H37P/R37aG/V38E/T39Y/V41R/D60aP/Y60bE/T97aI/L
      97bA/H99Q/C122S/Y149R

<400> 705
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Trp Arg Pro Gly Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
```

```
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 706
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      N26D/F30Y/R35Y/R36H/H37E/V38E/T39F/Y40F/V41R/K61E/
      T97aI/L97bA/H99Q/R110dS/P114S/C122S/Y149R/M157K

<400> 706
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asp Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Tyr His Glu Arg Gly Gly Ser Glu Phe Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Glu Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Ser Cys Ala Gln
            100                 105                 110
Ser Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
```

```
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 707
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Y/R36H/H37N/V38E/T39F/Y40F/V41R/K61E/R72H/
T97aI/L97bA/H99Q/C122S/Y149R/M157K/Q169K

<400> 707

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Tyr His Asn Arg Gly Gly Ser Glu Phe Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Glu Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
His Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
```

```
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Lys Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 708
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35Y/R36H/H37E/V38E/T39F/Y40F/V41R/K61E/T97aI
      /L97bA/H99Q/C122S/Y149R/M157K/T242A

<400> 708
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Tyr His Glu Arg Gly Gly Ser Glu Phe Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Glu Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
```

```
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Ala Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 709
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35Q/R36H/H37G/R37aE/V38E/T39F/Y40F/V41R/D60a
      S/Y60bP/T97aE/L97bA/H99Q/C122S/Y149R/M157K

<400> 709
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Gln His Gly Glu Gly Gly Ser Glu Phe Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Ser Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
```

```
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 710
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35M/R36H/H37D/R37aD/V38E/T39Y/Y40F/V41R/D60a
      P/Y60bS/T97aE/L97bA/H99Q/C122S/Y149R/M157K

<400> 710
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Met His Asp Asp Gly Gly Ser Glu Tyr Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
```

```
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 711
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35Q/R36H/H37G/R37aN/V38E/T39Y/Y40F/V41R/Y60b
      A/T97aE/L97bA/H99Q/C122S/Y149R/M157K

<400> 711
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Gln His Gly Asn Gly Gly Ser Glu Tyr Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Ala Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
```

```
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 712
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/R36H/H37G/R37aE/V38E/T39Y/Y40F/V41R/D60a
P/Y60bS/T97aE/L97bA/H99Q/C122S/Y149R/M157K

<400> 712

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Gln His Gly Glu Gly Gly Ser Glu Tyr Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
```

```
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 713
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36H/H37D/R37aE/V38E/T39Y/Y40F/V41R/D60a
E/Y60bF/T97aE/L97bA/H99Q/C122S/Y149R/M157K

<400> 713

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp His Asp Glu Gly Gly Ser Glu Tyr Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Glu Phe Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
```

Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 714
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/R36H/H37Y/R37aE/V38E/T39Y/Y40F/V41R/D60a
S/Y60bP/T97aE/L97bA/H99Q/C122S/Y149R/M157K

<400> 714
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Gln His Tyr Glu Gly Gly Ser Glu Tyr Phe Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Ser Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 715
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/R36H/H37Y/R37aD/V38E/T39Y/Y40F/V41R/Y60b
V/T97aE/L97bA/H99Q/C122S/Y149R/M157K

<400> 715
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Gln His Tyr Asp Gly Gly Ser Glu Tyr Phe Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Val Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 716
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35A/R36H/H37T/R37aD/V38E/T39Y/Y40L/V41R/D60a
P/Y60bE/T97aE/L97bA/H99Q/C122S/Y149R/M157K

<400> 716

Ile	Ile	Gly	Gly	Glu	Phe	Thr	Thr	Ile	Glu	Asn	Gln	Pro	Trp	Tyr	Ala
1			5					10						15	
Ala	Ile	Tyr	Ala	His	Thr	Asp	Gly	Gly	Ser	Glu	Tyr	Leu	Arg	Cys	Gly
		20					25					30			
Gly	Ser	Leu	Ile	Ser	Pro	Cys	Trp	Val	Ile	Ser	Ala	Thr	His	Cys	Phe
	35					40					45				
Ile	Pro	Glu	Pro	Lys	Lys	Glu	Asp	Tyr	Ile	Val	Tyr	Leu	Gly	Arg	Ser
50					55					60					
Arg	Leu	Asn	Ser	Asn	Thr	Gln	Gly	Glu	Met	Lys	Phe	Glu	Val	Glu	Asn
65				70					75						80
Leu	Ile	Leu	His	Lys	Asp	Tyr	Ser	Ala	Asp	Glu	Ala	Ala	Gln	His	Asn
			85					90					95		
Asp	Ile	Ala	Leu	Leu	Lys	Ile	Arg	Ser	Lys	Glu	Gly	Arg	Cys	Ala	Gln
		100					105					110			
Pro	Ser	Arg	Thr	Ile	Gln	Thr	Ile	Ser	Leu	Pro	Ser	Met	Tyr	Asn	Asp
	115					120					125				
Pro	Gln	Phe	Gly	Thr	Ser	Cys	Glu	Ile	Thr	Gly	Phe	Gly	Lys	Glu	Asn
130					135					140					
Ser	Thr	Asp	Arg	Leu	Tyr	Pro	Glu	Gln	Leu	Lys	Lys	Thr	Val	Val	Lys
145				150					155						160
Leu	Ile	Ser	His	Arg	Glu	Cys	Gln	Gln	Pro	His	Tyr	Tyr	Gly	Ser	Glu
			165					170					175		
Val	Thr	Thr	Lys	Met	Leu	Cys	Ala	Ala	Asp	Pro	Gln	Trp	Lys	Thr	Asp
		180					185					190			
Ser	Cys	Gln	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Cys	Ser	Leu	Gln	Gly
	195					200					205				
Arg	Met	Thr	Leu	Thr	Gly	Ile	Val	Ser	Trp	Gly	Arg	Gly	Cys	Ala	Leu
210					215					220					
Lys	Asp	Lys	Pro	Gly	Val	Tyr	Thr	Arg	Val	Ser	His	Phe	Leu	Pro	Trp
225				230					235						240
Ile	Arg	Ser	His	Thr	Lys	Glu	Glu	Asn	Gly	Leu	Ala	Leu			
			245					250							

<210> 717
<211> 253

<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36H/H37S/V38E/T39Y/Y40F/V41R/Y60bN/T97a
E/L97bA/H99Q/C122S/N145S/S146V/T147M/D148G/Y149Q/L
150F/M157K

<400> 717
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Trp His Ser Arg Gly Gly Ser Glu Tyr Phe Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Ser
130 135 140
Val Met Gly Gln Phe Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 718
<211> 253
<212> PRT

<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/R36H/H37G/R37aE/V38E/T39F/Y40F/V41R/D60a
P/Y60bS/T97aE/L97bA/H99Q/C122S/Y149R/M157K

<400> 718

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Gln His Gly Glu Gly Gly Ser Glu Phe Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 719
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/R36H/H37G/R37aL/V38E/T39N/Y40F/V41R/D60a
P/Y60bT/T97aE/L97bA/H99Q/C122S/Y149R/M157K

<400> 719
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Gln His Gly Leu Gly Gly Ser Glu Asn Phe Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Pro Thr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 720
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)

protease domain
F30Y/R35E/R36H/H37D/R37aN/V38E/T39Y/Y40F/V41R/Y60b
N/T97aE/L97bA/H99Q/C122S/Y149R/M157K

<400> 720

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Glu His Asp Asn Gly Gly Ser Glu Tyr Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 721
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R36H/H37M/R37aD/V38E/T39G/Y40F/V41R/D60aP/Y60

bE/T97aE/L97bA/H99Q/C122S/Y149R/M157K

<400> 721
```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg His Met Asp Gly Gly Ser Glu Gly Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 722
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36H/H37E/R37aP/V38E/T39Y/Y40F/V41R/Y60b
N/T97aE/L97bA/H99Q/C122S/Y149Q/M157K

<400> 722
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1   5   10   15
Ala Ile Tyr Trp His Glu Pro Gly Gly Ser Glu Tyr Phe Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Gln Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 723
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35Q/R36H/H37D/R37aE/V38E/T39Y/Y40F/V41R/D60a
      E/Y60bG/T97aE/L97bA/H99Q/C122S/Y149R/M157K

<400> 723
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala

```
 1               5                  10                  15
Ala Ile Tyr Gln His Asp Glu Gly Gly Ser Glu Tyr Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Glu Gly Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 724
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Y/R36H/H37P/R37aQ/V38E/T39Y/Y40F/V41R/Y60b
H/T97aE/L97bA/H99Q/C122S/Y149R/M157K

<400> 724

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Tyr His Pro Gln Gly Gly Ser Glu Tyr Phe Arg Cys Gly
```

```
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp His Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 725
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35F/R36H/H37D/R37aD/V38E/T39H/Y40F/V41R/D60a
      P/Y60bA/T97aE/L97bA/H99Q/C122S/Y149R/M157K

<400> 725
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Phe His Asp Asp Gly Gly Ser Glu His Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
```

```
        35                  40                  45
Ile Pro Ala Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 726
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/R36H/H37Y/R37aE/V38E/T39Y/Y40F/V41R/D60a
E/Y60bA/T97aE/L97bA/H99Q/C122S/Y149R/M157K

<400> 726

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Gln His Tyr Glu Gly Gly Ser Glu Tyr Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Glu Ala Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
```

```
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 727
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36H/H37P/R37aD/V38E/T39Y/Y40F/V41R/D60a
E/Y60bS/T97aE/L97bA/H99Q/C122S/Y149R/M157K

<400> 727

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp His Pro Asp Gly Gly Ser Glu Tyr Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Glu Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
```

65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 728
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35Q/R36H/H37G/R37aE/V38E/T39Y/Y40F/V41R/D60a
A/Y60bS/T97aE/L97bA/H99Q/C122S/Y149R/M157K

<400> 728
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Gln His Gly Glu Gly Gly Ser Glu Tyr Phe Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Ala Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn

```
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 729
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35M/R36H/H37G/R37aE/V38E/T39Y/Y40F/V41R/D60a
P/Y60bS/T97aE/L97bA/H99Q/C122S/Y149R/M157K

<400> 729

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Met His Gly Glu Gly Gly Ser Glu Tyr Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
```

```
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 730
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R36H/H37D/R37aE/V38E/T39Y/Y40F/V41R/Y60bN/T97
      aE/L97bA/H99Q/C122S/Y149R/M157K

<400> 730
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg His Asp Glu Gly Gly Ser Glu Tyr Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
```

```
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 731
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R35W/R36H/H37P/R37aQ/V38E/T39Y/Y40F/V41R/Y60b
Q/T97aE/L97bA/H99Q/C122S/Y149R/M157K

<400> 731

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp His Pro Gln Gly Gly Ser Glu Tyr Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
```

```
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 732
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      F30Y/R35W/R36H/H37P/R37aE/V38E/T39Y/Y40F/V41R/Y60b
      A/T97aE/L97bA/H99Q/C122S/Y149R/M157K

<400> 732
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Trp His Pro Glu Gly Gly Ser Glu Tyr Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Ala Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Lys Thr Val Val Lys
```

```
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 733
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aA/Y60bP/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 733

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Ala Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
```

```
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 734
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35L/H37D/R37aS/V38E/T39Y/V41R/D60aP/Y60bD/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 734

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Leu Arg Asp Ser Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
```

```
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 735
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35M/H37G/R37aD/V38E/T39W/V41R/D60aP/Y60bD/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 735

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Met Arg Gly Asp Gly Gly Ser Glu Trp Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
```

```
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 736
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37G/R37aP/V38E/T39Y/V41R/D60aP/Y60bE/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 736

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Gly Pro Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
```

```
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 737
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35A/H37G/R37aE/V38E/T39F/V41R/D60aE/Y60bP/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 737

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Ala Arg Gly Glu Gly Gly Ser Glu Phe Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Glu Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
```

225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 738
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37S/R37aE/V38E/T39Y/V41R/D60aP/Y60bS/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 738
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Gln Arg Ser Glu Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Pro Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu

245 250

<210> 739
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37T/R37aP/V38E/T39Y/V41R/D60aE/Y60bD/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 739
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Gln Arg Thr Pro Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Glu Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 740
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37G/R37aE/V38E/T39H/V41R/D60aP/Y60bA/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 740
```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Gly Glu Gly Gly Ser Glu His Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Ala Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 741

<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35W/H37D/R37aS/V38E/T39Y/V41R/D60aE/Y60bS/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 741
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Trp Arg Asp Ser Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Glu Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 742
<211> 253
<212> PRT

<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37G/R37aE/V38E/T39Y/V41R/D60aP/Y60bT/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 742

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Gly Glu Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Thr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 743
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aG/Y60bS/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 743
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Gly Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 744
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)

protease domain
R35W/H37P/R37aN/V38E/T39Y/V41R/D60aP/Y60bL/D97T/T9
7aE/L97bG/A98S/H99L/C122S

<400> 744
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Trp Arg Pro Asn Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Pro Leu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Thr Glu Gly Ser Leu His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 745
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35W/H37P/R37aN/V38E/T39Y/V41K/D60aP/Y60bD/T97aI/L

97bA/H99Q/C122S/Y151L/Q192A

<400> 745
```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Trp Arg Pro Asn Gly Gly Ser Glu Tyr Tyr Lys Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Ala Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 746
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Y/H37V/R37aW/V38E/T39Y/V41R/D60aP/Y60bE/T97aI/L
97bA/H99Q/C122S/Y151L/Q192T

<400> 746
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Tyr Arg Val Trp Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Pro Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 747
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35W/H37P/R37aN/V38E/T39Y/V41K/D60aP/Y60bD/T97aI/L
      97bA/H99Q/C122S/Y151L/Q192T

<400> 747
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala

```
 1               5                  10                  15
Ala Ile Tyr Trp Arg Pro Asn Gly Gly Ser Glu Tyr Tyr Lys Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 748
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
H37T/R37aL/V38E/T39Y/V41R/D60aP/Y60bD/T97aI/L97bA/
H99Q/C122S/Y151L/Q192R

<400> 748

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg Thr Leu Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
```

```
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Arg Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 749
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35Y/H37S/R37aP/V38E/T39Y/V41R/D60aP/Y60bD/T97aI/L
      97bA/H99Q/C122S/Y151L

<400> 749
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Tyr Arg Ser Pro Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
```

```
        35                  40                  45
Ile Pro Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 750
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Y/H37S/R37aP/V38E/T39Y/V41R/D60aP/Y60bD/T97aI/L
97bA/H99Q/C122S/Y151L/Q192H

<400> 750

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Tyr Arg Ser Pro Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
```

```
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys His Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 751
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35A/H37E/R37aG/V38E/T39Y/V41R/D60aP/Y60bD/T97aI/L
97bA/H99Q/C122S/Y151L

<400> 751

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Ala Arg Glu Gly Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
```

```
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 752
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35W/H37G/R37aE/V38E/T39Y/V41R/D60aP/Y60bD/T97aI/L
97bA/H99Q/C122S/Y151L/Q192T

<400> 752

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Trp Arg Gly Glu Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
```

```
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 753
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Y/H37S/R37aP/V38E/T39Y/V41R/D60aP/Y60bD/T97aI/L
97bA/H99Q/C122S

<400> 753

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Tyr Arg Ser Pro Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
```

```
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 754
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35A/H37T/R37aD/V38E/T39Y/V41R/D60aP/Y60bD/T97aI/L
      97bA/H99Q/C122S/Y151L/Q192S

<400> 754
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Ala Arg Thr Asp Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
```

```
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Ser Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 755
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/L97bR/H99E/C122S/E175D/R217A/K224S

<400> 755
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
```

Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Ala Gly Cys Ala Leu
210 215 220
Lys Asp Ser Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 756
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/L97bR/H99E/C122S/Y172F/E175D/R217E

<400> 756
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Glu His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Phe Gly Ser Asp

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                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 757
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/L97bR/H99Q/C122S/E175D/R217E/K224R

<400> 757
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
```

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Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 758
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/L97bR/H99E/C122S/E175D/R217A/K224Q

<400> 758
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Ala Gly Cys Ala Leu
```

```
    210                 215                 220
Lys Asp Gln Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 759
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/L97bR/H99L/C122S/E175D/R217E/K224S

<400> 759

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Leu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Ser Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
```

```
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 760
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/L97bR/H99E/C122S/E175D/R217E/K224R

<400> 760
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 761
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/L97bR/H99E/C122S/E175D/R217S/K224S

<400> 761
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Glu His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Ser Gly Cys Ala Leu
210 215 220
Lys Asp Ser Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 762
<211> 253

<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/L97bR/H99V/C122S/E175D/R217E/K224N

<400> 762
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Val His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
210 215 220
Lys Asp Asn Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 763
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38D/L97bV/H99L/C122S/E175D/K224S

<400> 763
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Val Ala Leu His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Ser Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 764
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38D/L97bR/H99L/C122S/E175D/R217E

<400> 764
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Leu His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 765
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/L97bG/H99Q/C122S/E175D/R217K/K224A

<400> 765
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15

```
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Lys Gly Cys Ala Leu
    210                 215                 220
Lys Asp Ala Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 766
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain V38D/L97bR/H99E/C122S/E175D/K224A

<400> 766
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
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```
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Ala Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 767
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38D/L97bR/H99E/C122S/E175D/K224S

<400> 767

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
```

```
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Ser Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 768
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38D/L97bV/H99E/C122S/K224S

<400> 768

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Val Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
```

```
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Ser Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 769
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38D/L97bK/H99L/C122S/R217E

<400> 769

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Lys Ala Leu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
```

```
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 770
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/L97bR/H99L/C122S/E175D/R217T/K224S

<400> 770

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Leu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
```

```
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Thr Gly Cys Ala Leu
    210                 215                 220
Lys Asp Ser Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 771
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38D/L97bV/H99L/C122S/K224A

<400> 771

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Val Ala Leu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
```

```
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Ala Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 772
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/L97bR/H99V/C122S/E175D/R217E/K224S

<400> 772

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Val His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
```

Lys Asp Ser Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 773
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38D/L97bG/H99Q/C122S/R217Q

<400> 773
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Gln Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 774
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/V38D/L97bA/H99Q/C122S/Y151L/M157T/Q192H

<400> 774
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Thr Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys His Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 775

<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/V38D/Y40H/V41K/L97bA/H99Q/C122S/Y151K/M157R/Q
192E

<400> 775
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Lys Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Lys Pro Glu Gln Leu Lys Arg Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Glu Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 776
<211> 253
<212> PRT

<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/V38D/Y40H/V41K/L97bA/H99Q/C122S/Y151K/M157S/Q
192E

<400> 776

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Lys Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Lys Pro Glu Gln Leu Lys Ser Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Glu Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 777
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/V38D/Y40H/V41K/L97bA/H99Q/C122S/Y151K/Q192E

<400> 777

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr His Lys Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Lys Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Glu Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 778
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain

F30M/V38D/Y40F/V41R/L97bA/H99Q/C122S/Y151G/Q192T

<400> 778
```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Met Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Gly Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 779
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/V38D/V41R/L97bA/H99Q/C122S/Y151M/M157R/Q192T

<400> 779

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Met Pro Glu Gln Leu Lys Arg Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 780
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30H/V38D/Y40P/V41K/L97bA/H99Q/C122S/Y151H/M157E/Q
192A

<400> 780

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp His Ala
 1               5                  10                  15
```

```
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Pro Lys Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu His Pro Glu Gln Leu Lys Glu Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Ala Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 781
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aH/V38E/T39S/D60aR/Y60bG/T97aE/L97bA/H99Q/C122S
/Y149T/Y151S

<400> 781

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His His Gly Gly Ser Glu Ser Tyr Val Cys Gly
            20                  25                  30
```

```
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Arg Gly Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Thr Leu Ser Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 782
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aH/V38E/T39A/V41R/D60aG/Y60bG/T97aI/L97bA/H99Q/
C122S/Y149V/Y151F/Q192R

<400> 782

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His His Gly Gly Ser Glu Ala Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
```

```
Ile Gly Gly Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Val Leu Phe Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Arg Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 783
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aH/V38E/T39H/V41R/D60aT/Y60bT/T97aI/L97bA/H99Q/
C122S/Y149M/Y151N/Q192T

<400> 783

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His His Gly Gly Ser Glu His Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Thr Thr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
```

```
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Met Leu Asn Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 784
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aH/V38E/T39G/V41A/D60aG/Y60bE/T97aE/L97bA/H99Q/
C122S/Y149R/Y151K/Q192T

<400> 784

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His His Gly Gly Ser Glu Gly Tyr Ala Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Gly Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
```

```
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Lys Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 785
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38E/T39D/V41A/D60aA/Y60bR/T97aE/L97bA/H99Q/C122S/
Y149W/Y151K/Q192T

<400> 785

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Asp Tyr Ala Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Ala Arg Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
```

```
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Trp Leu Lys Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 786
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38E/T39A/V41R/D60aH/Y60bH/T97aI/L97bA/H99Q/C122S/
Y149M/Y151N/Q192T

<400> 786

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Ala Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile His His Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
```

```
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Met Leu Asn Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 787
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38E/T39F/V41R/Y60bN/T97aE/L97bA/H99Q/C122S/Y149A/
Y151G/Q192T

<400> 787

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Phe Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
```

```
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Ala Leu Gly Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 788
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38E/T39D/V41A/D60aS/Y60bR/T97aE/L97bA/H99Q/C122S/
Y149W/Y151K/Q192T

<400> 788

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Asp Tyr Ala Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Ser Arg Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
```

```
Ser Thr Asp Trp Leu Lys Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 789
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R37aH/V38E/V41A/Y60bS/T97aE/L97bA/H99Q/C122S/Y149A
      /Y151M/Q192T

<400> 789
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His His Gly Gly Ser Glu Thr Tyr Ala Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Ala Leu Met Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
```

```
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 790
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R37aH/V38E/T39S/V41A/D60aG/Y60bE/T97aE/L97bA/H99Q/
      C122S/Y149S/Y151H

<400> 790
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His His Gly Gly Ser Glu Ser Tyr Ala Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Gly Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Ser Leu His Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
```

```
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 791
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R37aP/V38E/T39G/V41R/Y60bR/T97aE/L97bA/H99Q/C122S/
      Y149T/Y151P/Q192T

<400> 791
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Pro Gly Gly Ser Glu Gly Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Arg Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Thr Leu Pro Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
```

```
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 792
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37Y/R37aP/V38E/T39Y/V41R/D60aQ/Y60bP/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 792

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Tyr Pro Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Gln Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
```

Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 793
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35N/H37S/R37aE/V38E/T39F/V41R/D60aP/Y60bE/T97aI/L
      97bA/H99Q/C122S/Y149R

<400> 793
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Asn Arg Ser Glu Gly Gly Ser Glu Phe Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Pro Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220

Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 794
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35H/H37P/R37aG/V38E/T39F/V41R/D60aP/Y60bE/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 794
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr His Arg Pro Gly Gly Gly Ser Glu Phe Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Pro Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240

Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 795
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37G/R37aD/V38E/T39Y/V41R/D60aP/Y60bA/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 795
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Gln Arg Gly Asp Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Pro Ala Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 796
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35L/H37D/R37aN/V38E/T39Y/V41R/D60aP/T97aI/L97bA/H
99Q/C122S/Y149R

<400> 796
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Leu Arg Asp Asn Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Pro Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 797
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35N/H37T/R37aY/V38E/T39Y/V41R/D60aP/Y60bE/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 797
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Asn Arg Thr Tyr Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Pro Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 798
<211> 253

<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37D/R37aK/V38E/T39F/V41R/D60aP/Y60bS/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 798
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Gln Arg Asp Lys Gly Gly Ser Glu Phe Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Pro Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 799
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37Y/R37aS/V38E/T39Y/V41R/D60aP/Y60bE/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 799
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Gln Arg Tyr Ser Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Pro Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 800
<211> 253
<212> PRT
<213> Artificial Sequence

<220>

<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37Y/R37aP/V38E/T39Y/V41R/D60aN/Y60bN/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 800
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Gln Arg Tyr Pro Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asn Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 801
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain

R35Q/H37S/R37aP/V38E/T39Y/V41R/D60aP/Y60bE/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 801
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Gln Arg Ser Pro Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Pro Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 802
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Y/H37D/V38E/T39W/V41R/D60aP/Y60bE/T97aI/L97bA/H
99Q/C122S/Y149R

<400> 802
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Tyr Arg Asp Arg Gly Gly Ser Glu Trp Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Pro Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 803
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38E/T39W/V41T/Y60bK/T97aE/L97bA/H99Q/C122S/Y149I/
      Y151G/Q192T

<400> 803

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Trp Tyr Thr Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Lys Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Ile Leu Gly Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 804
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38E/T39W/V41T/D60aP/Y60bQ/T97aE/L97bA/H99Q/C122S/
Y149V/Y151G/Q192T

<400> 804

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
```

```
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Trp Tyr Thr Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Val Leu Gly Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 805
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38E/T39W/V41T/D60aP/Y60bW/T97aI/L97bA/H99Q/C122S/
Y149L/Y151G/Q192T

<400> 805

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Trp Tyr Thr Cys Gly
            20                  25                  30
```

```
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Trp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Leu Leu Gly Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 806
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38E/T39W/V41Q/Y60bE/T97aE/L97bA/H99Q/C122S/Y149I/
Y151G/Q192T

<400> 806

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Trp Tyr Gln Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
```

```
Ile Asp Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Ile Leu Gly Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 807
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38E/T39L/V41R/D60aP/Y60bD/T97aI/L97bA/H99Q/C122S/
Y149V/Y151L/Q192T

<400> 807

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Leu Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
```

```
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Val Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 808
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38D/L97bR/H99M/C122S/E175D/R217E

<400> 808

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Met His Asn
                85                  90                  95
```

```
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 809
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/L97bR/H99M/C122S/E175D/R217E/K224R

<400> 809

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Met His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
```

```
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 810
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38D/L97bR/C122S/E175D/R217E/K224R

<400> 810

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala His His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
```

```
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 811
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/L97bR/H99L/C122S/E175D/R217E/K224R

<400> 811

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Leu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
```

```
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 812
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain V38D/L97bT/H99L/C122S/E175D/R217K

<400> 812
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Thr Ala Leu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
```

Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Lys Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 813
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain V38D/L97bR/H99L/C122S/E175D/K224A

<400> 813
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Leu His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Ala Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240

Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 814
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38D/L97bM/H99S/C122S/K224S

<400> 814
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Met Ala Ser His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Ser Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 815
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38D/L97bK/H99L/C122S/E175D/K224A

<400> 815
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Lys Ala Leu His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Ala Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 816
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/L97bR/H99V/C122S/E175D/R217E/K224R

<400> 816
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Val His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
210 215 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 817
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)

protease domain V38D/L97bT/H99E/C122S/E175D/K224S

<400> 817
```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Thr Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Ser Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 818
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41R/Y60bK/T97aS/L97bR/H99E/C122S/Y151L/E175D
/Q192T/R217E/K224R

<400> 818
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Lys Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ser Arg Ala Glu His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210   215   220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 819
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/V41Q/D60aK/Y60bD/T97aA/L97bR/H99E/C122S/Y151L
      /E175D/Q192Y/R217E/K224R

<400> 819
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala

```
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Gln Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Lys Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ala Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Tyr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 820
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41Q/D60aP/Y60bS/T97aS/L97bR/H99E/C122S/Y151L
/E175D/Q192Y/R217E/K224R

<400> 820

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Gln Cys Gly
```

```
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ser Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Tyr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 821
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41R/Y60bR/T97aW/L97bR/H99E/C122S/E175D/R217E
/K224R

<400> 821

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
```

```
        35                  40                  45
Ile Asp Arg Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Trp Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 822
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41R/Y60bS/T97aI/L97bR/H99E/C122S/Y151L/E175D
/Q192F/R217E/K224R

<400> 822

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
```

```
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Phe Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 823
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41L/Y60bP/T97aM/L97bR/H99E/C122S/Y151L/E175D
/R217E/K224R

<400> 823

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
```

```
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Met Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 824
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41Q/D60aH/Y60bS/T97aW/L97bR/H99E/C122S/Y151L
/E175D/R217E/K224R

<400> 824

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Gln Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile His Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Trp Arg Ala Glu His Asn
```

```
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 825
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41K/D60aN/Y60bN/L97bR/H99E/C122S/Y151L/E175D
/Q192H/R217E/K224R

<400> 825

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Lys Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asn Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
```

```
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys His Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 826
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/V41Q/Y60bR/T97aW/L97bR/H99E/C122S/Y151L/E175D
      /Q192T/R217E/K224R

<400> 826
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Gln Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Arg Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Trp Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
```

```
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 827
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/V41L/L97bG/H99Q/C122S/Y151L/R217Q

<400> 827
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
```

```
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Gln Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 828
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/V41Q/L97bG/H99Q/C122S/Y151L/Q192S/R217A

<400> 828
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Gln Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
```

```
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Ser Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Ala Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 829
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R37aS/V38D/V41Q/L97bG/H99Q/C122S/Y151L/R217T

<400> 829
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Ser Gly Gly Ser Asp Thr Tyr Gln Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
```

```
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Thr Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 830
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/V41R/L97bG/H99Q/C122S/Y151L/R217A

<400> 830
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Ala Gly Cys Ala Leu
```

    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 831
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/V41R/L97bG/H99Q/C122S/Y151L/R217E

<400> 831
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240

Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 832
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/V38D/V41R/T97aS/L97bA/H99Q/C122S/Y151L

<400> 832
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Gln Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ser Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 833
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41Q/L97bG/H99Q/C122S/Y151L/R217T

<400> 833
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Gln Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Thr Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 834
<211> 253

<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/V38D/V41R/L97bG/H99Q/C122S/Y151L

<400> 834

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 835
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35S/V38D/V41R/L97bA/H99Q/C122S/Y151L

<400> 835
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Ser Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 836
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain

R35S/V38D/V41L/L97bG/H99Q/C122S/Y151L/R217Q

<400> 836
```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Ser Arg His Arg Gly Gly Ser Asp Thr Tyr Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Gln Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 837
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41R/L97bG/H99Q/C122S/Y151L/Q192S/R217A

<400> 837

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Ser Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Ala Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 838
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35S/V38D/Y40Q/V41R/Y60bS/L97bG/H99Q/C122S

<400> 838

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Ser Arg His Arg Gly Gly Ser Asp Thr Gln Arg Cys Gly
```

```
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 839
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35K/V38D/Y40H/V41R/Y60bS/L97bG/H99Q/C122S

<400> 839

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Lys Arg His Arg Gly Gly Ser Asp Thr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
```

```
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 840
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/V38D/Y40L/V41L/Y60bP/L97bG/H99Q/C122S

<400> 840

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg His Arg Gly Gly Ser Asp Thr Leu Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
```

65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 841
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35S/V38D/Y40H/V41L/Y60bD/L97bG/H99Q/C122S

<400> 841
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Ser Arg His Arg Gly Gly Ser Asp Thr His Leu Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
85 90 95

```
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 842
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/V41R/Y60bN/T97aL/L97bR/H99E/C122S/Y151L/E175D
      /Q192T/R217E/K224R

<400> 842
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Leu Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
```

```
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 843
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41Q/Y60bR/T97aF/L97bR/H99Q/C122S/Y151L/E175D
/Q192H/R217E/K224R

<400> 843

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Gln Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Arg Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Phe Arg Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
```

```
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys His Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 844
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41R/D60aP/Y60bD/T97aP/L97bR/H99Q/C122S/Y151L
/E175D/Q192R/R217E/K224R

<400> 844

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Pro Arg Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
```

Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Arg Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
210 215 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 845
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41Q/Y60bP/T97aW/L97bR/H99Q/C122S/Y151L/E175D
/Q192K/R217E/K224R

<400> 845
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Gln Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Trp Arg Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160

```
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Lys Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 846
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R37aS/V38D/V41R/Y60bT/T97aD/L97bR/H99Q/C122S/Y151L
      /E175D/Q192A/R217E/K224R

<400> 846
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Ser Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Thr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Asp Arg Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
```

```
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Ala Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 847
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/V41K/D60aE/Y60bP/T97aA/L97bR/H99L/C122S/Y151L
      /E175D/Q192R/R217E/K224R

<400> 847
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Lys Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Glu Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ala Arg Ala Leu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
```

```
Ser Cys Arg Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 848
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R37aS/V38D/V41R/D60aS/Y60bP/L97bR/H99Q/C122S/Y151L
      /E175D/Q192R/R217E/K224R

<400> 848
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Ser Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Ser Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Arg Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
```

Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210   215   220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 849
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/V41R/Y60bR/L97bR/H99E/C122S/Y151L/E175D/Q192T
      /R217E/K224R

<400> 849
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Arg Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Glu His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210   215   220

Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 850
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41R/D60aP/Y60bD/T97aW/L97bR/H99Q/C122S/Y151L
/E175D/Q192A/R217E/K224R

<400> 850
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Pro Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Trp Arg Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Ala Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
210 215 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240

Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 851
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41Q/D60aN/Y60bP/L97bR/H99L/C122S/Y151L/E175D
/Q192R/R217E/K224R

<400> 851
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Gln Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asn Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Leu His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Arg Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
210 215 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 852
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41Q/D60aN/Y60bP/T97aN/L97bR/H99I/C122S/Y151L
/E175D/Q192R/R217E/K224R

<400> 852
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Gln Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asn Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Asn Arg Ala Ile His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Arg Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
210 215 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 853
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41Q/Y60bP/T97aY/L97bR/H99L/C122S/Y151L/E175D
/Q192K/R217E/K224R

<400> 853
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Gln Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Tyr Arg Ala Leu His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Lys Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
210 215 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 854
<211> 253

<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41R/Y60bR/L97bR/H99L/C122S/Y151L/E175D/Q192T
/R217E/K224R

<400> 854
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Arg Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Leu His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
210 215 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 855
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41R/Y60bR/L97bR/H99L/C122S/Y151L/E175D/Q192Y
/R217E/K224R

<400> 855
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Arg Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Leu His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Tyr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
210 215 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 856
<211> 253
<212> PRT
<213> Artificial Sequence

<220>

<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain V38D/V41R/L97bT/C122S/Y151F/R217E

<400> 856
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Thr Ala His His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Phe Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 857
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41K/L97bA/H99L/C122S/Y151R/R217E

<400> 857
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Lys Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Leu His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Arg Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 858
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/V41R/L97bN/H99E/C122S/E175D/Q192M/R217E

<400> 858
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15

```
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Asn Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Met Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 859
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36H/V38D/T97aR/L97bG/H99Q/C122S/E175F

<400> 859

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
```

```
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Arg Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Phe
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 860
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35S/V38D/V41L/D60aP/Y60bW/L97bG/H99Q/C122S

<400> 860

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Ser Arg His Arg Gly Gly Ser Asp Thr Tyr Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Trp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
```

Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 861
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41R/D60aQ/Y60bP/L97bG/H99Q/C122S

<400> 861
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Gln Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn

```
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 862
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/V38D/Y40H/V41L/Y60bD/L97bG/H99Q/C122S

<400> 862

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg His Arg Gly Gly Ser Asp Thr His Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
```

```
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 863
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R37aS/V38D/V41R/D60aT/Y60bN/L97bG/H99Q/C122S

<400> 863
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Ser Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Thr Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
```

```
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 864
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35K/V38D/Y40H/Y60bP/L97bG/H99Q/C122S

<400> 864
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Lys Arg His Arg Gly Gly Ser Asp Thr His Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
```

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Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 865
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35Q/V38D/Y40M/V41R/Y60bA/L97bG/H99Q/C122S

<400> 865
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg His Arg Gly Gly Ser Asp Thr Met Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Ala Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
```

```
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 866
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35K/V38D/Y40F/V41R/Y60bT/L97bG/H99Q/C122S

<400> 866
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Lys Arg His Arg Gly Gly Ser Asp Thr Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Thr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
```

Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 867
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35Q/V38D/Y40F/V41T/Y60bP/L97bG/H99Q/C122S

<400> 867
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Gln Arg His Arg Gly Gly Ser Asp Thr Phe Thr Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp

225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 868
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/T39W/Y40L/V41R/T97aL/L97bA/H99Q/C122S

<400> 868
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Trp Leu Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Leu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 869
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/T39F/Y40L/V41R/T97aW/L97bA/H99Q/C122S

<400> 869
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Phe Leu Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Trp Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 870

<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/T39Y/Y40Q/V41L/T97aY/L97bA/H99Q/C122S

<400> 870

Ile	Ile	Gly	Gly	Glu	Phe	Thr	Thr	Ile	Glu	Asn	Gln	Pro	Trp	Phe	Ala
1				5				10						15	
Ala	Ile	Tyr	Arg	Arg	His	Arg	Gly	Gly	Ser	Asp	Tyr	Gln	Leu	Cys	Gly
			20					25					30		
Gly	Ser	Leu	Ile	Ser	Pro	Cys	Trp	Val	Ile	Ser	Ala	Thr	His	Cys	Phe
		35					40					45			
Ile	Asp	Tyr	Pro	Lys	Lys	Glu	Asp	Tyr	Ile	Val	Tyr	Leu	Gly	Arg	Ser
	50					55					60				
Arg	Leu	Asn	Ser	Asn	Thr	Gln	Gly	Glu	Met	Lys	Phe	Glu	Val	Glu	Asn
65					70					75					80
Leu	Ile	Leu	His	Lys	Asp	Tyr	Ser	Ala	Asp	Tyr	Ala	Ala	Gln	His	Asn
				85					90					95	
Asp	Ile	Ala	Leu	Leu	Lys	Ile	Arg	Ser	Lys	Glu	Gly	Arg	Cys	Ala	Gln
			100					105					110		
Pro	Ser	Arg	Thr	Ile	Gln	Thr	Ile	Ser	Leu	Pro	Ser	Met	Tyr	Asn	Asp
		115					120					125			
Pro	Gln	Phe	Gly	Thr	Ser	Cys	Glu	Ile	Thr	Gly	Phe	Gly	Lys	Glu	Asn
	130					135					140				
Ser	Thr	Asp	Tyr	Leu	Tyr	Pro	Glu	Gln	Leu	Lys	Met	Thr	Val	Val	Lys
145					150					155					160
Leu	Ile	Ser	His	Arg	Glu	Cys	Gln	Gln	Pro	His	Tyr	Tyr	Gly	Ser	Glu
				165					170					175	
Val	Thr	Thr	Lys	Met	Leu	Cys	Ala	Ala	Asp	Pro	Gln	Trp	Lys	Thr	Asp
			180					185					190		
Ser	Cys	Gln	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Cys	Ser	Leu	Gln	Gly
		195					200					205			
Arg	Met	Thr	Leu	Thr	Gly	Ile	Val	Ser	Trp	Gly	Arg	Gly	Cys	Ala	Leu
	210					215					220				
Lys	Asp	Lys	Pro	Gly	Val	Tyr	Thr	Arg	Val	Ser	His	Phe	Leu	Pro	Trp
225					230					235					240
Ile	Arg	Ser	His	Thr	Lys	Glu	Glu	Asn	Gly	Leu	Ala	Leu			
				245					250						

<210> 871
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aS/V38D/T39Y/Y40M/V41R/T97aL/L97bA/H99Q/C122S

<400> 871
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Ser Gly Gly Ser Asp Tyr Met Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Leu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 872
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)

protease domain
V38D/T39L/Y40L/V41R/T97aV/L97bA/H99Q/C122S

<400> 872
```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Leu Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Val Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 873
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/T39L/Y40L/V41R/T97aI/L97bA/H99Q/C122S

<400> 873
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Leu Leu Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 874
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/T39L/Y40L/V41R/T97aW/L97bA/H99Q/C122S

<400> 874
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15

```
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Leu Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Trp Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 875
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/T39Y/Y40H/V41R/T97aI/L97bA/H99Q/C122S

<400> 875
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Tyr His Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
```

```
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 876
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/T39Y/Y40L/V41R/T97aW/L97bA/H99Q/C122S

<400> 876

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Tyr Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
```

```
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Trp Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 877
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/T39Y/Y40M/V41R/T97aW/L97bA/H99Q/C122S

<400> 877

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Tyr Met Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Trp Ala Ala Gln His Asn
```

```
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 878
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/T39Y/Y40L/V41R/T97aE/L97bA/H99Q/C122S

<400> 878

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Tyr Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
```

```
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 879
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/T39Y/Y40M/V41R/T97aE/L97bA/H99Q/C122S

<400> 879
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Tyr Met Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
```

```
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 880
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35S/V38D/V41T/L97bR/H99Q/C122S/Y151L/R217E

<400> 880
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Ser Arg His Arg Gly Gly Ser Asp Thr Tyr Thr Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
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Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 881
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/V41R/L97bR/H99Q/C122S/Y151L/R217E

<400> 881
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
```

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            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 882
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41R/L97bR/H99E/C122S/Y151L/R217E

<400> 882

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
```

```
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 883
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35H/V38D/V41Q/L97bR/H99Q/C122S/Y151L/R217V

<400> 883

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr His Arg His Arg Gly Gly Ser Asp Thr Tyr Gln Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
```

225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 884
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/V41R/L97bR/H99Q/C122S/Y151L/R217V

<400> 884
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 885
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aS/V38D/V41R/L97bR/H99Q/C122S/Y151L/Q192T/R217V

<400> 885
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Ser Gly Gly Ser Asp Thr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 886

<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/T39Y/Y40L/V41K/L97bR/H99L/C122S/E175D

<400> 886

Ile	Ile	Gly	Gly	Glu	Phe	Thr	Thr	Ile	Glu	Asn	Gln	Pro	Trp	Phe	Ala
1				5				10						15	
Ala	Ile	Tyr	Arg	Arg	His	Arg	Gly	Gly	Ser	Asp	Tyr	Leu	Lys	Cys	Gly
			20					25					30		
Gly	Ser	Leu	Ile	Ser	Pro	Cys	Trp	Val	Ile	Ser	Ala	Thr	His	Cys	Phe
		35					40					45			
Ile	Asp	Tyr	Pro	Lys	Lys	Glu	Asp	Tyr	Ile	Val	Tyr	Leu	Gly	Arg	Ser
	50					55					60				
Arg	Leu	Asn	Ser	Asn	Thr	Gln	Gly	Glu	Met	Lys	Phe	Glu	Val	Glu	Asn
65					70					75					80
Leu	Ile	Leu	His	Lys	Asp	Tyr	Ser	Ala	Asp	Thr	Arg	Ala	Leu	His	Asn
				85					90					95	
Asp	Ile	Ala	Leu	Leu	Lys	Ile	Arg	Ser	Lys	Glu	Gly	Arg	Cys	Ala	Gln
			100					105					110		
Pro	Ser	Arg	Thr	Ile	Gln	Thr	Ile	Ser	Leu	Pro	Ser	Met	Tyr	Asn	Asp
		115					120					125			
Pro	Gln	Phe	Gly	Thr	Ser	Cys	Glu	Ile	Thr	Gly	Phe	Gly	Lys	Glu	Asn
	130					135					140				
Ser	Thr	Asp	Tyr	Leu	Tyr	Pro	Glu	Gln	Leu	Lys	Met	Thr	Val	Val	Lys
145					150					155					160
Leu	Ile	Ser	His	Arg	Glu	Cys	Gln	Gln	Pro	His	Tyr	Tyr	Gly	Ser	Asp
				165					170					175	
Val	Thr	Thr	Lys	Met	Leu	Cys	Ala	Ala	Asp	Pro	Gln	Trp	Lys	Thr	Asp
			180					185					190		
Ser	Cys	Gln	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Cys	Ser	Leu	Gln	Gly
		195					200					205			
Arg	Met	Thr	Leu	Thr	Gly	Ile	Val	Ser	Trp	Gly	Arg	Gly	Cys	Ala	Leu
	210					215					220				
Lys	Asp	Lys	Pro	Gly	Val	Tyr	Thr	Arg	Val	Ser	His	Phe	Leu	Pro	Trp
225					230					235					240
Ile	Arg	Ser	His	Thr	Lys	Glu	Glu	Asn	Gly	Leu	Ala	Leu			
				245					250						

<210> 887
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37G/R37aN/V38F/T39H/V41Q/Y60bR/T97aL/L97bR/H
99E/C122S/Y151L/E175D/Q192T/R217E/K224R

<400> 887
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Gln Arg Gly Asn Gly Gly Ser Phe His Tyr Gln Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Arg Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Leu Arg Ala Glu His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
210 215 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 888
<211> 253
<212> PRT
<213> Artificial Sequence

<220>

<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
H37N/R37aD/V38Y/T39F/V41Q/Y60bR/T97aW/L97bR/H99E/C
122S/Y151L/E175D/Q192T/R217E/K224R

<400> 888
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg Asn Asp Gly Gly Ser Tyr Phe Tyr Gln Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Arg Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Trp Arg Ala Glu His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
210 215 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 889
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain

H37A/R37aE/V38F/T39L/V41Q/Y60bR/T97aF/L97bR/H99E/C
122S/Y151L/E175D/Q192T/R217E/K224R

<400> 889
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg Ala Glu Gly Gly Ser Phe Leu Tyr Gln Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Arg Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Phe Arg Ala Glu His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210   215   220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 890
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35K/H37G/R37aE/G37bS/V38F/T39H/V41Q/Y60bR/T97aW/L
97bR/H99E/C122S/Y151L/E175D/Q192T/R217E/K224R

<400> 890
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Lys Arg Gly Glu Ser Gly Ser Phe His Tyr Gln Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Arg Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Trp Arg Ala Glu His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210   215   220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 891
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      H37A/R37aE/V38F/T39L/V41Q/Y60bR/T97aW/L97bR/H99E/C
      122S/Y151L/E175D/Q192T/R217E/K224R

<400> 891

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg Ala Glu Gly Gly Ser Phe Leu Tyr Gln Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Arg Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Trp Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 892
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
H37N/R37aE/V38F/T39L/V41Q/Y60bR/T97aW/L97bR/H99E/C
122S/Y151L/E175D/Q192T/R217E/K224R

<400> 892

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
```

```
Ala Ile Tyr Arg Arg Asn Glu Gly Gly Ser Phe Leu Tyr Gln Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Arg Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Trp Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 893
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35G/H37T/R37aE/V38T/T39Y/V41Q/Y60bR/T97aF/L97bR/H
99E/C122S/Y151L/E175D/Q192T/R217E/K224R

<400> 893

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gly Arg Thr Glu Gly Gly Ser Thr Tyr Tyr Gln Cys Gly
            20                  25                  30
```

```
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Arg Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Phe Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 894
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35K/H37S/R37aE/V38F/T39Y/V41Q/Y60bR/T97aL/L97bR/H
99E/C122S/Y151L/E175D/Q192T/R217E/K224R

<400> 894

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Lys Arg Ser Glu Gly Gly Ser Phe Tyr Tyr Gln Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
```

```
Ile Asp Arg Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Leu Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 895
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
H37A/R37aE/V38Y/T39Y/V41Q/Y60bR/T97aV/L97bR/H99E/C
122S/Y151L/E175D/Q192T/R217E/K224R

<400> 895

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg Ala Glu Gly Gly Ser Tyr Tyr Tyr Gln Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Arg Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
```

```
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Val Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 896
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
H37D/R37aD/V38Y/T39Y/V41Q/Y60bR/T97aL/L97bR/H99E/C
122S/Y151L/E175D/Q192T/R217E/K224R

<400> 896

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg Asp Asp Gly Gly Ser Tyr Tyr Tyr Gln Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Arg Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
```

```
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Leu Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 897
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
H37A/R37aD/V38Y/T39Y/V41Q/Y60bR/T97aD/L97bR/H99E/C
122S/Y151L/E175D/Q192T/R217E/K224R

<400> 897

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg Ala Asp Gly Gly Ser Tyr Tyr Tyr Gln Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Arg Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Asp Arg Ala Glu His Asn
                85                  90                  95
```

```
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 898
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
H37S/R37aD/V38H/T39L/V41Q/Y60bR/T97aW/L97bR/H99E/C
122S/Y151L/E175D/Q192T/R217E/K224R

<400> 898

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg Ser Asp Gly Gly Ser His Leu Tyr Gln Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Arg Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Trp Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
```

```
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 899
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
H37G/R37aD/V38Y/T39H/V41Q/Y60bR/T97aD/L97bR/H99E/C
122S/Y151L/E175D/Q192T/R217E/K224R

<400> 899

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg Gly Asp Gly Gly Ser Tyr His Tyr Gln Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Arg Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Asp Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
```

```
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 900
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
H37G/R37aD/G37bD/V38F/T39H/V41R/Y60bK/T97aS/L97bR/
H99E/C122S/Y151L/E175D/Q192T/R217E/K224R

<400> 900

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg Gly Asp Asp Gly Ser Phe His Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Lys Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ser Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
```

```
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 901
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35Q/H37G/R37aE/V38Y/T39H/V41R/Y60bK/T97aS/L97bR/H
      99E/C122S/Y151L/E175D/Q192T/R217E/K224R

<400> 901
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Gly Glu Gly Gly Ser Tyr His Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Lys Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ser Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
```

```
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 902
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35K/H37A/R37aE/V38H/T39Y/V41R/Y60bK/T97aS/L97bR/H
      99E/C122S/Y151L/E175D/Q192T/R217E/K224R

<400> 902
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Lys Arg Ala Glu Gly Gly Ser His Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Lys Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ser Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
```

Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210   215   220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 903
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35Q/H37G/R37aE/V38Y/T39F/V41R/Y60bK/T97aS/L97bR/H
      99E/C122S/Y151L/E175D/Q192T/R217E/K224R

<400> 903
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Gln Arg Gly Glu Gly Gly Ser Tyr Phe Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Lys Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ser Arg Ala Glu His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190

```
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 904
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35Q/H37G/R37aE/V38W/T39Y/V41R/Y60bK/T97aS/L97bR/H
      99E/C122S/Y151L/E175D/Q192T/R217E/K224R

<400> 904
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Gly Glu Gly Gly Ser Trp Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Lys Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ser Arg Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Asp
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Thr Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
```

```
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Arg Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 905
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R36L/V38D/T39R/Y40L/V41T/L97bD/H99P/C122S/R217S

<400> 905
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Leu His Arg Gly Gly Ser Asp Arg Leu Thr Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Asp Ala Pro His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Ser Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
```

225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 906
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/T39V/V41R/L97bV/H99E/C122S/R217E

<400> 906
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Val Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Val Ala Glu His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 907
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aH/V38D/T39M/Y40A/V41K/L97bR/H99Q/C122S/R217E

<400> 907
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His His Gly Gly Ser Asp Met Ala Lys Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 908

<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36S/V38D/T39H/Y40L/V41R/L97bV/H99V/C122S/R217Q

<400> 908

Ile	Ile	Gly	Gly	Glu	Phe	Thr	Thr	Ile	Glu	Asn	Gln	Pro	Trp	Phe	Ala
1			5					10						15	
Ala	Ile	Tyr	Arg	Ser	His	Arg	Gly	Gly	Ser	Asp	His	Leu	Arg	Cys	Gly
		20					25					30			
Gly	Ser	Leu	Ile	Ser	Pro	Cys	Trp	Val	Ile	Ser	Ala	Thr	His	Cys	Phe
	35					40					45				
Ile	Asp	Tyr	Pro	Lys	Lys	Glu	Asp	Tyr	Ile	Val	Tyr	Leu	Gly	Arg	Ser
	50				55					60					
Arg	Leu	Asn	Ser	Asn	Thr	Gln	Gly	Glu	Met	Lys	Phe	Glu	Val	Glu	Asn
65				70					75					80	
Leu	Ile	Leu	His	Lys	Asp	Tyr	Ser	Ala	Asp	Thr	Val	Ala	Val	His	Asn
			85					90					95		
Asp	Ile	Ala	Leu	Leu	Lys	Ile	Arg	Ser	Lys	Glu	Gly	Arg	Cys	Ala	Gln
		100					105					110			
Pro	Ser	Arg	Thr	Ile	Gln	Thr	Ile	Ser	Leu	Pro	Ser	Met	Tyr	Asn	Asp
	115					120					125				
Pro	Gln	Phe	Gly	Thr	Ser	Cys	Glu	Ile	Thr	Gly	Phe	Gly	Lys	Glu	Asn
	130				135					140					
Ser	Thr	Asp	Tyr	Leu	Tyr	Pro	Glu	Gln	Leu	Lys	Met	Thr	Val	Val	Lys
145				150					155					160	
Leu	Ile	Ser	His	Arg	Glu	Cys	Gln	Gln	Pro	His	Tyr	Tyr	Gly	Ser	Glu
			165					170					175		
Val	Thr	Thr	Lys	Met	Leu	Cys	Ala	Ala	Asp	Pro	Gln	Trp	Lys	Thr	Asp
		180					185					190			
Ser	Cys	Gln	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Cys	Ser	Leu	Gln	Gly
	195					200					205				
Arg	Met	Thr	Leu	Thr	Gly	Ile	Val	Ser	Trp	Gly	Gln	Gly	Cys	Ala	Leu
	210				215					220					
Lys	Asp	Lys	Pro	Gly	Val	Tyr	Thr	Arg	Val	Ser	His	Phe	Leu	Pro	Trp
225				230					235					240	
Ile	Arg	Ser	His	Thr	Lys	Glu	Glu	Asn	Gly	Leu	Ala	Leu			
			245					250							

<210> 909
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36S/V38D/T39K/Y40F/V41R/L97bN/H99E/C122S/R217S

<400> 909
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Ser His Arg Gly Gly Ser Asp Lys Phe Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Asn Ala Glu His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Ser Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 910
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)

protease domain
V38D/T39K/Y40F/V41Q/L97bI/H99S/C122S/R217T

<400> 910

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Lys Phe Gln Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ile Ala Ser His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Thr Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 911
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36H/V38D/T39R/Y40F/V41R/H99S/C122S/R217T

<400> 911
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg His His Arg Gly Gly Ser Asp Arg Phe Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala Ser His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Thr Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 912
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R37aP/V38D/T39Y/V41R/L97bV/H99Q/C122S/R217T

<400> 912
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15

```
Ala Ile Tyr Arg Arg His Pro Gly Gly Ser Asp Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Val Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Thr Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 913
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36S/V38D/T39K/Y40M/V41K/L97bI/C122S/R217E

<400> 913

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Ser His Arg Gly Gly Ser Asp Lys Met Lys Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
```

```
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ile Ala His His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 914
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/T39H/Y40F/V41K/L97bM/H99T/C122S/R217E

<400> 914

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp His Phe Lys Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
```

```
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Met Ala Thr His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 915
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36S/V38D/T39K/Y40M/V41K/L97bH/H99T/C122S/R217S

<400> 915

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Ser His Arg Gly Gly Ser Asp Lys Met Lys Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr His Ala Thr His Asn
```

```
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Ser Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 916
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/T39L/Y40L/V41K/L97bH/H99L/C122S/R217A

<400> 916

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Leu Leu Lys Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr His Ala Leu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
```

```
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Ala Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 917
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38D/T39F/Y40L/V41K/L97bT/H99S/C122S/R217T

<400> 917

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Phe Leu Lys Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Thr Ala Ser His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
```

```
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Thr Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 918
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36S/V38D/T39A/V41R/L97bV/H99S/C122S/R217T

<400> 918

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Ser His Arg Gly Gly Ser Asp Ala Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Val Ala Ser His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
```

Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Thr Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 919
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R37aH/V38D/T39R/Y40F/L97bT/C122S/R217E

<400> 919
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His His Gly Gly Ser Asp Arg Phe Val Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Thr Ala His His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp

```
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 920
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36S/V38D/T39K/Y40F/V41R/L97bI/H99E/C122S/R217S

<400> 920

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Ser His Arg Gly Gly Ser Asp Lys Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ile Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
```

```
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Ser Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 921
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36S/V38D/T39A/Y40F/V41R/L97bA/H99E/C122S/R217T

<400> 921

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Ser His Arg Gly Gly Ser Asp Ala Phe Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Thr Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
```

225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 922
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35Q/H37Y/R37aE/V38E/T39Y/V41R/L97bG/H99S/C122S

<400> 922
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Ser His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 923
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aS/V38D/T39L/Y40L/V41R/L97bM/H99L/C122S/R217S

<400> 923
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Ser Gly Gly Ser Asp Leu Leu Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Met Ala Leu His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Ser Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 924

<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36S/V38D/T39L/Y40L/V41R/L97bI/H99E/C122S/R217T

<400> 924

Ile	Ile	Gly	Gly	Glu	Phe	Thr	Thr	Ile	Glu	Asn	Gln	Pro	Trp	Phe	Ala
1			5					10						15	
Ala	Ile	Tyr	Arg	Ser	His	Arg	Gly	Gly	Ser	Asp	Leu	Leu	Arg	Cys	Gly
		20					25					30			
Gly	Ser	Leu	Ile	Ser	Pro	Cys	Trp	Val	Ile	Ser	Ala	Thr	His	Cys	Phe
	35					40					45				
Ile	Asp	Tyr	Pro	Lys	Lys	Glu	Asp	Tyr	Ile	Val	Tyr	Leu	Gly	Arg	Ser
	50				55					60					
Arg	Leu	Asn	Ser	Asn	Thr	Gln	Gly	Glu	Met	Lys	Phe	Glu	Val	Glu	Asn
65				70					75					80	
Leu	Ile	Leu	His	Lys	Asp	Tyr	Ser	Ala	Asp	Thr	Ile	Ala	Glu	His	Asn
			85					90					95		
Asp	Ile	Ala	Leu	Leu	Lys	Ile	Arg	Ser	Lys	Glu	Gly	Arg	Cys	Ala	Gln
		100					105					110			
Pro	Ser	Arg	Thr	Ile	Gln	Thr	Ile	Ser	Leu	Pro	Ser	Met	Tyr	Asn	Asp
	115					120					125				
Pro	Gln	Phe	Gly	Thr	Ser	Cys	Glu	Ile	Thr	Gly	Phe	Gly	Lys	Glu	Asn
	130				135					140					
Ser	Thr	Asp	Tyr	Leu	Tyr	Pro	Glu	Gln	Leu	Lys	Met	Thr	Val	Val	Lys
145				150					155					160	
Leu	Ile	Ser	His	Arg	Glu	Cys	Gln	Gln	Pro	His	Tyr	Tyr	Gly	Ser	Glu
			165					170					175		
Val	Thr	Thr	Lys	Met	Leu	Cys	Ala	Ala	Asp	Pro	Gln	Trp	Lys	Thr	Asp
		180					185					190			
Ser	Cys	Gln	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Cys	Ser	Leu	Gln	Gly
	195					200					205				
Arg	Met	Thr	Leu	Thr	Gly	Ile	Val	Ser	Trp	Gly	Thr	Gly	Cys	Ala	Leu
	210				215					220					
Lys	Asp	Lys	Pro	Gly	Val	Tyr	Thr	Arg	Val	Ser	His	Phe	Leu	Pro	Trp
225				230					235					240	
Ile	Arg	Ser	His	Thr	Lys	Glu	Glu	Asn	Gly	Leu	Ala	Leu			
			245					250							

<210> 925
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aS/V38D/T39Y/Y40F/V41R/H99L/C122S/R217T

<400> 925
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Ser Gly Gly Ser Asp Tyr Phe Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala Leu His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Thr Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 926
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)

protease domain
V38D/T39Y/Y40L/V41R/L97bI/H99E/C122S/R217E

<400> 926

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Tyr Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ile Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 927
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aP/V38D/T39L/Y40I/V41R/H99L/C122S/R217Q

<400> 927
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Arg His Pro Gly Gly Ser Asp Leu Ile Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala Leu His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Gln Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 928
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38D/T39V/Y40L/V41S/H99V/C122S/R217V

<400> 928
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15

```
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Asp Val Leu Ser Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala Val His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 929
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R37aS/V38D/T39V/V41E/L97bG/H99Q/C122S/R217T

<400> 929
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Ser Gly Gly Ser Asp Val Tyr Glu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
```

```
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Thr Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 930
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36S/V38D/T39S/V41R/L97bI/H99E/C122S/R217T

<400> 930

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Ser His Arg Gly Gly Ser Asp Ser Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
```

```
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ile Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Thr Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 931
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aS/V38D/T39G/V41R/L97bM/H99E/C122S/R217S

<400> 931

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Ser Gly Gly Ser Asp Gly Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Met Ala Glu His Asn
```

```
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Ser Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 932
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aS/V38D/T39Y/V41R/L97bI/H99E/C122S/R217T

<400> 932

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Ser Gly Gly Ser Asp Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ile Ala Glu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
```

```
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Thr Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 933
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35E/R37aD/V38E/Y40Q/V41L/Y60bN/L97bA/H99Q/C122S/Y
149R

<400> 933

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Glu Arg His Asp Gly Gly Ser Glu Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Asn Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
```

```
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 934
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35S/R37aD/V38E/Y40Q/V41L/L97bA/H99Q/C122S/Y149R

<400> 934
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Ser Arg His Asp Gly Gly Ser Glu Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
```

```
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 935
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35V/R37aD/V38E/Y40Q/V41L/Y60bG/T97aE/L97bA/H99Q/C
122S/Y149R

<400> 935

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Val Arg His Asp Gly Gly Ser Glu Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Gly Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
```

```
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 936
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35S/R37aD/V38E/Y40Q/V41L/Y60bV/T97aL/L97bA/H99Q/C
122S/Y149L

<400> 936

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Ser Arg His Asp Gly Gly Ser Glu Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Val Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Leu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Leu Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
```

```
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 937
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R37aP/V38E/Y40Q/V41L/Y60bE/L97bA/H99Q/C122S/Y149R

<400> 937
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Pro Gly Gly Ser Glu Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
```

Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 938
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35M/R37aQ/V38E/Y40Q/V41L/Y60bE/T97aE/L97bA/H99Q/C
      122S/Y149R

<400> 938
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Met Arg His Gln Gly Gly Ser Glu Thr Gln Leu Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220

```
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 939
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35S/R37aD/V38E/Y40Q/V41L/Y60bT/T97aE/L97bA/H99Q/C
122S/Y149R

<400> 939

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Ser Arg His Asp Gly Gly Ser Glu Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Thr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
```

Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 940
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35S/R37aA/V38E/Y40Q/V41L/L97bA/H99Q/C122S/Y149V

<400> 940
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Ser Arg His Ala Gly Gly Ser Glu Thr Gln Leu Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Val Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 941
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35K/R37aD/V38E/Y40Q/V41L/Y60bE/L97bA/H99Q/C122S/Y
149R

<400> 941
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Lys Arg His Asp Gly Gly Ser Glu Thr Gln Leu Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Glu Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 942

<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35V/R37aE/V38E/Y40Q/V41L/Y60bS/T97aE/L97bA/H99Q/C
122S/Y149R

<400> 942
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Val Arg His Glu Gly Gly Ser Glu Thr Gln Leu Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Ser Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 943
<211> 253
<212> PRT

<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35A/R37aE/V38E/Y40Q/V41L/L97bA/H99Q/C122S/Y149R

<400> 943
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Ala Arg His Glu Gly Gly Ser Glu Thr Gln Leu Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 944
<211> 253
<212> PRT
<213> Artificial Sequence

<220>

<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aD/V38E/Y40Q/V41L/Y60bP/T97aE/L97bA/H99Q/C122S/
Y149R

<400> 944
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Asp Gly Gly Ser Glu Thr Gln Leu Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 945
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain

R35S/R37aD/V38E/Y40Q/V41L/T97aD/L97bA/H99Q/C122S/Y
149K

<400> 945

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Ser Arg His Asp Gly Gly Ser Glu Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Asp Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Lys Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 946
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35A/R37aD/V38E/Y40Q/V41L/Y60bV/T97aE/L97bA/H99Q/C
122S/Y149K

<400> 946
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Ala Arg His Asp Gly Gly Ser Glu Thr Gln Leu Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Val Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Lys Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 947
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R37aD/V38E/Y40Q/V41L/Y60bP/T97aV/L97bA/H99Q/C122S/
      Y149K

<400> 947

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Asp Gly Gly Ser Glu Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Val Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Lys Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 948
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35S/R37aD/V38E/Y40Q/V41L/T97aE/L97bA/H99Q/C122S/Y
149R

<400> 948

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
```

```
Ala Ile Tyr Ser Arg His Asp Gly Gly Ser Glu Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Glu Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 949
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aS/V38E/Y40V/V41R/H99L/C122S/Y151L/R217V

<400> 949

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Ser Gly Gly Ser Glu Thr Val Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
```

```
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala Leu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 950
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38E/Y40L/V41R/H99L/C122S/Y151L/R217S

<400> 950

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Thr Leu Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
```

```
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala Leu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Ser Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 951
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36L/V38E/Y40Q/V41R/L97bG/H99Q/C122S/Y151P/R217S

<400> 951

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Leu His Arg Gly Gly Ser Glu Thr Gln Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
```

```
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Pro Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Ser Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 952
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aS/V38E/V41R/L97bG/H99Q/C122S/R217V

<400> 952

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Ser Gly Gly Ser Glu Thr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
```

```
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 953
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38E/Y40A/V41L/L97bG/H99Q/C122S/R217T

<400> 953

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Thr Ala Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
```

```
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Thr Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 954
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38E/Y40H/V41Q/L97bG/H99Q/C122S/R217T

<400> 954
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Thr His Gln Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
```

```
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Thr Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 955
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38E/Y40H/V41T/L97bG/H99Q/C122S/R217T

<400> 955
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Thr His Thr Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
```

```
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Thr Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 956
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38E/Y40Q/V41L/L97bG/H99Q/C122S/Y151P/R217T

<400> 956
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Pro Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
```

```
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Thr Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 957
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38E/Y40Q/V41L/L97bG/H99Q/C122S/R217T

<400> 957

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Thr Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
```

225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 958
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36S/V38E/Y40Q/V41R/L97bG/H99L/C122S/Y151P/R217E

<400> 958
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Ser His Arg Gly Gly Ser Glu Thr Gln Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Leu His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Pro Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 959
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38E/Y40P/V41L/L97bG/H99L/C122S/Y151Q/R217E

<400> 959
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Thr Pro Leu Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Leu His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Gln Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Glu Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 960

<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aS/V38E/Y40H/V41T/L97bG/H99Q/C122S/R217T

<400> 960

Ile	Ile	Gly	Gly	Glu	Phe	Thr	Thr	Ile	Glu	Asn	Gln	Pro	Trp	Phe	Ala
1			5					10						15	
Ala	Ile	Tyr	Arg	Arg	His	Ser	Gly	Gly	Ser	Glu	Thr	His	Thr	Cys	Gly
		20					25					30			
Gly	Ser	Leu	Ile	Ser	Pro	Cys	Trp	Val	Ile	Ser	Ala	Thr	His	Cys	Phe
	35					40					45				
Ile	Asp	Tyr	Pro	Lys	Lys	Glu	Asp	Tyr	Ile	Val	Tyr	Leu	Gly	Arg	Ser
	50				55					60					
Arg	Leu	Asn	Ser	Asn	Thr	Gln	Gly	Glu	Met	Lys	Phe	Glu	Val	Glu	Asn
65				70					75					80	
Leu	Ile	Leu	His	Lys	Asp	Tyr	Ser	Ala	Asp	Thr	Gly	Ala	Gln	His	Asn
			85					90					95		
Asp	Ile	Ala	Leu	Leu	Lys	Ile	Arg	Ser	Lys	Glu	Gly	Arg	Cys	Ala	Gln
		100					105					110			
Pro	Ser	Arg	Thr	Ile	Gln	Thr	Ile	Ser	Leu	Pro	Ser	Met	Tyr	Asn	Asp
	115					120					125				
Pro	Gln	Phe	Gly	Thr	Ser	Cys	Glu	Ile	Thr	Gly	Phe	Gly	Lys	Glu	Asn
	130				135					140					
Ser	Thr	Asp	Tyr	Leu	Tyr	Pro	Glu	Gln	Leu	Lys	Met	Thr	Val	Val	Lys
145				150					155					160	
Leu	Ile	Ser	His	Arg	Glu	Cys	Gln	Gln	Pro	His	Tyr	Tyr	Gly	Ser	Glu
			165					170					175		
Val	Thr	Thr	Lys	Met	Leu	Cys	Ala	Ala	Asp	Pro	Gln	Trp	Lys	Thr	Asp
		180					185					190			
Ser	Cys	Gln	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Cys	Ser	Leu	Gln	Gly
	195					200					205				
Arg	Met	Thr	Leu	Thr	Gly	Ile	Val	Ser	Trp	Gly	Thr	Gly	Cys	Ala	Leu
	210				215					220					
Lys	Asp	Lys	Pro	Gly	Val	Tyr	Thr	Arg	Val	Ser	His	Phe	Leu	Pro	Trp
225				230					235					240	
Ile	Arg	Ser	His	Thr	Lys	Glu	Glu	Asn	Gly	Leu	Ala	Leu			
			245					250							

<210> 961
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aS/V38E/Y40P/V41L/L97bG/H99Q/C122S/Y151Q/R217T

<400> 961
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Ser Gly Gly Ser Glu Thr Pro Leu Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Gln Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Thr Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 962
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)

protease domain
R37aS/V38E/Y40Q/V41L/L97bG/C122S/Y151P/R217T

<400> 962

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Ser Gly Gly Ser Glu Thr Gln Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala His His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Pro Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Thr Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 963
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R36S/V38E/Y40L/V41N/L97bG/H99Q/C122S/Y151L/R217T

<400> 963
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr Arg Ser His Arg Gly Gly Ser Glu Thr Leu Asn Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Thr Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 964
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35S/V38E/L97bR/C122S/Y151L/R217V/H241N

<400> 964
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15

```
Ala Ile Tyr Ser Arg His Arg Gly Gly Ser Glu Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala His His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser Asn Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 965
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35S/V38E/H99Q/C122S/S146F/Y151L/V159L/K179N/Q192R
      /R217V/T242S

<400> 965
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Ser Arg His Arg Gly Gly Ser Glu Thr Tyr Val Cys Gly
            20                  25                  30
```

```
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Phe Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Leu Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Asn Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Arg Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Ser Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 966
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
F30Y/R37aH/V38E/H99Q/C122S/Y151L/R217V

<400> 966

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His His Gly Gly Ser Glu Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
```

```
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 967
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain R35H/V38E/L97bR/C122S/Y151L/R217V

<400> 967

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr His Arg His Arg Gly Gly Ser Glu Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala His His Asn
```

```
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 968
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38E/T56I/H99Q/C122S/Y151L/S190G/R217V

<400> 968

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Ile His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
```

```
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Gly Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 969
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain F30Y/V38E/L97bR/C122S/Y151L/R217V

<400> 969
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Tyr Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Thr Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala His His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
```

```
Ser Thr Asp Tyr Leu Leu Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Val Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 970
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38E/T39S/V41L/Y60bP/L97bG/H99Q/C122S

<400> 970
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Ser Tyr Leu Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Asp Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
```

```
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 971
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38E/T39R/D60aP/Y60bD/L97bG/H99Q/C122S

<400> 971
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Arg Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
```

```
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 972
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38E/T39W/V41R/D60aP/Y60bD/L97bA/H99L/C122S

<400> 972
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Trp Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Asp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Leu His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
```

```
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 973
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      V38E/T39Y/V41R/D60aW/Y60bP/L97bR/H99I/C122S

<400> 973
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Trp Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Arg Ala Ile His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
```

Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 974
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38E/T39H/D60aP/Y60bK/L97bG/H99Q/C122S

<400> 974
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu His Tyr Val Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Pro Lys Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 975
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38E/T39L/V41R/D60aN/Y60bP/L97bG/H99Q/C122S

<400> 975
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Leu Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Asn Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 976
<211> 253

<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38E/T39H/D60aP/Y60bW/L97bG/H99Q/C122S

<400> 976

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu His Tyr Val Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Trp Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 977
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
V38E/T39W/V41R/D60aW/Y60bP/L97bG/H99L/C122S

<400> 977
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
1 5 10 15
Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Glu Trp Tyr Arg Cys Gly
20 25 30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
35 40 45
Ile Trp Pro Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
50 55 60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65 70 75 80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Gly Ala Leu His Asn
85 90 95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
100 105 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
115 120 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
130 135 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145 150 155 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
165 170 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
180 185 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
195 200 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
210 215 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225 230 235 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
245 250

<210> 978
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain

R35H/V38E/T39Y/V41R/D60aP/Y60bQ/L97bA/H99Q/C122S/I
138V/E167K

<400> 978
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr His Arg His Arg Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Val Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Lys Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 979
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35H/V38E/T39Y/V41R/D60aP/Y60bQ/L97bA/H99Q/C122S/T
158S/E167K

<400> 979
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1   5   10   15
Ala Ile Tyr His Arg His Arg Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20   25   30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35   40   45
Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50   55   60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65   70   75   80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85   90   95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100   105   110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115   120   125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130   135   140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Ser Val Val Lys
145   150   155   160
Leu Ile Ser His Arg Lys Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165   170   175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180   185   190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195   200   205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210   215   220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225   230   235   240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245   250

<210> 980
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35H/G37bD/V38E/T39Y/V41R/D60aP/Y60bQ/L97bA/H99Q/C
      122S/T158S

<400> 980

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr His Arg His Arg Asp Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Ser Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 981
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35H/V38E/T39Y/V41R/D60aP/Y60bQ/L97bA/H99Q/C122S/T
158A

<400> 981

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
```

```
Ala Ile Tyr His Arg His Arg Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Ala Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 982
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35H/V38E/T39Y/V41R/T56A/D60aP/Y60bQ/L97bA/H99Q/C1
22S

<400> 982

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr His Arg His Arg Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
```

```
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Ala His Cys Phe
        35                  40                  45
Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 983
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35H/V38E/T39Y/V41R/T56S/D60aP/Y60bQ/L97bA/H99Q/C1
22S/T158S

<400> 983

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr His Arg His Arg Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Ser His Cys Phe
        35                  40                  45
```

```
Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Ser Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 984
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aH/V38E/T39Y/V41R/T56A/D60aP/Y60bQ/L97bA/H99Q/C
122S/T158A

<400> 984

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His His Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Ala His Cys Phe
        35                  40                  45
Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
```

```
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Ala Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 985
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R37aH/V38E/T39Y/V41R/D60aP/Y60bQ/L97bA/H99Q/C122S

<400> 985

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Arg Arg His His Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
```

```
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250
```

<210> 986
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
protease domain
R35H/V38E/T39Y/V41R/D60aP/Y60bQ/P60cS/L97bA/H99Q/C
122S/I138V/E167K

<400> 986

```
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr His Arg His Arg Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
        35                  40                  45
Ile Pro Gln Ser Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
```

```
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
        115                 120                 125
Pro Gln Phe Gly Thr Ser Cys Glu Val Thr Gly Phe Gly Lys Glu Asn
    130                 135                 140
Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
145                 150                 155                 160
Leu Ile Ser His Arg Lys Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
                165                 170                 175
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
                245                 250


<210> 987
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      protease domain
      R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aP/Y60bQ/T97aI/L
      97bA/C122C/H99Q/Y149R

<400> 987
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
 1               5                  10                  15
Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
            20                  25                  30
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
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Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
    50                  55                  60
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
65                  70                  75                  80
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
                85                  90                  95
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
            100                 105                 110
Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr Asn Asp
```

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Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
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Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
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Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
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Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
            180                 185                 190
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
        195                 200                 205
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
    210                 215                 220
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
225                 230                 235                 240
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<210> 988
<211> 6418
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<220>
<223> pE5 plasmid

<400> 988

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<210> 989
<211> 6
<212> PRT
<213> Artificial Sequence

<220>

<223> HIS tag

<400> 989
His His His His His His
 1   5

<210> 990
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> HIS tag-SUMO

<400> 990
Met Gly His His His His His His Gly Ser Leu Gln Asp Ser Glu Val
 1   5   10   15
Asn Gln Glu Ala Lys Pro Glu Val Lys Pro Glu Val Lys Pro Glu Thr
            20   25   30
His Ile Asn Leu Lys Val Ser Asp Gly Ser Ser Glu Ile Phe Phe Lys
        35   40   45
Ile Lys Lys Thr Thr Pro Leu Arg Arg Leu Met Glu Ala Phe Ala Lys
    50   55   60
Arg Gln Gly Lys Glu Met Asp Ser Leu Arg Phe Leu Tyr Asp Gly Ile
65   70   75   80
Arg Ile Gln Ala Asp Gln Ala Pro Glu Asp Leu Asp Met Glu Asp Asn
                85   90   95
Asp Ile Ile Glu Ala His Arg Glu Gln Ile Gly Gly
            100   105

<210> 991
<211> 585
<212> PRT
<213> Homo sapiens

<220>
<223> human serum albumin

<220>

<400> 991
Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu
 1   5   10   15
Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln
            20   25   30
Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu

```
        35                  40                  45
Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
    50                  55                  60
Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65                  70                  75                  80
Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
                85                  90                  95
Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
            100                 105                 110
Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
        115                 120                 125
Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
    130                 135                 140
Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145                 150                 155                 160
Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
                165                 170                 175
Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
            180                 185                 190
Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
        195                 200                 205
Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
    210                 215                 220
Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225                 230                 235                 240
Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
                245                 250                 255
Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
            260                 265                 270
Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
        275                 280                 285
Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
    290                 295                 300
Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305                 310                 315                 320
Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
                325                 330                 335
Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
            340                 345                 350
Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
        355                 360                 365
Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro
    370                 375                 380
Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385                 390                 395                 400
Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
                405                 410                 415
Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
```

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            420                 425                 430
Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
        435                 440                 445
Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
    450                 455                 460
Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465                 470                 475                 480
Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
                485                 490                 495
Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
            500                 505                 510
Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
        515                 520                 525
Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
    530                 535                 540
Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545                 550                 555                 560
Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val
                565                 570                 575
Ala Ala Ser Gln Ala Ala Leu Gly Leu
            580                 585


<210> 992
<211> 226
<212> PRT
<213> Homo sapiens

<220>
<223> Immunoglobulin Gamma-1 heavy chain (FC)

<400> 992
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
 1               5                  10                  15
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
            20                  25                  30
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
        35                  40                  45
Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
    50                  55                  60
His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65                  70                  75                  80
Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
                85                  90                  95
Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
            100                 105                 110
Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
        115                 120                 125
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Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
    130                 135                 140
Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145                 150                 155                 160
Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
                165                 170                 175
Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
            180                 185                 190
Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
        195                 200                 205
His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
    210                 215                 220
Pro Gly
225


<210> 993
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<223> Anti-Type-II collagen Antibody scFv Fragment

<400> 993
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Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30
Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45
Gly Met Ile His Pro Ser Asp Ser Glu Thr Arg Leu Ser Gln Lys Phe
    50                  55                  60
Lys Asp Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65                  70                  75                  80
Met Gln Leu Ser Ser Pro Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Leu Lys Pro Gly Gly Thr Trp Phe Ala Tyr Trp Gly Gln Gly
            100                 105                 110
Thr Leu Val Thr Val Ser Ala Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125
Ser Gly Gly Gly Gly Ser Gly Gly Ser Asp Ile Val Leu Thr Gln Ser
    130                 135                 140
Pro Ala Ser Leu Thr Val Ser Leu Gly Gln Arg Ala Thr Ile Ser Cys
145                 150                 155                 160
Arg Ala Ser Lys Ser Val Asp Ser Tyr Gly Asn Ser Phe Met Glu Trp
                165                 170                 175
Tyr Gln Gln Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Arg Ala
```

```
            180                 185                 190
Ser Asn Leu Glu Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205
Arg Thr Asp Phe Thr Leu Thr Ile Asn Pro Val Glu Ala Asp Asp Val
    210                 215                 220
Ala Thr Tyr Tyr Cys Gln Gln Ser Asn Glu Asp Pro Tyr Thr Phe Gly
225                 230                 235                 240
Gly Gly Thr Lys Leu Glu Ile Lys
                245
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<210> 994
<211> 103
<212> PRT
<213> Artificial Sequence

<220>
<223> human Tumor necrosis factor-stimulated gene-6
(TSG-6) aa residues 32-134 (HABP)

<400> 994

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Glu Arg Ala Ala Gly Val Tyr His Arg Glu Ala Arg Ser Gly Lys Tyr
 1               5                  10                  15
Lys Leu Thr Tyr Ala Glu Ala Lys Ala Val Cys Glu Phe Glu Gly Gly
            20                  25                  30
His Leu Ala Thr Tyr Lys Gln Leu Glu Ala Ala Arg Lys Ile Gly Phe
        35                  40                  45
His Val Cys Ala Ala Gly Trp Met Ala Lys Gly Arg Val Gly Tyr Pro
    50                  55                  60
Ile Val Lys Pro Gly Pro Asn Cys Gly Phe Gly Lys Thr Gly Ile Ile
65                  70                  75                  80
Asp Tyr Gly Ile Arg Leu Asn Arg Ser Glu Arg Trp Asp Ala Tyr Cys
                85                  90                  95
Tyr Asn Pro His Ala Lys Glu
            100
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<210> 995
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Furin activation sequence

<400> 995

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Gln Cys Gly Gln Lys Thr Leu Arg Arg Arg Lys Arg
 1               5                  10
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<210> 996
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Furin activation sequence

<400> 996
Gln Ser Gly Gln Lys Thr Leu Arg Arg Arg Lys Arg
 1   5   10

<210> 997
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      activation sequence

<400> 997
Gln Cys Gly Gln Lys Thr Leu Arg Pro Arg Phe Lys
 1   5   10

<210> 998
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> UROKINASE-TYPE PLASMINOGEN ACTIVATOR (u-PA)
      activation sequence

<400> 998
Gln Ser Gly Gln Lys Thr Leu Arg Pro Arg Phe Lys
 1   5   10

<210> 999
<211> 20
<212> PRT
<213> Mus musculus

<220>
<223> Ig kappa chain V-III region signal peptide
(IgGkSP)

<400> 999
Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
1 5 10 15
Gly Ser Thr Gly
20

<210> 1000
<211> 20
<212> PRT
<213> Homo sapiens

<220>
<223> human IL2 Signal Peptide (hIL2SP)

<400> 1000
Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
1 5 10 15
Val Thr Asn Ser
20

<210> 1001
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> GGGGS linker

<400> 1001
Gly Gly Gly Gly Ser
1 5

<210> 1002
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> GGSSGG linker

<400> 1002

Gly Gly Ser Ser Gly Gly
 1   5

<210> 1003
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> AGS linker

<400> 1003
Ala Gly Ser
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<210> 1004
<211> 514
<212> PRT
<213> Artificial Sequence

<220>
<223> IgGkSP-FC-AGS-uPA
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97bA/H99Q/Y149R fusion

<400> 1004
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Gly Ser Thr Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
            20   25   30
Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
        35   40   45
Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
    50   55   60
Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
65   70   75   80
Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
                85   90   95
Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
            100   105   110
Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
        115   120   125
Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
    130   135   140
Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys
145   150   155   160

```
Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
                165                 170                 175
Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
            180                 185                 190
Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
        195                 200                 205
Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
    210                 215                 220
Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
225                 230                 235                 240
Leu Ser Leu Ser Pro Gly Ala Gly Ser Gln Cys Gly Gln Lys Thr Leu
                245                 250                 255
Arg Pro Arg Phe Lys Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn
            260                 265                 270
Gln Pro Trp Phe Ala Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu
        275                 280                 285
Tyr Tyr Arg Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser
    290                 295                 300
Ala Thr His Cys Phe Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val
305                 310                 315                 320
Tyr Leu Gly Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys
                325                 330                 335
Phe Glu Val Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile
            340                 345                 350
Ala Ala Gln His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu
        355                 360                 365
Gly Arg Cys Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro
    370                 375                 380
Ser Met Tyr Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly
385                 390                 395                 400
Phe Gly Lys Glu Asn Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys
                405                 410                 415
Met Thr Val Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His
            420                 425                 430
Tyr Tyr Gly Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro
        435                 440                 445
Gln Trp Lys Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val
    450                 455                 460
Cys Ser Leu Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly
465                 470                 475                 480
Arg Gly Cys Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser
                485                 490                 495
His Phe Leu Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu
            500                 505                 510
Ala Leu
```

<210> 1005
<211> 431
<212> PRT
<213> Artificial Sequence

<220>
<223> IgGkSP-uPA
R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aP/Y60bQ/T97aI/L
97bA/H99Q/Y149R

<400> 1005

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Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
 1               5                  10                  15
Gly Ser Thr Gly Ser Asn Glu Leu His Gln Val Pro Ser Asn Cys Asp
            20                  25                  30
Cys Leu Asn Gly Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile
        35                  40                  45
His Trp Cys Asn Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile
    50                  55                  60
Asp Lys Ser Lys Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly
65                  70                  75                  80
Lys Ala Ser Thr Asp Thr Met Gly Arg Pro Cys Leu Pro Trp Asn Ser
                85                  90                  95
Ala Thr Val Leu Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu
            100                 105                 110
Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg
        115                 120                 125
Arg Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln
    130                 135                 140
Glu Cys Met Val His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro
145                 150                 155                 160
Pro Glu Glu Leu Lys Phe Gln Cys Gly Gln Lys Thr Leu Arg Pro Arg
                165                 170                 175
Phe Lys Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp
            180                 185                 190
Phe Ala Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Tyr Tyr Arg
        195                 200                 205
Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His
    210                 215                 220
Cys Phe Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly
225                 230                 235                 240
Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val
                245                 250                 255
Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln
            260                 265                 270
His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys
        275                 280                 285
Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr
```

```
    290                 295                 300
Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys
305                 310                 315                 320
Glu Asn Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val
                325                 330                 335
Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly
            340                 345                 350
Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys
        355                 360                 365
Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu
    370                 375                 380
Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys
385                 390                 395                 400
Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu
                405                 410                 415
Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu
            420                 425                 430


<210> 1006
<211> 505
<212> PRT
<213> Artificial Sequence

<220>
<223> hIL2ss-uPA
      R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aP/Y60bQ/T97aI/L
      97bA/H99Q/C122S/Y149R-IgG1Fc

<400> 1006
Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
 1               5                  10                  15
Val Thr Asn Ser Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln
            20                  25                  30
Pro Trp Phe Ala Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Tyr
        35                  40                  45
Tyr Arg Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala
    50                  55                  60
Thr His Cys Phe Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr
65                  70                  75                  80
Leu Gly Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe
                85                  90                  95
Glu Val Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala
            100                 105                 110
Ala Gln His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly
        115                 120                 125
Arg Cys Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser
    130                 135                 140
```

```
Met Tyr Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe
145                 150                 155                 160
Gly Lys Glu Asn Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met
                165                 170                 175
Thr Val Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr
            180                 185                 190
Tyr Gly Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln
        195                 200                 205
Trp Lys Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys
    210                 215                 220
Ser Leu Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg
225                 230                 235                 240
Gly Cys Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His
                245                 250                 255
Phe Leu Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala
            260                 265                 270
Leu Gly Gly Ser Ser Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys
        275                 280                 285
Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
    290                 295                 300
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
305                 310                 315                 320
Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
                325                 330                 335
Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
            340                 345                 350
Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
        355                 360                 365
His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
    370                 375                 380
Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
385                 390                 395                 400
Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
                405                 410                 415
Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
            420                 425                 430
Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
        435                 440                 445
Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
    450                 455                 460
Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
465                 470                 475                 480
Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
                485                 490                 495
Gln Lys Ser Leu Ser Leu Ser Pro Gly
            500                 505
```

<210> 1007
<211> 864
<212> PRT
<213> Artificial Sequence

<220>
<223> hIL2ss-uPA
R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aP/Y60bQ/T97aI/L
97bA/H99Q/C122S/Y149R-HSA

<400> 1007
Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
 1   5   10   15
Val Thr Asn Ser Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln
            20   25   30
Pro Trp Phe Ala Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Tyr
        35   40   45
Tyr Arg Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala
    50   55   60
Thr His Cys Phe Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr
65   70   75   80
Leu Gly Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe
                85   90   95
Glu Val Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala
            100   105   110
Ala Gln His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly
        115   120   125
Arg Cys Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser
    130   135   140
Met Tyr Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe
145   150   155   160
Gly Lys Glu Asn Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met
                165   170   175
Thr Val Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr
            180   185   190
Tyr Gly Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln
        195   200   205
Trp Lys Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys
    210   215   220
Ser Leu Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg
225   230   235   240
Gly Cys Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His
                245   250   255
Phe Leu Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala
            260   265   270
Leu Gly Gly Ser Ser Gly Gly Asp Ala His Lys Ser Glu Val Ala His
        275   280   285
Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile

```
    290                 295                 300
Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys
305                 310                 315                 320
Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu
                325                 330                 335
Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys
            340                 345                 350
Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp
        355                 360                 365
Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His
    370                 375                 380
Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp
385                 390                 395                 400
Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys
                405                 410                 415
Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu
            420                 425                 430
Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys
        435                 440                 445
Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu
    450                 455                 460
Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala
465                 470                 475                 480
Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala
                485                 490                 495
Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys
            500                 505                 510
Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp
        515                 520                 525
Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys
    530                 535                 540
Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys
545                 550                 555                 560
Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu
                565                 570                 575
Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys
            580                 585                 590
Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met
        595                 600                 605
Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu
    610                 615                 620
Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys
625                 630                 635                 640
Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe
                645                 650                 655
Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu
            660                 665                 670
Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val
```

```
        675                 680                 685
Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu
    690                 695                 700
Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro
705                 710                 715                 720
Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu
                725                 730                 735
Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val
            740                 745                 750
Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser
        755                 760                 765
Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu
    770                 775                 780
Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg
785                 790                 795                 800
Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys Pro
                805                 810                 815
Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala
            820                 825                 830
Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala
        835                 840                 845
Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
    850                 855                 860
```

<210> 1008
<211> 864
<212> PRT
<213> Artificial Sequence

<220>
<223> hIL2ss-uPA
R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aP/Y60bQ/T97aI/L
97bA/H99Q/C122S/Y149R-C2scFv

<400> 1008

```
Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
 1               5                  10                  15
Val Thr Asn Ser Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln
            20                  25                  30
Pro Trp Phe Ala Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Tyr
        35                  40                  45
Tyr Arg Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala
    50                  55                  60
Thr His Cys Phe Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr
65                  70                  75                  80
Leu Gly Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe
                85                  90                  95
```

```
Glu Val Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala
            100                 105                 110
Ala Gln His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly
        115                 120                 125
Arg Cys Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser
    130                 135                 140
Met Tyr Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe
145                 150                 155                 160
Gly Lys Glu Asn Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met
                165                 170                 175
Thr Val Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr
            180                 185                 190
Tyr Gly Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln
        195                 200                 205
Trp Lys Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys
    210                 215                 220
Ser Leu Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg
225                 230                 235                 240
Gly Cys Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His
                245                 250                 255
Phe Leu Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala
            260                 265                 270
Leu Gly Gly Ser Ser Gly Gly Asp Ala His Lys Ser Glu Val Ala His
        275                 280                 285
Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile
    290                 295                 300
Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys
305                 310                 315                 320
Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu
                325                 330                 335
Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys
            340                 345                 350
Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp
        355                 360                 365
Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His
    370                 375                 380
Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp
385                 390                 395                 400
Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys
                405                 410                 415
Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu
            420                 425                 430
Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys
        435                 440                 445
Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu
    450                 455                 460
Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala
465                 470                 475                 480
```

```
Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala
                485                 490                 495
Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys
            500                 505                 510
Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp
        515                 520                 525
Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys
    530                 535                 540
Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys
545                 550                 555                 560
Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu
                565                 570                 575
Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys
            580                 585                 590
Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met
        595                 600                 605
Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu
    610                 615                 620
Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys
625                 630                 635                 640
Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe
                645                 650                 655
Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu
            660                 665                 670
Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val
        675                 680                 685
Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu
    690                 695                 700
Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro
705                 710                 715                 720
Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu
                725                 730                 735
Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val
            740                 745                 750
Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser
        755                 760                 765
Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu
    770                 775                 780
Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg
785                 790                 795                 800
Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys Pro
                805                 810                 815
Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala
            820                 825                 830
Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala
        835                 840                 845
Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
    850                 855                 860
```

<210> 1009
<211> 382
<212> PRT
<213> Artificial Sequence

<220>
<223> hIL2ss-uPA
R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aP/Y60bQ/T97aI/L
97bA/H99Q/C122S/Y149R-HABD

<400> 1009
Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
 1   5   10   15
Val Thr Asn Ser Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln
            20   25   30
Pro Trp Phe Ala Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Tyr
        35   40   45
Tyr Arg Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala
    50   55   60
Thr His Cys Phe Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr
65   70   75   80
Leu Gly Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe
                85   90   95
Glu Val Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala
            100   105   110
Ala Gln His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly
        115   120   125
Arg Cys Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser
    130   135   140
Met Tyr Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe
145   150   155   160
Gly Lys Glu Asn Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met
                165   170   175
Thr Val Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr
            180   185   190
Tyr Gly Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln
        195   200   205
Trp Lys Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys
    210   215   220
Ser Leu Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg
225   230   235   240
Gly Cys Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His
                245   250   255
Phe Leu Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala
            260   265   270
Leu Gly Gly Ser Ser Gly Gly Glu Arg Ala Ala Gly Val Tyr His Arg

```
        275                 280                 285
Glu Ala Arg Ser Gly Lys Tyr Lys Leu Thr Tyr Ala Glu Ala Lys Ala
    290                 295                 300
Val Cys Glu Phe Glu Gly Gly His Leu Ala Thr Tyr Lys Gln Leu Glu
305                 310                 315                 320
Ala Ala Arg Lys Ile Gly Phe His Val Cys Ala Ala Gly Trp Met Ala
                325                 330                 335
Lys Gly Arg Val Gly Tyr Pro Ile Val Lys Pro Gly Pro Asn Cys Gly
            340                 345                 350
Phe Gly Lys Thr Gly Ile Ile Asp Tyr Gly Ile Arg Leu Asn Arg Ser
        355                 360                 365
Glu Arg Trp Asp Ala Tyr Cys Tyr Asn Pro His Ala Lys Glu
    370                 375                 380


<210> 1010
<211> 516
<212> PRT
<213> Artificial Sequence

<220>
<223> IgGkSP-Furin-uPA
      R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aP/Y60bQ/T97aI/L
      97bA/H99Q/C122S/Y149R-FC

<400> 1010
Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
 1               5                  10                  15
Gly Ser Thr Gly Gln Ser Gly Gln Lys Thr Leu Arg Arg Lys Arg Ile
            20                  25                  30
Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala Ala
        35                  40                  45
Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Tyr Tyr Arg Cys Gly Gly
    50                  55                  60
Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe Ile
65                  70                  75                  80
Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser Arg
                85                  90                  95
Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn Leu
            100                 105                 110
Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn Asp
        115                 120                 125
Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro
    130                 135                 140
Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro
145                 150                 155                 160
Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser
                165                 170                 175
```

```
Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu
            180                 185                 190
Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val
        195                 200                 205
Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser
    210                 215                 220
Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg
225                 230                 235                 240
Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys
                245                 250                 255
Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile
            260                 265                 270
Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu Gly Gly Ser Ser
        275                 280                 285
Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
    290                 295                 300
Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
305                 310                 315                 320
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
                325                 330                 335
Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
            340                 345                 350
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
        355                 360                 365
Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
    370                 375                 380
Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
385                 390                 395                 400
Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
                405                 410                 415
Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
            420                 425                 430
Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
        435                 440                 445
Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
    450                 455                 460
Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
465                 470                 475                 480
Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
                485                 490                 495
Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
            500                 505                 510
Leu Ser Pro Gly
        515
```

<210> 1011
<211> 663

<212> PRT
<213> Artificial Sequence

<220>
<223> IgGkSP-uPA
R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aP/Y60bQ/T97aI/L
97bA/H99Q/Y149R-FC

<400> 1011
```
Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
 1               5                  10                  15
Gly Ser Thr Gly Ser Asn Glu Leu His Gln Val Pro Ser Asn Cys Asp
            20                  25                  30
Cys Leu Asn Gly Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile
        35                  40                  45
His Trp Cys Asn Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile
    50                  55                  60
Asp Lys Ser Lys Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly
65                  70                  75                  80
Lys Ala Ser Thr Asp Thr Met Gly Arg Pro Cys Leu Pro Trp Asn Ser
                85                  90                  95
Ala Thr Val Leu Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu
            100                 105                 110
Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg
        115                 120                 125
Arg Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln
    130                 135                 140
Glu Cys Met Val His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro
145                 150                 155                 160
Pro Glu Glu Leu Lys Phe Gln Cys Gly Gln Lys Thr Leu Arg Pro Arg
                165                 170                 175
Phe Lys Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp
            180                 185                 190
Phe Ala Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Tyr Tyr Arg
        195                 200                 205
Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His
    210                 215                 220
Cys Phe Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly
225                 230                 235                 240
Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val
                245                 250                 255
Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln
            260                 265                 270
His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys
        275                 280                 285
Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr
    290                 295                 300
Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys
```

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305                 310                 315                 320
Glu Asn Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val
                325                 330                 335
Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly
            340                 345                 350
Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys
        355                 360                 365
Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu
    370                 375                 380
Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys
385                 390                 395                 400
Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu
                405                 410                 415
Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu Gly
            420                 425                 430
Gly Ser Ser Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
        435                 440                 445
Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
    450                 455                 460
Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
465                 470                 475                 480
Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
                485                 490                 495
Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
            500                 505                 510
Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
        515                 520                 525
Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
    530                 535                 540
Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
545                 550                 555                 560
Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr
                565                 570                 575
Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
            580                 585                 590
Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
        595                 600                 605
Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
    610                 615                 620
Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
625                 630                 635                 640
Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
                645                 650                 655
Ser Leu Ser Leu Ser Pro Gly
            660
```

<210> 1012

<211> 505
<212> PRT
<213> Artificial Sequence

<220>
<223> hIL2ss-uPA -FC

<400> 1012
Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
 1   5   10   15
Val Thr Asn Ser Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln
            20   25   30
Pro Trp Phe Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr
        35   40   45
Tyr Val Cys Gly Gly Ser Leu Met Ser Pro Cys Trp Val Ile Ser Ala
    50   55   60
Thr His Cys Phe Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr
65   70   75   80
Leu Gly Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe
                85   90   95
Glu Val Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu
            100   105   110
Ala His His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly
        115   120   125
Arg Cys Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser
    130   135   140
Met Tyr Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe
145   150   155   160
Gly Lys Glu Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met
                165   170   175
Thr Val Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr
            180   185   190
Tyr Gly Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln
        195   200   205
Trp Lys Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys
    210   215   220
Ser Leu Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg
225   230   235   240
Gly Cys Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His
                245   250   255
Phe Leu Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala
            260   265   270
Leu Gly Gly Ser Ser Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys
        275   280   285
Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
    290   295   300
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
305   310   315   320

```
Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
                325                 330                 335
Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
            340                 345                 350
Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
        355                 360                 365
His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
    370                 375                 380
Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
385                 390                 395                 400
Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
                405                 410                 415
Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
            420                 425                 430
Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
        435                 440                 445
Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
    450                 455                 460
Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
465                 470                 475                 480
Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
                485                 490                 495
Gln Lys Ser Leu Ser Leu Ser Pro Gly
            500                 505
```

<210> 1013
<211> 864
<212> PRT
<213> Artificial Sequence

<220>
<223> hIL2ss-uPA -HSA

<400> 1013

```
Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
 1               5                  10                  15
Val Thr Asn Ser Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln
            20                  25                  30
Pro Trp Phe Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr
        35                  40                  45
Tyr Val Cys Gly Gly Ser Leu Met Ser Pro Cys Trp Val Ile Ser Ala
    50                  55                  60
Thr His Cys Phe Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr
65                  70                  75                  80
Leu Gly Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe
                85                  90                  95
Glu Val Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu
```

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            100                 105                 110
Ala His His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly
        115                 120                 125
Arg Cys Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser
    130                 135                 140
Met Tyr Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe
145                 150                 155                 160
Gly Lys Glu Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met
                165                 170                 175
Thr Val Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr
            180                 185                 190
Tyr Gly Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln
        195                 200                 205
Trp Lys Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys
    210                 215                 220
Ser Leu Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg
225                 230                 235                 240
Gly Cys Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His
                245                 250                 255
Phe Leu Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala
            260                 265                 270
Leu Gly Gly Ser Ser Gly Gly Asp Ala His Lys Ser Glu Val Ala His
        275                 280                 285
Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile
    290                 295                 300
Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys
305                 310                 315                 320
Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu
                325                 330                 335
Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys
            340                 345                 350
Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp
        355                 360                 365
Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His
    370                 375                 380
Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp
385                 390                 395                 400
Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys
                405                 410                 415
Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu
            420                 425                 430
Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys
        435                 440                 445
Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu
    450                 455                 460
Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala
465                 470                 475                 480
Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala
```

```
                485                 490                 495
Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys
            500                 505                 510
Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp
        515                 520                 525
Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys
    530                 535                 540
Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys
545                 550                 555                 560
Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu
                565                 570                 575
Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys
            580                 585                 590
Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met
        595                 600                 605
Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu
    610                 615                 620
Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys
625                 630                 635                 640
Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe
                645                 650                 655
Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu
            660                 665                 670
Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val
        675                 680                 685
Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu
    690                 695                 700
Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro
705                 710                 715                 720
Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu
                725                 730                 735
Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val
            740                 745                 750
Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser
        755                 760                 765
Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu
    770                 775                 780
Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg
785                 790                 795                 800
Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys Pro
                805                 810                 815
Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala
            820                 825                 830
Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala
        835                 840                 845
Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
    850                 855                 860
```

<210> 1014
<211> 1022
<212> PRT
<213> Artificial Sequence

<220>
<223> IgGkSP-Furin-u-PA
R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aP/Y60bQ/T97aI/L
97bA/H99Q/Y149R-HSA

<400> 1014
Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
 1   5   10   15
Gly Ser Thr Gly Ser Asn Glu Leu His Gln Val Pro Ser Asn Cys Asp
            20   25   30
Cys Leu Asn Gly Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile
        35   40   45
His Trp Cys Asn Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile
    50   55   60
Asp Lys Ser Lys Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly
65   70   75   80
Lys Ala Ser Thr Asp Thr Met Gly Arg Pro Cys Leu Pro Trp Asn Ser
                85   90   95
Ala Thr Val Leu Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu
            100   105   110
Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg
        115   120   125
Arg Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln
    130   135   140
Glu Cys Met Val His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro
145   150   155   160
Pro Glu Glu Leu Lys Phe Gln Cys Gly Gln Lys Thr Leu Arg Arg Arg
                165   170   175
Lys Arg Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp
            180   185   190
Phe Ala Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Tyr Tyr Arg
        195   200   205
Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His
    210   215   220
Cys Phe Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly
225   230   235   240
Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val
                245   250   255
Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln
            260   265   270
His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys
        275   280   285

```
Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr
    290                 295                 300
Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys
305                 310                 315                 320
Glu Asn Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val
                325                 330                 335
Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly
            340                 345                 350
Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys
        355                 360                 365
Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu
    370                 375                 380
Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys
385                 390                 395                 400
Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu
                405                 410                 415
Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu Gly
            420                 425                 430
Gly Ser Ser Gly Gly Asp Ala His Lys Ser Glu Val Ala His Arg Phe
        435                 440                 445
Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe
    450                 455                 460
Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val
465                 470                 475                 480
Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala
                485                 490                 495
Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys
            500                 505                 510
Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys
        515                 520                 525
Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp
    530                 535                 540
Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met
545                 550                 555                 560
Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu
                565                 570                 575
Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu
            580                 585                 590
Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala
        595                 600                 605
Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp
    610                 615                 620
Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu
625                 630                 635                 640
Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu
                645                 650                 655
Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val
            660                 665                 670
```

```
Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu Leu
        675                 680                 685
Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn
    690                 695                 700
Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu
705                 710                 715                 720
Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro
                725                 730                 735
Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val
            740                 745                 750
Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu
        755                 760                 765
Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu
    770                 775                 780
Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala
785                 790                 795                 800
Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro
                805                 810                 815
Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe
            820                 825                 830
Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr
        835                 840                 845
Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser
    850                 855                 860
Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala
865                 870                 875                 880
Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln
                885                 890                 895
Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys
            900                 905                 910
Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu
        915                 920                 925
Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe
    930                 935                 940
Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile
945                 950                 955                 960
Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala
                965                 970                 975
Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val
            980                 985                 990
Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu
        995                 1000                1005
Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
    1010                1015                1020
```

<210> 1015
<211> 1022

<212> PRT
<213> Artificial Sequence

<220>
<223> IgGkSP-u-PA activation-u-PA
R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aP/Y60bQ/T97aI/L
97bA/H99Q/Y149R-HSA

<400> 1015
Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
 1   5   10   15
Gly Ser Thr Gly Ser Asn Glu Leu His Gln Val Pro Ser Asn Cys Asp
            20   25   30
Cys Leu Asn Gly Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile
        35   40   45
His Trp Cys Asn Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile
    50   55   60
Asp Lys Ser Lys Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly
65   70   75   80
Lys Ala Ser Thr Asp Thr Met Gly Arg Pro Cys Leu Pro Trp Asn Ser
                85   90   95
Ala Thr Val Leu Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu
            100   105   110
Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg
        115   120   125
Arg Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln
    130   135   140
Glu Cys Met Val His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro
145   150   155   160
Pro Glu Glu Leu Lys Phe Gln Cys Gly Gln Lys Thr Leu Arg Pro Arg
                165   170   175
Phe Lys Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp
            180   185   190
Phe Ala Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Tyr Tyr Arg
        195   200   205
Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His
    210   215   220
Cys Phe Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly
225   230   235   240
Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val
                245   250   255
Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln
            260   265   270
His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys
        275   280   285
Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr
    290   295   300
Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys

```
305                 310                 315                 320
Glu Asn Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val
                325                 330                 335
Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly
            340                 345                 350
Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys
        355                 360                 365
Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu
    370                 375                 380
Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys
385                 390                 395                 400
Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu
                405                 410                 415
Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu Gly
            420                 425                 430
Gly Ser Ser Gly Gly Asp Ala His Lys Ser Glu Val Ala His Arg Phe
        435                 440                 445
Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe
    450                 455                 460
Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val
465                 470                 475                 480
Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala
                485                 490                 495
Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys
            500                 505                 510
Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys
        515                 520                 525
Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp
    530                 535                 540
Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met
545                 550                 555                 560
Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu
                565                 570                 575
Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu
            580                 585                 590
Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala
        595                 600                 605
Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp
    610                 615                 620
Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu
625                 630                 635                 640
Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu
                645                 650                 655
Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val
            660                 665                 670
Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu Leu
        675                 680                 685
Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn
```

```
    690                 695                 700
Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu
705                 710                 715                 720
Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro
                725                 730                 735
Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val
            740                 745                 750
Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu
        755                 760                 765
Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu
    770                 775                 780
Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala
785                 790                 795                 800
Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro
                805                 810                 815
Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe
            820                 825                 830
Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr
        835                 840                 845
Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser
    850                 855                 860
Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala
865                 870                 875                 880
Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln
                885                 890                 895
Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys
            900                 905                 910
Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu
        915                 920                 925
Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe
    930                 935                 940
Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile
945                 950                 955                 960
Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala
                965                 970                 975
Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val
            980                 985                 990
Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu
        995                 1000                1005
Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
    1010                1015                1020
```

<210> 1016
<211> 876
<212> PRT
<213> Artificial Sequence

<220>
<223> IgGkSP-furin activation-uPA
R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aP/Y60bQ/T97aI/L
97bA/H99Q/C122S/Y149R-linker-HSA

<400> 1016

```
Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
 1               5                  10                  15
Gly Ser Thr Gly Gln Ser Gly Gln Lys Thr Leu Arg Arg Arg Lys Arg
            20                  25                  30
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
        35                  40                  45
Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
    50                  55                  60
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
65                  70                  75                  80
Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
                85                  90                  95
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
            100                 105                 110
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
        115                 120                 125
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
    130                 135                 140
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
145                 150                 155                 160
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
                165                 170                 175
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
            180                 185                 190
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
        195                 200                 205
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
    210                 215                 220
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
225                 230                 235                 240
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
                245                 250                 255
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
            260                 265                 270
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu Gly Gly Ser
        275                 280                 285
Ser Gly Gly Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp
    290                 295                 300
Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln
305                 310                 315                 320
Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu
                325                 330                 335
```

```
Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn
            340                 345                 350
Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val
        355                 360                 365
Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys
    370                 375                 380
Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn
385                 390                 395                 400
Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr
                405                 410                 415
Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu
            420                 425                 430
Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe
        435                 440                 445
Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp
    450                 455                 460
Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly
465                 470                 475                 480
Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys
                485                 490                 495
Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln
            500                 505                 510
Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp
        515                 520                 525
Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys
    530                 535                 540
Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp
545                 550                 555                 560
Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu
                565                 570                 575
Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp
            580                 585                 590
Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys
        595                 600                 605
Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu
    610                 615                 620
Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu
625                 630                 635                 640
Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp
                645                 650                 655
Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val
            660                 665                 670
Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln
        675                 680                 685
Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys
    690                 695                 700
Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn
705                 710                 715                 720
```

```
Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg
                725                 730                 735
Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys
            740                 745                 750
Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys
        755                 760                 765
Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val
    770                 775                 780
Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe
785                 790                 795                 800
His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys
                805                 810                 815
Gln Thr Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys
            820                 825                 830
Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys
        835                 840                 845
Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys
    850                 855                 860
Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
865                 870                 875


<210> 1017
<211> 972
<212> PRT
<213> Artificial Sequence

<220>
<223> IgGkSS-HIS-SUMO-uPA
      R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aP/Y60bQ/T97aI/L
      97bA/H99Q/C122S/Y149R-linker-HSA

<400> 1017
Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
 1               5                  10                  15
Gly Ser Thr Gly Asp Gly His His His His His His Gly Ser Leu Gln
            20                  25                  30
Asp Ser Glu Val Asn Gln Glu Ala Lys Pro Glu Val Lys Pro Glu Val
        35                  40                  45
Lys Pro Glu Thr His Ile Asn Leu Lys Val Ser Asp Gly Ser Ser Glu
    50                  55                  60
Ile Phe Phe Lys Ile Lys Lys Thr Thr Pro Leu Arg Arg Leu Met Glu
65                  70                  75                  80
Ala Phe Ala Lys Arg Gln Gly Lys Glu Met Asp Ser Leu Thr Phe Leu
                85                  90                  95
Tyr Asp Gly Ile Glu Ile Gln Ala Asp Gln Thr Pro Glu Asp Leu Asp
            100                 105                 110
Met Glu Asp Asn Asp Ile Ile Glu Ala His Arg Glu Gln Ile Gly Gly
```

```
        115                 120                 125
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
    130                 135                 140
Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
145                 150                 155                 160
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
                165                 170                 175
Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
            180                 185                 190
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
        195                 200                 205
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
    210                 215                 220
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
225                 230                 235                 240
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
                245                 250                 255
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
            260                 265                 270
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
        275                 280                 285
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
    290                 295                 300
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
305                 310                 315                 320
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
                325                 330                 335
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
            340                 345                 350
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
        355                 360                 365
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu Gly Gly Ser
    370                 375                 380
Ser Gly Gly Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp
385                 390                 395                 400
Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln
                405                 410                 415
Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu
            420                 425                 430
Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn
        435                 440                 445
Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val
    450                 455                 460
Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys
465                 470                 475                 480
Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn
                485                 490                 495
Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr
```

```
            500                 505                 510
Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu
        515                 520                 525
Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe
    530                 535                 540
Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp
545                 550                 555                 560
Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly
                565                 570                 575
Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys
            580                 585                 590
Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln
        595                 600                 605
Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp
    610                 615                 620
Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys
625                 630                 635                 640
Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp
                645                 650                 655
Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu
            660                 665                 670
Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp
        675                 680                 685
Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys
    690                 695                 700
Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu
705                 710                 715                 720
Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu
                725                 730                 735
Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp
            740                 745                 750
Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val
        755                 760                 765
Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln
    770                 775                 780
Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys
785                 790                 795                 800
Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn
                805                 810                 815
Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg
            820                 825                 830
Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys
        835                 840                 845
Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys
    850                 855                 860
Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val
865                 870                 875                 880
Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe
```

```
                885                 890                 895
His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys
            900                 905                 910
Gln Thr Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys
        915                 920                 925
Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys
    930                 935                 940
Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys
945                 950                 955                 960
Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
                965                 970
```

<210> 1018
<211> 613
<212> PRT
<213> Artificial Sequence

<220>
<223> IgGkSS-HIS-SUMO-uPA
R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aP/Y60bQ/T97aI/L
97bA/H99Q/C122S/Y149R-linker-FC

<400> 1018

```
Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
 1               5                  10                  15
Gly Ser Thr Gly Asp Gly His His His His His His Gly Ser Leu Gln
            20                  25                  30
Asp Ser Glu Val Asn Gln Glu Ala Lys Pro Glu Val Lys Pro Glu Val
        35                  40                  45
Lys Pro Glu Thr His Ile Asn Leu Lys Val Ser Asp Gly Ser Ser Glu
    50                  55                  60
Ile Phe Phe Lys Ile Lys Lys Thr Thr Pro Leu Arg Arg Leu Met Glu
65                  70                  75                  80
Ala Phe Ala Lys Arg Gln Gly Lys Glu Met Asp Ser Leu Thr Phe Leu
                85                  90                  95
Tyr Asp Gly Ile Glu Ile Gln Ala Asp Gln Thr Pro Glu Asp Leu Asp
            100                 105                 110
Met Glu Asp Asn Asp Ile Ile Glu Ala His Arg Glu Gln Ile Gly Gly
        115                 120                 125
Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala
    130                 135                 140
Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Tyr Tyr Arg Cys Gly
145                 150                 155                 160
Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe
                165                 170                 175
Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser
            180                 185                 190
```

```
Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn
        195                 200                 205
Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn
    210                 215                 220
Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln
225                 230                 235                 240
Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp
                245                 250                 255
Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn
            260                 265                 270
Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys
        275                 280                 285
Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu
    290                 295                 300
Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp
305                 310                 315                 320
Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly
                325                 330                 335
Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu
            340                 345                 350
Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp
        355                 360                 365
Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu Gly Gly Ser
    370                 375                 380
Ser Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
385                 390                 395                 400
Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
                405                 410                 415
Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
            420                 425                 430
Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
        435                 440                 445
Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
    450                 455                 460
Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
465                 470                 475                 480
Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
                485                 490                 495
Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
            500                 505                 510
Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
        515                 520                 525
Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
    530                 535                 540
Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
545                 550                 555                 560
Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
                565                 570                 575
```

```
Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
            580                 585                 590
Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
        595                 600                 605
Ser Leu Ser Pro Gly
    610


<210> 1019
<211> 1002
<212> PRT
<213> Artificial Sequence

<220>
<223> uPA N-term-uPA activation-u-PA
      R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aP/Y60bQ/T97aI/L
      97bA/H99Q/Y149R-HSA

<400> 1019
Ser Asn Glu Leu His Gln Val Pro Ser Asn Cys Asp Cys Leu Asn Gly
 1               5                  10                  15
Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile His Trp Cys Asn
            20                  25                  30
Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile Asp Lys Ser Lys
        35                  40                  45
Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly Lys Ala Ser Thr
    50                  55                  60
Asp Thr Met Gly Arg Pro Cys Leu Pro Trp Asn Ser Ala Thr Val Leu
65                  70                  75                  80
Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu Gln Leu Gly Leu
                85                  90                  95
Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg Arg Arg Pro Trp
            100                 105                 110
Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln Glu Cys Met Val
        115                 120                 125
His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro Pro Glu Glu Leu
    130                 135                 140
Lys Phe Gln Cys Gly Gln Lys Thr Leu Arg Pro Arg Phe Lys Ile Ile
145                 150                 155                 160
Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala Ala Ile
                165                 170                 175
Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Tyr Tyr Arg Cys Gly Gly Ser
            180                 185                 190
Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe Ile Pro
        195                 200                 205
Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser Arg Leu
    210                 215                 220
Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn Leu Ile
```

```
225                 230                 235                 240
Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn Asp Ile
                245                 250                 255
Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser
            260                 265                 270
Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr Asn Asp Pro Gln
        275                 280                 285
Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr
    290                 295                 300
Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile
305                 310                 315                 320
Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr
                325                 330                 335
Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys
            340                 345                 350
Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met
        355                 360                 365
Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys Asp
    370                 375                 380
Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg
385                 390                 395                 400
Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu Gly Gly Ser Ser Gly
                405                 410                 415
Gly Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly
            420                 425                 430
Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu
        435                 440                 445
Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr
    450                 455                 460
Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp
465                 470                 475                 480
Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr
                485                 490                 495
Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu
            500                 505                 510
Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn
        515                 520                 525
Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe
    530                 535                 540
His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala
545                 550                 555                 560
Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys
                565                 570                 575
Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala
            580                 585                 590
Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala
        595                 600                 605
Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly
```

```
    610                 615                 620
Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe
625                 630                 635                 640
Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr
                645                 650                 655
Lys Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp
            660                 665                 670
Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile
        675                 680                 685
Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser
    690                 695                 700
His Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro
705                 710                 715                 720
Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr
                725                 730                 735
Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala
            740                 745                 750
Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys
        755                 760                 765
Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His
    770                 775                 780
Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu
785                 790                 795                 800
Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly
                805                 810                 815
Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val
            820                 825                 830
Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly
        835                 840                 845
Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro
    850                 855                 860
Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu
865                 870                 875                 880
His Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu
                885                 890                 895
Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu
            900                 905                 910
Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala
        915                 920                 925
Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr
    930                 935                 940
Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln
945                 950                 955                 960
Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys
                965                 970                 975
Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu
            980                 985                 990
Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
```

995 1000

<210> 1020
<211> 326
<212> PRT
<213> Homo sapiens

<220>
<223> hIgG2 heavy chain constant

<400> 1020
Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
1 5 10 15
Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30
Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45
Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60
Leu Ser Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr
65 70 75 80
Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95
Thr Val Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro
100 105 110
Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
115 120 125
Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
130 135 140
Val Ser His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly
145 150 155 160
Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn
165 170 175
Ser Thr Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp
180 185 190
Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro
195 200 205
Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu
210 215 220
Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
225 230 235 240
Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
245 250 255
Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
260 265 270
Thr Pro Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
275 280 285

```
Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
    290                 295                 300
Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
305                 310                 315                 320
Ser Leu Ser Pro Gly Lys
                325


<210> 1021
<211> 377
<212> PRT
<213> Homo sapiens

<220>
<223> hIgG3 heavy chain constant

<400> 1021
Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
 1               5                  10                  15
Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
            20                  25                  30
Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
        35                  40                  45
Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50                  55                  60
Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65                  70                  75                  80
Tyr Thr Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
                85                  90                  95
Arg Val Glu Leu Lys Thr Pro Leu Gly Asp Thr Thr His Thr Cys Pro
            100                 105                 110
Arg Cys Pro Glu Pro Lys Ser Cys Asp Thr Pro Pro Pro Cys Pro Arg
        115                 120                 125
Cys Pro Glu Pro Lys Ser Cys Asp Thr Pro Pro Pro Cys Pro Arg Cys
    130                 135                 140
Pro Glu Pro Lys Ser Cys Asp Thr Pro Pro Pro Cys Pro Arg Cys Pro
145                 150                 155                 160
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
                165                 170                 175
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
            180                 185                 190
Val Val Asp Val Ser His Glu Asp Pro Glu Val Gln Phe Lys Trp Tyr
        195                 200                 205
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
    210                 215                 220
Gln Tyr Asn Ser Thr Phe Arg Val Val Ser Val Leu Thr Val Leu His
225                 230                 235                 240
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
```

```
                245                 250                 255
Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln
            260                 265                 270
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met
        275                 280                 285
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
    290                 295                 300
Ser Asp Ile Ala Val Glu Trp Glu Ser Ser Gly Gln Pro Glu Asn Asn
305                 310                 315                 320
Tyr Asn Thr Thr Pro Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu
                325                 330                 335
Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Ile
            340                 345                 350
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn Arg Phe Thr Gln
        355                 360                 365
Lys Ser Leu Ser Leu Ser Pro Gly Lys
    370                 375


<210> 1022
<211> 327
<212> PRT
<213> Homo sapiens

<220>
<223> hIgG4 heavy chain constant

<400> 1022
Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
 1               5                  10                  15
Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
            20                  25                  30
Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
        35                  40                  45
Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
    50                  55                  60
Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr
65                  70                  75                  80
Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
                85                  90                  95
Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro Ala Pro
            100                 105                 110
Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
        115                 120                 125
Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
    130                 135                 140
Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
145                 150                 155                 160
```

```
Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
                165                 170                 175
Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
            180                 185                 190
Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
        195                 200                 205
Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
    210                 215                 220
Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys
225                 230                 235                 240
Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
                245                 250                 255
Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
            260                 265                 270
Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
        275                 280                 285
Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
    290                 295                 300
Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
305                 310                 315                 320
Leu Ser Leu Ser Leu Gly Lys
                325
```

<210> 1023
<211> 227
<212> PRT
<213> Homo sapiens

<220>
<223> Immunoglobulin Gamma-1 heavy chain (FC)

<400> 1023

```
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
 1               5                  10                  15
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
            20                  25                  30
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
        35                  40                  45
Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
    50                  55                  60
His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65                  70                  75                  80
Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
                85                  90                  95
Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
            100                 105                 110
Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
```

```
        115                 120                 125
Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
    130                 135                 140
Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145                 150                 155                 160
Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
                165                 170                 175
Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
            180                 185                 190
Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
        195                 200                 205
His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
    210                 215                 220
Pro Gly Lys
225
```

<210> 1024
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> SSSSG linker

<400> 1024
Ser Ser Ser Ser Gly
 1   5

<210> 1025
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> GKSSGSGSESKS linker

<400> 1025
Gly Lys Ser Ser Gly Ser Gly Ser Glu Ser Lys Ser
 1   5   10

<210> 1026
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> GGSTSGSGKSSEGKG linker

<400> 1026
Gly Gly Ser Thr Ser Gly Ser Gly Lys Ser Ser Glu Gly Lys Gly
 1   5   10   15

<210> 1027
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> GSTSGSGKSSSEGSGSTKG linker

<400> 1027
Gly Ser Thr Ser Gly Ser Gly Lys Ser Ser Ser Glu Gly Ser Gly Ser
 1   5   10   15
Thr Lys Gly

<210> 1028
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> GSTSGSGKPGSGEGSTKG linker

<400> 1028
Gly Ser Thr Ser Gly Ser Gly Lys Pro Gly Ser Gly Glu Gly Ser Thr
 1   5   10   15
Lys Gly

<210> 1029
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> EGKSSGSGSESKEF linker

<400> 1029
Glu Gly Lys Ser Ser Gly Ser Gly Ser Glu Ser Lys Glu Phe

 1   5   10

<210> 1030
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> AAPA linker

<400> 1030
Ala Ala Pro Ala
 1

<210> 1031
<211> 100
<212> PRT
<213> Artificial Sequence

<220>
<223> SUMO

<400> 1031
Gly Ser Leu Gln Asp Ser Glu Val Asn Gln Glu Ala Lys Pro Glu Val
 1   5   10   15
Lys Pro Glu Val Lys Pro Glu Thr His Ile Asn Leu Lys Val Ser Asp
            20   25   30
Gly Ser Ser Glu Ile Phe Phe Lys Ile Lys Lys Thr Thr Pro Leu Arg
        35   40   45
Arg Leu Met Glu Ala Phe Ala Lys Arg Gln Gly Lys Glu Met Asp Ser
    50   55   60
Leu Arg Phe Leu Tyr Asp Gly Ile Arg Ile Gln Ala Asp Gln Ala Pro
65   70   75   80
Glu Asp Leu Asp Met Glu Asp Asn Asp Ile Ile Glu Ala His Arg Glu
                85   90   95
Gln Ile Gly Gly
            100

<210> 1032
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> DG-6xHIS-SUMO

<400> 1032
Asp Gly His His His His His His Gly Ser Leu Gln Asp Ser Glu Val
 1   5   10   15
Asn Gln Glu Ala Lys Pro Glu Val Lys Pro Glu Val Lys Pro Glu Thr
            20   25   30
His Ile Asn Leu Lys Val Ser Asp Gly Ser Ser Glu Ile Phe Phe Lys
        35   40   45
Ile Lys Lys Thr Thr Pro Leu Arg Arg Leu Met Glu Ala Phe Ala Lys
    50   55   60
Arg Gln Gly Lys Glu Met Asp Ser Leu Thr Phe Leu Tyr Asp Gly Ile
65   70   75   80
Glu Ile Gln Ala Asp Gln Thr Pro Glu Asp Leu Asp Met Glu Asp Asn
                85   90   95
Asp Ile Ile Glu Ala His Arg Glu Gln Ile Gly Gly
            100   105

<210> 1033
<211> 100
<212> PRT
<213> Artificial Sequence

<220>
<223> SUMO

<400> 1033
Gly Ser Leu Gln Asp Ser Glu Val Asn Gln Glu Ala Lys Pro Glu Val
 1   5   10   15
Lys Pro Glu Val Lys Pro Glu Thr His Ile Asn Leu Lys Val Ser Asp
            20   25   30
Gly Ser Ser Glu Ile Phe Phe Lys Ile Lys Lys Thr Thr Pro Leu Arg
        35   40   45
Arg Leu Met Glu Ala Phe Ala Lys Arg Gln Gly Lys Glu Met Asp Ser
    50   55   60
Leu Thr Phe Leu Tyr Asp Gly Ile Glu Ile Gln Ala Asp Gln Thr Pro
65   70   75   80
Glu Asp Leu Asp Met Glu Asp Asn Asp Ile Ile Glu Ala His Arg Glu
                85   90   95
Gln Ile Gly Gly
            100

<210> 1034
<211> 505
<212> PRT
<213> Artificial Sequence

<220>
<223> hIL2ss-uPA -FC

<400> 1034

```
Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
 1               5                  10                  15
Val Thr Asn Ser Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln
            20                  25                  30
Pro Trp Phe Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr
        35                  40                  45
Tyr Val Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala
    50                  55                  60
Thr His Cys Phe Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr
65                  70                  75                  80
Leu Gly Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe
                85                  90                  95
Glu Val Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu
            100                 105                 110
Ala His His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly
        115                 120                 125
Arg Cys Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser
    130                 135                 140
Met Tyr Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe
145                 150                 155                 160
Gly Lys Glu Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met
                165                 170                 175
Thr Val Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr
            180                 185                 190
Tyr Gly Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln
        195                 200                 205
Trp Lys Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys
    210                 215                 220
Ser Leu Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg
225                 230                 235                 240
Gly Cys Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His
                245                 250                 255
Phe Leu Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala
            260                 265                 270
Leu Gly Gly Ser Ser Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys
        275                 280                 285
Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
    290                 295                 300
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
305                 310                 315                 320
Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
                325                 330                 335
Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
            340                 345                 350
```

```
Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
        355                 360                 365
His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
    370                 375                 380
Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
385                 390                 395                 400
Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
                405                 410                 415
Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
            420                 425                 430
Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
        435                 440                 445
Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
    450                 455                 460
Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
465                 470                 475                 480
Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
                485                 490                 495
Gln Lys Ser Leu Ser Leu Ser Pro Gly
            500                 505


<210> 1035
<211> 867
<212> PRT
<213> Artificial Sequence

<220>
<223> hIL2ss-uPA -HSA

<400> 1035
Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
 1               5                  10                  15
Val Thr Asn Ser Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln
            20                  25                  30
Pro Trp Phe Ala Ala Ile Tyr Arg Arg His Arg Gly Gly Ser Val Thr
        35                  40                  45
Tyr Val Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala
    50                  55                  60
Thr His Cys Phe Ile Asp Tyr Pro Lys Lys Glu Asp Tyr Ile Val Tyr
65                  70                  75                  80
Leu Gly Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe
                85                  90                  95
Glu Val Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Thr Leu
            100                 105                 110
Ala His His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly
        115                 120                 125
Arg Cys Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser
```

```
    130                 135                 140
Met Tyr Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe
145                 150                 155                 160
Gly Lys Glu Asn Ser Thr Asp Tyr Leu Tyr Pro Glu Gln Leu Lys Met
                165                 170                 175
Thr Val Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr
            180                 185                 190
Tyr Gly Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln
        195                 200                 205
Trp Lys Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys
    210                 215                 220
Ser Leu Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg
225                 230                 235                 240
Gly Cys Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His
                245                 250                 255
Phe Leu Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala
            260                 265                 270
Leu Gly Gly Ser Ser Gly Gly Asp Ala His Lys Ser Glu Val Ala His
        275                 280                 285
Arg Phe Lys Asp Leu Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile
    290                 295                 300
Ala Phe Ala Gln Tyr Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys
305                 310                 315                 320
Leu Val Asn Glu Val Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu
                325                 330                 335
Ser Ala Glu Asn Cys Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys
            340                 345                 350
Leu Cys Thr Val Ala Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp
        355                 360                 365
Cys Cys Ala Lys Gln Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His
    370                 375                 380
Lys Asp Asp Asn Pro Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp
385                 390                 395                 400
Val Met Cys Thr Ala Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys
                405                 410                 415
Tyr Leu Tyr Glu Ile Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu
            420                 425                 430
Leu Leu Phe Phe Ala Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys
        435                 440                 445
Gln Ala Ala Asp Lys Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu
    450                 455                 460
Arg Asp Glu Gly Lys Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala
465                 470                 475                 480
Ser Leu Gln Lys Phe Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala
                485                 490                 495
Arg Leu Ser Gln Arg Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys
            500                 505                 510
Leu Val Thr Asp Leu Thr Lys Val His Thr Glu Cys Cys His Gly Asp
```

```
        515                 520                 525
Leu Leu Glu Cys Ala Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys
    530                 535                 540
Glu Asn Gln Asp Ser Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys
545                 550                 555                 560
Pro Leu Leu Glu Lys Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu
                565                 570                 575
Met Pro Ala Asp Leu Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys
            580                 585                 590
Asp Val Cys Lys Asn Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met
        595                 600                 605
Phe Leu Tyr Glu Tyr Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu
    610                 615                 620
Leu Leu Arg Leu Ala Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys
625                 630                 635                 640
Ala Ala Ala Asp Pro His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe
                645                 650                 655
Lys Pro Leu Val Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu
            660                 665                 670
Leu Phe Glu Gln Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val
        675                 680                 685
Arg Tyr Thr Lys Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu
    690                 695                 700
Val Ser Arg Asn Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro
705                 710                 715                 720
Glu Ala Lys Arg Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu
                725                 730                 735
Asn Gln Leu Cys Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val
            740                 745                 750
Thr Lys Cys Cys Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser
        755                 760                 765
Ala Leu Glu Val Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu
    770                 775                 780
Thr Phe Thr Phe His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg
785                 790                 795                 800
Gln Ile Lys Lys Gln Thr Ala Leu Val Glu Leu Val Lys His Lys Pro
                805                 810                 815
Lys Ala Thr Lys Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala
            820                 825                 830
Phe Val Glu Lys Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala
        835                 840                 845
Glu Glu Gly Lys Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
    850                 855                 860
Ser Pro Gly
865
```

<210> 1036

<211> 663
<212> PRT
<213> Artificial Sequence

<220>
<223> IgGkSP-uPA N-term-furin activation-u-PA
R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aP/Y60bQ/T97aI/L
97bA/H99Q/Y149R-linker-Fc

<400> 1036
Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
 1   5   10   15
Gly Ser Thr Gly Ser Asn Glu Leu His Gln Val Pro Ser Asn Cys Asp
            20   25   30
Cys Leu Asn Gly Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile
        35   40   45
His Trp Cys Asn Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile
    50   55   60
Asp Lys Ser Lys Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly
65   70   75   80
Lys Ala Ser Thr Asp Thr Met Gly Arg Pro Cys Leu Pro Trp Asn Ser
                85   90   95
Ala Thr Val Leu Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu
            100   105   110
Gln Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg
        115   120   125
Arg Arg Pro Trp Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln
    130   135   140
Glu Cys Met Val His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro
145   150   155   160
Pro Glu Glu Leu Lys Phe Gln Cys Gly Gln Lys Thr Leu Arg Arg Arg
                165   170   175
Lys Arg Ile Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp
            180   185   190
Phe Ala Ala Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Tyr Tyr Arg
        195   200   205
Cys Gly Gly Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His
    210   215   220
Cys Phe Ile Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly
225   230   235   240
Arg Ser Arg Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val
                245   250   255
Glu Asn Leu Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln
            260   265   270
His Asn Asp Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys
        275   280   285
Ala Gln Pro Ser Arg Thr Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr
    290   295   300

```
Asn Asp Pro Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys
305                 310                 315                 320
Glu Asn Ser Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val
                325                 330                 335
Val Lys Leu Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly
            340                 345                 350
Ser Glu Val Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys
        355                 360                 365
Thr Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu
    370                 375                 380
Gln Gly Arg Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys
385                 390                 395                 400
Ala Leu Lys Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu
                405                 410                 415
Pro Trp Ile Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu Gly
            420                 425                 430
Gly Ser Ser Gly Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
        435                 440                 445
Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
    450                 455                 460
Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
465                 470                 475                 480
Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
                485                 490                 495
Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
            500                 505                 510
Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
        515                 520                 525
Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
    530                 535                 540
Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
545                 550                 555                 560
Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr
                565                 570                 575
Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
            580                 585                 590
Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
        595                 600                 605
Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
    610                 615                 620
Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
625                 630                 635                 640
Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
                645                 650                 655
Ser Leu Ser Leu Ser Pro Gly
            660
```

<210> 1037
<211> 361
<212> PRT
<213> Artificial Sequence

<220>
<223> HHHHHH-SUMO-uPA
R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aP/Y60bQ/T97aI/L
97bA/H99Q/Y149R

<400> 1037
Met Gly His His His His His His Gly Ser Leu Gln Asp Ser Glu Val
 1   5   10   15
Asn Gln Glu Ala Lys Pro Glu Val Lys Pro Glu Val Lys Pro Glu Thr
            20   25   30
His Ile Asn Leu Lys Val Ser Asp Gly Ser Ser Glu Ile Phe Phe Lys
        35   40   45
Ile Lys Lys Thr Thr Pro Leu Arg Arg Leu Met Glu Ala Phe Ala Lys
    50   55   60
Arg Gln Gly Lys Glu Met Asp Ser Leu Arg Phe Leu Tyr Asp Gly Ile
65   70   75   80
Arg Ile Gln Ala Asp Gln Ala Pro Glu Asp Leu Asp Met Glu Asp Asn
                85   90   95
Asp Ile Ile Glu Ala His Arg Glu Gln Ile Gly Gly Ile Ile Gly Gly
            100   105   110
Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala Ala Ile Tyr Gln
        115   120   125
Arg Tyr Glu Gly Gly Ser Glu Tyr Tyr Arg Cys Gly Gly Ser Leu Ile
    130   135   140
Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe Ile Pro Gln Pro
145   150   155   160
Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser Arg Leu Asn Ser
                165   170   175
Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn Leu Ile Leu His
            180   185   190
Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn Asp Ile Ala Leu
        195   200   205
Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser Arg Thr
    210   215   220
Ile Gln Thr Ile Cys Leu Pro Ser Met Tyr Asn Asp Pro Gln Phe Gly
225   230   235   240
Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr Asp Arg
                245   250   255
Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile Ser His
            260   265   270
Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr Thr Lys
        275   280   285
Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys Gln Gly

```
    290                 295                 300
Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met Thr Leu
305                 310                 315                 320
Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys Asp Lys Pro
                325                 330                 335
Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg Ser His
            340                 345                 350
Thr Lys Glu Glu Asn Gly Leu Ala Leu
        355                 360
```

<210> 1038
<211> 361
<212> PRT
<213> Artificial Sequence

<220>
<223> HHHHHH-SUMO-uPA
R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aP/Y60bQ/T97aI/L
97bA/H99Q/C122S/Y149R

<400> 1038

```
Met Gly His His His His His His Gly Ser Leu Gln Asp Ser Glu Val
 1               5                  10                  15
Asn Gln Glu Ala Lys Pro Glu Val Lys Pro Glu Val Lys Pro Glu Thr
            20                  25                  30
His Ile Asn Leu Lys Val Ser Asp Gly Ser Ser Glu Ile Phe Phe Lys
        35                  40                  45
Ile Lys Lys Thr Thr Pro Leu Arg Arg Leu Met Glu Ala Phe Ala Lys
    50                  55                  60
Arg Gln Gly Lys Glu Met Asp Ser Leu Arg Phe Leu Tyr Asp Gly Ile
65                  70                  75                  80
Arg Ile Gln Ala Asp Gln Ala Pro Glu Asp Leu Asp Met Glu Asp Asn
                85                  90                  95
Asp Ile Ile Glu Ala His Arg Glu Gln Ile Gly Gly Ile Ile Gly Gly
            100                 105                 110
Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala Ala Ile Tyr Gln
        115                 120                 125
Arg Tyr Glu Gly Gly Ser Glu Tyr Tyr Arg Cys Gly Gly Ser Leu Ile
    130                 135                 140
Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe Ile Pro Gln Pro
145                 150                 155                 160
Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser Arg Leu Asn Ser
                165                 170                 175
Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn Leu Ile Leu His
            180                 185                 190
Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn Asp Ile Ala Leu
        195                 200                 205
```

```
Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser Arg Thr
    210                 215                 220
Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln Phe Gly
225                 230                 235                 240
Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr Asp Arg
                245                 250                 255
Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile Ser His
            260                 265                 270
Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr Thr Lys
        275                 280                 285
Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys Gln Gly
    290                 295                 300
Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met Thr Leu
305                 310                 315                 320
Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys Asp Lys Pro
                325                 330                 335
Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg Ser His
            340                 345                 350
Thr Lys Glu Glu Asn Gly Leu Ala Leu
        355                 360


<210> 1039
<211> 366
<212> PRT
<213> Artificial Sequence

<220>
<223> HHHHHH-SUMO-uPA
      R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aP/Y60bQ/T97aI/L
      97bA/H99Q/C122S/Y149R-GGSCK

<400> 1039
Met Gly His His His His His His Gly Ser Leu Gln Asp Ser Glu Val
 1               5                  10                  15
Asn Gln Glu Ala Lys Pro Glu Val Lys Pro Glu Val Lys Pro Glu Thr
            20                  25                  30
His Ile Asn Leu Lys Val Ser Asp Gly Ser Ser Glu Ile Phe Phe Lys
        35                  40                  45
Ile Lys Lys Thr Thr Pro Leu Arg Arg Leu Met Glu Ala Phe Ala Lys
    50                  55                  60
Arg Gln Gly Lys Glu Met Asp Ser Leu Arg Phe Leu Tyr Asp Gly Ile
65                  70                  75                  80
Arg Ile Gln Ala Asp Gln Ala Pro Glu Asp Leu Asp Met Glu Asp Asn
                85                  90                  95
Asp Ile Ile Glu Ala His Arg Glu Gln Ile Gly Gly Ile Ile Gly Gly
            100                 105                 110
Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala Ala Ile Tyr Gln
```

```
        115                 120                 125
Arg Tyr Glu Gly Gly Ser Glu Tyr Tyr Arg Cys Gly Gly Ser Leu Ile
    130                 135                 140
Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe Ile Pro Gln Pro
145                 150                 155                 160
Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser Arg Leu Asn Ser
                165                 170                 175
Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn Leu Ile Leu His
            180                 185                 190
Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn Asp Ile Ala Leu
        195                 200                 205
Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro Ser Arg Thr
    210                 215                 220
Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro Gln Phe Gly
225                 230                 235                 240
Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser Thr Asp Arg
                245                 250                 255
Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu Ile Ser His
            260                 265                 270
Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val Thr Thr Lys
        275                 280                 285
Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser Cys Gln Gly
    290                 295                 300
Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg Met Thr Leu
305                 310                 315                 320
Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys Asp Lys Pro
                325                 330                 335
Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile Arg Ser His
            340                 345                 350
Thr Lys Glu Glu Asn Gly Leu Ala Leu Gly Gly Ser Cys Lys
        355                 360                 365


<210> 1040
<211> 875
<212> PRT
<213> Artificial Sequence

<220>
<223> IgGkSP-furin activation-uPA
      R35Q/H37Y/R37aE/V38E/T39Y/V41R/D60aP/Y60bQ/T97aI/L
      97bA/H99Q/C122S/Y149R-linker-HSA

<400> 1040
Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
 1               5                  10                  15
Gly Ser Thr Gly Gln Ser Gly Gln Lys Thr Leu Arg Arg Lys Arg Ile
            20                  25                  30
```

```
Ile Gly Gly Glu Phe Thr Thr Ile Glu Asn Gln Pro Trp Phe Ala Ala
        35                  40                  45
Ile Tyr Gln Arg Tyr Glu Gly Gly Ser Glu Tyr Tyr Arg Cys Gly Gly
    50                  55                  60
Ser Leu Ile Ser Pro Cys Trp Val Ile Ser Ala Thr His Cys Phe Ile
65                  70                  75                  80
Pro Gln Pro Lys Lys Glu Asp Tyr Ile Val Tyr Leu Gly Arg Ser Arg
                85                  90                  95
Leu Asn Ser Asn Thr Gln Gly Glu Met Lys Phe Glu Val Glu Asn Leu
            100                 105                 110
Ile Leu His Lys Asp Tyr Ser Ala Asp Ile Ala Ala Gln His Asn Asp
        115                 120                 125
Ile Ala Leu Leu Lys Ile Arg Ser Lys Glu Gly Arg Cys Ala Gln Pro
    130                 135                 140
Ser Arg Thr Ile Gln Thr Ile Ser Leu Pro Ser Met Tyr Asn Asp Pro
145                 150                 155                 160
Gln Phe Gly Thr Ser Cys Glu Ile Thr Gly Phe Gly Lys Glu Asn Ser
                165                 170                 175
Thr Asp Arg Leu Tyr Pro Glu Gln Leu Lys Met Thr Val Val Lys Leu
            180                 185                 190
Ile Ser His Arg Glu Cys Gln Gln Pro His Tyr Tyr Gly Ser Glu Val
        195                 200                 205
Thr Thr Lys Met Leu Cys Ala Ala Asp Pro Gln Trp Lys Thr Asp Ser
    210                 215                 220
Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Ser Leu Gln Gly Arg
225                 230                 235                 240
Met Thr Leu Thr Gly Ile Val Ser Trp Gly Arg Gly Cys Ala Leu Lys
                245                 250                 255
Asp Lys Pro Gly Val Tyr Thr Arg Val Ser His Phe Leu Pro Trp Ile
            260                 265                 270
Arg Ser His Thr Lys Glu Glu Asn Gly Leu Ala Leu Gly Gly Ser Ser
        275                 280                 285
Gly Gly Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu
    290                 295                 300
Gly Glu Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr
305                 310                 315                 320
Leu Gln Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val
                325                 330                 335
Thr Glu Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys
            340                 345                 350
Asp Lys Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala
        355                 360                 365
Thr Leu Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln
    370                 375                 380
Glu Pro Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro
385                 390                 395                 400
Asn Leu Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala
                405                 410                 415
```

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Phe His Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile
            420                 425                 430
Ala Arg Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala
        435                 440                 445
Lys Arg Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys
    450                 455                 460
Ala Ala Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys
465                 470                 475                 480
Ala Ser Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe
                485                 490                 495
Gly Glu Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg
            500                 505                 510
Phe Pro Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu
        515                 520                 525
Thr Lys Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala
    530                 535                 540
Asp Asp Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser
545                 550                 555                 560
Ile Ser Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys
                565                 570                 575
Ser His Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu
            580                 585                 590
Pro Ser Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn
        595                 600                 605
Tyr Ala Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr
    610                 615                 620
Ala Arg Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala
625                 630                 635                 640
Lys Thr Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro
                645                 650                 655
His Glu Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu
            660                 665                 670
Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu
        675                 680                 685
Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys
    690                 695                 700
Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu
705                 710                 715                 720
Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met
                725                 730                 735
Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val
            740                 745                 750
Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr
        755                 760                 765
Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp
    770                 775                 780
Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His
785                 790                 795                 800
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Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln
                805                 810                 815
Thr Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu
            820                 825                 830
Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys
        835                 840                 845
Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys
    850                 855                 860
Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
865                 870                 875


<210> 1041
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Furin activation sequence

<400> 1041
Gln Ser Gly Lys Thr Leu Arg Arg Lys Arg
 1               5                  10


<210> 1042
<211> 146
<212> PRT
<213> uPA N-terminus

<400> 1042
Ser Asn Glu Leu His Gln Val Pro Ser Asn Cys Asp Cys Leu Asn Gly
 1               5                  10                  15
Gly Thr Cys Val Ser Asn Lys Tyr Phe Ser Asn Ile His Trp Cys Asn
            20                  25                  30
Cys Pro Lys Lys Phe Gly Gly Gln His Cys Glu Ile Asp Lys Ser Lys
        35                  40                  45
Thr Cys Tyr Glu Gly Asn Gly His Phe Tyr Arg Gly Lys Ala Ser Thr
    50                  55                  60
Asp Thr Met Gly Arg Pro Cys Leu Pro Trp Asn Ser Ala Thr Val Leu
65                  70                  75                  80
Gln Gln Thr Tyr His Ala His Arg Ser Asp Ala Leu Gln Leu Gly Leu
                85                  90                  95
Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Asn Arg Arg Arg Pro Trp
            100                 105                 110
Cys Tyr Val Gln Val Gly Leu Lys Pro Leu Val Gln Glu Cys Met Val
        115                 120                 125
His Asp Cys Ala Asp Gly Lys Lys Pro Ser Ser Pro Pro Glu Glu Leu
```

    130   135   140
Lys Phe
145

<210> 1043
<211> 255
<212> PRT
<213> Artificial Sequence

<220>
<223> Chain A, IG GAMMA-1 CHAIN C REGION

<400> 1043
Met Lys Lys Thr Ala Ile Ala Ile Ala Val Ala Leu Ala Gly Phe Ala
 1   5   10   15
Thr Val Ala Gln Ala Asp Val Glu Ser Lys Ser Cys Asp Lys Thr His
            20   25   30
Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
        35   40   45
Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
    50   55   60
Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
65   70   75   80
Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
                85   90   95
Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
            100   105   110
Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
        115   120   125
Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
    130   135   140
Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
145   150   155   160
Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
                165   170   175
Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
            180   185   190
Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
        195   200   205
Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
    210   215   220
Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
225   230   235   240
His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                245   250   255

<210> 1044
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Furin

<400> 1044
Gln Ser Gly Gln Lys Thr Leu Arg Arg Lys Arg
 1   5   10