SEQUENCE LISTING

<110> CSL Behring Recombinant Facility AG

<120> Truncated Von Willebrand Factor Polypeptides for Extravascular Administration in the Treatment or Prophylaxis of a Blood Coagulation Disorder

<130> SP100952SGM

<150> EP 16198497.6
<151> 2016-11-11

<160> 8

<170> PatentIn version 3.5

<210> 1
<211> 5616
<212> DNA
<213> Artificial Sequence

<220>
<223> DNA encoding construct VWF fragment - G/S Linker - albumin

<220>
<221> misc_feature
<222> (1)..(6)
<223> EcoRI restriction enzyme cleavage site

<220>
<221> misc_feature
<222> (32)..(3757)
<223> coding sequence for VWF amino acids 1 to 1242

<220>
<221> misc_feature
<222> (3758)..(3850)
<223> coding sequence for glycine/serine linker

<220>
<221> misc_feature
<222> (3851)..(5608)
<223> coding sequence for human albumin

<220>
<221> misc_feature
<222> (5609)..(5616)
<223> NotI restriction enzyme cleavage site

<400> 1
gaattcccgc agccctcatt tgcaggggaa gatgattcct gccagatttg ccggggtgct 60

gcttgctctg gccctcattt tgccagggac cctttgtgca gaaggaactc gcggcaggtc 120

atccacggcc cgatgcagcc ttttcggaag tgacttcgtc aacacctttg atgggagcat 180

gtacagcttt gcgggatact gcagttacct cctggcaggg ggctgccaga aacgctcctt 240

ctcgattatt ggggacttcc agaatggcaa gagagtgagc ctctccgtgt atcttgggga 300

atttttgac atccatttgt ttgtcaatgg taccgtgaca caggggacc aaagagtctc 360

catgccctat gcctccaaag ggctgtatct agaaactgag gctgggtact acaagctgtc 420

cggtgaggcc tatggctttg tggccaggat cgatggcagc ggcaactttc aagtcctgct 480

gtcagacaga tacttcaaca agacctgcgg gctgtgtggc aactttaaca tctttgctga 540

agatgacttt atgacccaag aagggacctt gacctcggac ccttatgact ttgccaactc 600

atgggctctg agcagtggag aacagtggtg tgaacgggca tctcctccca gcagctcatg 660

caacatctcc tctggggaaa tgcagaaggg cctgtgggag cagtgccagc ttctgaagag 720

cacctcggtg tttgcccgct gccaccctct ggtggacccc gagccttttg tggccctgtg 780

tgagaagact ttgtgtgagt gtgctggggg gctggagtgc gcctgccctg ccctcctgga 840

gtacgcccgg acctgtgccc aggagggaat ggtgctgtac ggctggaccg accacagcgc 900

gtgcagccca gtgtgccctg ctggtatgga gtataggcag tgtgtgtccc cttgcgccag 960

gacctgccag agcctgcaca tcaatgaaat gtgtcaggag cgatgcgtgg atggctgcag 1020

ctgccctgag ggacagctcc tggatgaagg cctctgcgtg gagagcaccg agtgtccctg 1080

cgtgcattcc ggaaagcgct accctcccgg cacctccctc tctcgagact gcaacacctg 1140

catttgccga aacagccagt ggatctgcag caatgaagaa tgtccagggg agtgccttgt 1200

cacaggtcaa tcacacttca agagctttga caacagatac ttcaccttca gtgggatctg 1260

ccagtacctg ctggcccggg attgccagga ccactccttc tccattgtca ttgagactgt 1320

ccagtgtgct gatgaccgcg acgctgtgtg cacccgctcc gtcaccgtcc ggctgcctgg 1380

cctgcacaac agccttgtga aactgaagca tggggcagga gttgccatgg atggccagga 1440

cgtccagctc cccctcctga aaggtgacct ccgcatccag catacagtga cggcctccgt 1500

gcgcctcagc tacggggagg acctgcagat ggactgggat ggccgcggga ggctgctggt 1560

gaagctgtcc cccgtctatg ccgggaagac ctgcggcctg tgtgggaatt acaatggcaa 1620

ccagggcgac gacttcctta ccccctctgg gctggcggag ccccgggtgg aggacttcgg 1680

gaacgcctgg aagctgcacg gggactgcca ggacctgcag aagcagcaca gcgatccctg 1740

cgccctcaac ccgcgcatga ccaggttctc cgaggaggcg tgcgcggtcc tgacgtcccc 1800

cacattcgag gcctgccatc gtgccgtcag cccgctgccc tacctgcgga actgccgcta 1860

cgacgtgtgc tcctgctcgg acggccgcga gtgcctgtgc ggcgccctgg ccagctatgc 1920

cgcggcctgc gcggggagag gcgtgcgcgt cgcgtggcgc gagccaggcc gctgtgagct 1980

gaactgcccg aaaggccagg tgtacctgca gtgcgggacc ccctgcaacc tgacctgccg 2040

ctctctctct tacccggatg aggaatgcaa tgaggcctgc ctggagggct gcttctgccc 2100

cccagggctc tacatggatg agagggggga ctgcgtgccc aaggcccagt gcccctgtta 2160

ctatgacggt gagatcttcc agccagaaga catcttctca gaccatcaca ccatgtgcta 2220

ctgtgaggat ggcttcatgc actgtaccat gagtggagtc cccggaagct tgctgcctga 2280

cgctgtcctc agcagtcccc tgtctcatcg cagcaaaagg agcctatcct gtcggccccc 2340

catggtcaag ctggtgtgtc ccgctgacaa cctgcgggct gaagggctcg agtgtaccaa 2400

aacgtgccag aactatgacc tggagtgcat gagcatgggc tgtgtctctg gctgcctctg 2460

ccccccgggc atggtccggc atgagaacag atgtgtggcc ctggaaaggt gtccctgctt 2520

ccatcagggc aaggagtatg cccctggaga aacagtgaag attggctgca acacttgtgt 2580

ctgtcgggac cggaagtgga actgcacaga ccatgtgtgt gatgccacgt gctccacgat 2640

cggcatggcc cactacctca ccttcgacgg gctcaaatac ctgttccccg gggagtgcca 2700

gtacgttctg gtgcaggatt actgcggcag taaccctggg acctttcgga tcctagtggg 2760

gaataaggga tgcagccacc cctcagtgaa atgcaagaaa cgggtcacca tcctggtgga 2820

gggaggagag attgagctgt ttgacgggga ggtgaatgtg aagaggccca tgaaggatga 2880

gactcacttt gaggtggtgg agtctggccg gtacatcatt ctgctgctgg gcaaagccct 2940

ctccgtggtc tgggaccgcc acctgagcat ctccgtggtc ctgaagcaga cataccagga 3000

gaaagtgtgt ggcctgtgtg ggaattttga tggcatccag aacaatgacc tcaccagcag 3060

caacctccaa gtggaggaag accctgtgga ctttgggaac tcctggaaag tgagctcgca 3120

gtgtgctgac accagaaaag tgcctctgga ctcatcccct gccacctgcc ataacaacat 3180

catgaagcag acgatggtgg attcctcctg tagaatcctt accagtgacg tcttccagga 3240

ctgcaacaag ctggtggacc ccgagccata tctggatgtc tgcatttacg acacctgctc 3300

ctgtgagtcc attggggact gcgcctgctt ctgcgacacc attgctgcct atgcccacgt 3360

gtgtgcccag catggcaagg tggtgacctg gaggacggcc acattgtgcc cccagagctg 3420

cgaggagagg aatctccggg agaacgggta tgagtgtgag tggcgctata acagctgtgc 3480

acctgcctgt caagtcacgt gtcagcaccc tgagccactg gcctgccctg tgcagtgtgt 3540

ggagggctgc catgcccact gccctccagg gaaaatcctg gatgagcttt tgcagacctg 3600

cgttgaccct gaagactgtc cagtgtgtga ggtggctggc cggcgttttg cctcaggaaa 3660

gaaagtcacc ttgaatccca gtgaccctga gcactgccag atttgccact gtgatgttgt 3720

caacctcacc tgtgaagcct gccaggagcc gggaggctcg agcgggggat ctggcgggtc 3780

tggaggctct ggagggtcgg gaggctctgg aggctctggg ggatctggcg ggtctggagg 3840

gtcgggatcc gatgcacaca agagtgaggt tgctcatcgg tttaaagatt tgggagaaga 3900

aaatttcaaa gccttggtgt tgattgcctt tgctcagtat cttcagcagt gtccatttga 3960

agatcatgta aaattagtga atgaagtaac tgaatttgca aaaacatgtg ttgctgatga 4020

gtcagctgaa aattgtgaca aatcacttca taccctttt ggagacaaat tatgcacagt 4080

tgcaactctt cgtgaaacct atggtgaaat ggctgactgc tgtgcaaaac aagaacctga 4140

gagaaatgaa tgcttcttgc aacacaaaga tgacaaccca aacctccccc gattggtgag 4200

accagaggtt gatgtgatgt gcactgcttt tcatgacaat gaagagacat ttttgaaaaa 4260

atacttatat gaaattgcca gaagacatcc ttacttttat gccccggaac tccttttctt 4320

tgctaaaagg tataaagctg cttttacaga atgttgccaa gctgctgata aagctgcctg 4380

cctgttgcca aagctcgatg aacttcggga tgaagggaag gcttcgtctg ccaaacagag 4440

actcaagtgt gccagtctcc aaaaatttgg agaaagagct ttcaaagcat gggcagtagc 4500

tcgcctgagc cagagatttc ccaaagctga gtttgcagaa gtttccaagt tagtgacaga 4560

tcttaccaaa gtccacacgg aatgctgcca tggagatctg cttgaatgtg ctgatgacag 4620

ggcggacctt gccaagtata tctgtgaaaa tcaagattcg atctccagta aactgaagga 4680

atgctgtgaa aaacctctgt tggaaaaatc ccactgcatt gccgaagtgg aaaatgatga 4740

gatgcctgct gacttgcctt cattagctgc tgattttgtt gaaagtaagg atgtttgcaa 4800

aaactatgct gaggcaaagg atgtcttcct gggcatgttt ttgtatgaat atgcaagaag 4860

gcatcctgat tactctgtcg tgctgctgct gagacttgcc aagacatatg aaaccactct 4920

agagaagtgc tgtgccgctg cagatcctca tgaatgctat gccaaagtgt tcgatgaatt 4980

taaacctctt gtggaagagc ctcagaattt aatcaaacaa aattgtgagc tttttgagca 5040

gcttggagag tacaaattcc agaatgcgct attagttcgt tacaccaaga aagtacccca 5100

agtgtcaact ccaactcttg tagaggtctc aagaaaccta ggaaaagtgg gcagcaaatg 5160

ttgtaaacat cctgaagcaa aaagaatgcc ctgtgcagaa gactatctat ccgtggtcct 5220

gaaccagtta tgtgtgttgc atgagaaaac gccagtaagt gacagagtca ccaaatgctg 5280

cacagaatcc ttggtgaaca ggcgaccatg cttttcagct ctggaagtcg atgaaacata 5340

cgttcccaaa gagtttaatg ctgaaacatt caccttccat gcagatatat gcacactttc 5400

tgagaaggag agacaaatca agaaacaaac tgcacttgtt gagctcgtga aacacaagcc 5460

caaggcaaca aaagagcaac tgaaagctgt tatggatgat ttcgcagctt ttgtagagaa 5520

gtgctgcaag gctgacgata aggagacctg ctttgccgag gagggtaaaa aacttgttgc 5580

tgcaagtcaa gctgccttag gcttataggc ggccgc 5616

<210> 2
<211> 1095
<212> PRT
<213> Artificial Sequence

<220>
<223> polypeptide encoded by SEQ ID NO:1

<220>
<221> MISC_FEATURE
<222> (1)..(479)
<223> VWF D´D3 region (VWF amino acids 764 - 1242)

<220>
<221> MISC_FEATURE
<222> (480)..(510)
<223> glycine/serine linker

<220>
<221> MISC_FEATURE
<222> (511)..(1095)
<223> human albumin

<400> 2

Ser Leu Ser Cys Arg Pro Pro Met Val Lys Leu Val Cys Pro Ala Asp
1 5 10 15

Asn Leu Arg Ala Glu Gly Leu Glu Cys Thr Lys Thr Cys Gln Asn Tyr

```
            20                  25                  30

Asp Leu Glu Cys Met Ser Met Gly Cys Val Ser Gly Cys Leu Cys Pro
        35                  40                  45

Pro Gly Met Val Arg His Glu Asn Arg Cys Val Ala Leu Glu Arg Cys
    50                  55                  60

Pro Cys Phe His Gln Gly Lys Glu Tyr Ala Pro Gly Glu Thr Val Lys
65                  70                  75                  80

Ile Gly Cys Asn Thr Cys Val Cys Arg Asp Arg Lys Trp Asn Cys Thr
                85                  90                  95

Asp His Val Cys Asp Ala Thr Cys Ser Thr Ile Gly Met Ala His Tyr
            100                 105                 110

Leu Thr Phe Asp Gly Leu Lys Tyr Leu Phe Pro Gly Glu Cys Gln Tyr
        115                 120                 125

Val Leu Val Gln Asp Tyr Cys Gly Ser Asn Pro Gly Thr Phe Arg Ile
    130                 135                 140

Leu Val Gly Asn Lys Gly Cys Ser His Pro Ser Val Lys Cys Lys Lys
145                 150                 155                 160

Arg Val Thr Ile Leu Val Glu Gly Gly Glu Ile Glu Leu Phe Asp Gly
                165                 170                 175

Glu Val Asn Val Lys Arg Pro Met Lys Asp Glu Thr His Phe Glu Val
            180                 185                 190

Val Glu Ser Gly Arg Tyr Ile Ile Leu Leu Leu Gly Lys Ala Leu Ser
        195                 200                 205

Val Val Trp Asp Arg His Leu Ser Ile Ser Val Val Leu Lys Gln Thr
    210                 215                 220

Tyr Gln Glu Lys Val Cys Gly Leu Cys Gly Asn Phe Asp Gly Ile Gln
225                 230                 235                 240

Asn Asn Asp Leu Thr Ser Ser Asn Leu Gln Val Glu Glu Asp Pro Val
                245                 250                 255

Asp Phe Gly Asn Ser Trp Lys Val Ser Ser Gln Cys Ala Asp Thr Arg
            260                 265                 270

Lys Val Pro Leu Asp Ser Ser Pro Ala Thr Cys His Asn Asn Ile Met
        275                 280                 285

Lys Gln Thr Met Val Asp Ser Ser Cys Arg Ile Leu Thr Ser Asp Val
```

290 295 300

Phe Gln Asp Cys Asn Lys Leu Val Asp Pro Glu Pro Tyr Leu Asp Val
305 310 315 320

Cys Ile Tyr Asp Thr Cys Ser Cys Glu Ser Ile Gly Asp Cys Ala Cys
325 330 335

Phe Cys Asp Thr Ile Ala Ala Tyr Ala His Val Cys Ala Gln His Gly
340 345 350

Lys Val Val Thr Trp Arg Thr Ala Thr Leu Cys Pro Gln Ser Cys Glu
355 360 365

Glu Arg Asn Leu Arg Glu Asn Gly Tyr Glu Cys Glu Trp Arg Tyr Asn
370 375 380

Ser Cys Ala Pro Ala Cys Gln Val Thr Cys Gln His Pro Glu Pro Leu
385 390 395 400

Ala Cys Pro Val Gln Cys Val Glu Gly Cys His Ala His Cys Pro Pro
405 410 415

Gly Lys Ile Leu Asp Glu Leu Leu Gln Thr Cys Val Asp Pro Glu Asp
420 425 430

Cys Pro Val Cys Glu Val Ala Gly Arg Arg Phe Ala Ser Gly Lys Lys
435 440 445

Val Thr Leu Asn Pro Ser Asp Pro Glu His Cys Gln Ile Cys His Cys
450 455 460

Asp Val Val Asn Leu Thr Cys Glu Ala Cys Gln Glu Pro Gly Gly Ser
465 470 475 480

Ser Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ser
485 490 495

Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Ser Asp Ala
500 505 510

His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu Asn
515 520 525

Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln Cys
530 535 540

Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe Ala
545 550 555 560

Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser Leu

565 570 575

His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg Glu
580 585 590

Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu Arg
595 600 605

Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro Arg
610 615 620

Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp Asn
625 630 635 640

Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg His
645 650 655

Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr Lys
660 665 670

Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys Leu
675 680 685

Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser Ala
690 695 700

Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg Ala
705 710 715 720

Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys Ala
725 730 735

Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val His
740 745 750

Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg Ala
755 760 765

Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser Lys
770 775 780

Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys Ile
785 790 795 800

Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu Ala
805 810 815

Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu Ala
820 825 830

Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg His

835 840 845

Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr Glu
850 855 860

Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys Tyr
865 870 875 880

Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln Asn
885 890 895

Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr Lys
900 905 910

Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln Val
915 920 925

Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val Gly
930 935 940

Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala Glu
945 950 955 960

Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu Lys
965 970 975

Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu Val
980 985 990

Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr Val
995 1000 1005

Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile
1010 1015 1020

Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
1025 1030 1035

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln
1040 1045 1050

Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys
1055 1060 1065

Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys
1070 1075 1080

Lys Leu Val Ala Ala Ser Gln Ala Ala Leu Gly Leu
1085 1090 1095

<210> 3

<211> 8442
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)..(8442)

<400> 3

```
atg att cct gcc aga ttt gcc ggg gtg ctg ctt gct ctg gcc ctc att          48
Met Ile Pro Ala Arg Phe Ala Gly Val Leu Leu Ala Leu Ala Leu Ile
1               5                   10                  15

ttg cca ggg acc ctt tgt gca gaa gga act cgc ggc agg tca tcc acg          96
Leu Pro Gly Thr Leu Cys Ala Glu Gly Thr Arg Gly Arg Ser Ser Thr
            20                  25                  30

gcc cga tgc agc ctt ttc gga agt gac ttc gtc aac acc ttt gat ggg         144
Ala Arg Cys Ser Leu Phe Gly Ser Asp Phe Val Asn Thr Phe Asp Gly
        35                  40                  45

agc atg tac agc ttt gcg gga tac tgc agt tac ctc ctg gca ggg ggc         192
Ser Met Tyr Ser Phe Ala Gly Tyr Cys Ser Tyr Leu Leu Ala Gly Gly
    50                  55                  60

tgc cag aaa cgc tcc ttc tcg att att ggg gac ttc cag aat ggc aag         240
Cys Gln Lys Arg Ser Phe Ser Ile Ile Gly Asp Phe Gln Asn Gly Lys
65                  70                  75                  80

aga gtg agc ctc tcc gtg tat ctt ggg gaa ttt ttt gac atc cat ttg         288
Arg Val Ser Leu Ser Val Tyr Leu Gly Glu Phe Phe Asp Ile His Leu
                85                  90                  95

ttt gtc aat ggt acc gtg aca cag ggg gac caa aga gtc tcc atg ccc         336
Phe Val Asn Gly Thr Val Thr Gln Gly Asp Gln Arg Val Ser Met Pro
            100                 105                 110

tat gcc tcc aaa ggg ctg tat cta gaa act gag gct ggg tac tac aag         384
Tyr Ala Ser Lys Gly Leu Tyr Leu Glu Thr Glu Ala Gly Tyr Tyr Lys
        115                 120                 125

ctg tcc ggt gag gcc tat ggc ttt gtg gcc agg atc gat ggc agc ggc         432
Leu Ser Gly Glu Ala Tyr Gly Phe Val Ala Arg Ile Asp Gly Ser Gly
    130                 135                 140

aac ttt caa gtc ctg ctg tca gac aga tac ttc aac aag acc tgc ggg         480
Asn Phe Gln Val Leu Leu Ser Asp Arg Tyr Phe Asn Lys Thr Cys Gly
145                 150                 155                 160

ctg tgt ggc aac ttt aac atc ttt gct gaa gat gac ttt atg acc caa         528
Leu Cys Gly Asn Phe Asn Ile Phe Ala Glu Asp Asp Phe Met Thr Gln
                165                 170                 175

gaa ggg acc ttg acc tcg gac cct tat gac ttt gcc aac tca tgg gct         576
Glu Gly Thr Leu Thr Ser Asp Pro Tyr Asp Phe Ala Asn Ser Trp Ala
            180                 185                 190

ctg agc agt gga gaa cag tgg tgt gaa cgg gca tct cct ccc agc agc         624
Leu Ser Ser Gly Glu Gln Trp Cys Glu Arg Ala Ser Pro Pro Ser Ser
        195                 200                 205

tca tgc aac atc tcc tct ggg gaa atg cag aag ggc ctg tgg gag cag         672
Ser Cys Asn Ile Ser Ser Gly Glu Met Gln Lys Gly Leu Trp Glu Gln
    210                 215                 220

tgc cag ctt ctg aag agc acc tcg gtg ttt gcc cgc tgc cac cct ctg         720
Cys Gln Leu Leu Lys Ser Thr Ser Val Phe Ala Arg Cys His Pro Leu
```

```
225                 230                 235                 240

gtg gac ccc gag cct ttt gtg gcc ctg tgt gag aag act ttg tgt gag        768
Val Asp Pro Glu Pro Phe Val Ala Leu Cys Glu Lys Thr Leu Cys Glu
                245                 250                 255

tgt gct ggg ggg ctg gag tgc gcc tgc cct gcc ctc ctg gag tac gcc        816
Cys Ala Gly Gly Leu Glu Cys Ala Cys Pro Ala Leu Leu Glu Tyr Ala
            260                 265                 270

cgg acc tgt gcc cag gag gga atg gtg ctg tac ggc tgg acc gac cac        864
Arg Thr Cys Ala Gln Glu Gly Met Val Leu Tyr Gly Trp Thr Asp His
        275                 280                 285

agc gcg tgc agc cca gtg tgc cct gct ggt atg gag tat agg cag tgt        912
Ser Ala Cys Ser Pro Val Cys Pro Ala Gly Met Glu Tyr Arg Gln Cys
    290                 295                 300

gtg tcc cct tgc gcc agg acc tgc cag agc ctg cac atc aat gaa atg        960
Val Ser Pro Cys Ala Arg Thr Cys Gln Ser Leu His Ile Asn Glu Met
305                 310                 315                 320

tgt cag gag cga tgc gtg gat ggc tgc agc tgc cct gag gga cag ctc       1008
Cys Gln Glu Arg Cys Val Asp Gly Cys Ser Cys Pro Glu Gly Gln Leu
                325                 330                 335

ctg gat gaa ggc ctc tgc gtg gag agc acc gag tgt ccc tgc gtg cat       1056
Leu Asp Glu Gly Leu Cys Val Glu Ser Thr Glu Cys Pro Cys Val His
            340                 345                 350

tcc gga aag cgc tac cct ccc ggc acc tcc ctc tct cga gac tgc aac       1104
Ser Gly Lys Arg Tyr Pro Pro Gly Thr Ser Leu Ser Arg Asp Cys Asn
        355                 360                 365

acc tgc att tgc cga aac agc cag tgg atc tgc agc aat gaa gaa tgt       1152
Thr Cys Ile Cys Arg Asn Ser Gln Trp Ile Cys Ser Asn Glu Glu Cys
    370                 375                 380

cca ggg gag tgc ctt gtc aca ggt caa tca cac ttc aag agc ttt gac       1200
Pro Gly Glu Cys Leu Val Thr Gly Gln Ser His Phe Lys Ser Phe Asp
385                 390                 395                 400

aac aga tac ttc acc ttc agt ggg atc tgc cag tac ctg ctg gcc cgg       1248
Asn Arg Tyr Phe Thr Phe Ser Gly Ile Cys Gln Tyr Leu Leu Ala Arg
                405                 410                 415

gat tgc cag gac cac tcc ttc tcc att gtc att gag act gtc cag tgt       1296
Asp Cys Gln Asp His Ser Phe Ser Ile Val Ile Glu Thr Val Gln Cys
            420                 425                 430

gct gat gac cgc gac gct gtg tgc acc cgc tcc gtc acc gtc cgg ctg       1344
Ala Asp Asp Arg Asp Ala Val Cys Thr Arg Ser Val Thr Val Arg Leu
        435                 440                 445

cct ggc ctg cac aac agc ctt gtg aaa ctg aag cat ggg gca gga gtt       1392
Pro Gly Leu His Asn Ser Leu Val Lys Leu Lys His Gly Ala Gly Val
    450                 455                 460

gcc atg gat ggc cag gac gtc cag ctc ccc ctc ctg aaa ggt gac ctc       1440
Ala Met Asp Gly Gln Asp Val Gln Leu Pro Leu Leu Lys Gly Asp Leu
465                 470                 475                 480

cgc atc cag cat aca gtg acg gcc tcc gtg cgc ctc agc tac ggg gag       1488
Arg Ile Gln His Thr Val Thr Ala Ser Val Arg Leu Ser Tyr Gly Glu
                485                 490                 495

gac ctg cag atg gac tgg gat ggc cgc ggg agg ctg ctg gtg aag ctg       1536
Asp Leu Gln Met Asp Trp Asp Gly Arg Gly Arg Leu Leu Val Lys Leu
```

```
            500                 505                 510

tcc ccc gtc tat gcc ggg aag acc tgc ggc ctg tgt ggg aat tac aat       1584
Ser Pro Val Tyr Ala Gly Lys Thr Cys Gly Leu Cys Gly Asn Tyr Asn
        515                 520                 525

ggc aac cag ggc gac gac ttc ctt acc ccc tct ggg ctg gcg gag ccc       1632
Gly Asn Gln Gly Asp Asp Phe Leu Thr Pro Ser Gly Leu Ala Glu Pro
    530                 535                 540

cgg gtg gag gac ttc ggg aac gcc tgg aag ctg cac ggg gac tgc cag       1680
Arg Val Glu Asp Phe Gly Asn Ala Trp Lys Leu His Gly Asp Cys Gln
545                 550                 555                 560

gac ctg cag aag cag cac agc gat ccc tgc gcc ctc aac ccg cgc atg       1728
Asp Leu Gln Lys Gln His Ser Asp Pro Cys Ala Leu Asn Pro Arg Met
                565                 570                 575

acc agg ttc tcc gag gag gcg tgc gcg gtc ctg acg tcc ccc aca ttc       1776
Thr Arg Phe Ser Glu Glu Ala Cys Ala Val Leu Thr Ser Pro Thr Phe
            580                 585                 590

gag gcc tgc cat cgt gcc gtc agc ccg ctg ccc tac ctg cgg aac tgc       1824
Glu Ala Cys His Arg Ala Val Ser Pro Leu Pro Tyr Leu Arg Asn Cys
        595                 600                 605

cgc tac gac gtg tgc tcc tgc tcg gac ggc cgc gag tgc ctg tgc ggc       1872
Arg Tyr Asp Val Cys Ser Cys Ser Asp Gly Arg Glu Cys Leu Cys Gly
    610                 615                 620

gcc ctg gcc agc tat gcc gcg gcc tgc gcg ggg aga ggc gtg cgc gtc       1920
Ala Leu Ala Ser Tyr Ala Ala Ala Cys Ala Gly Arg Gly Val Arg Val
625                 630                 635                 640

gcg tgg cgc gag cca ggc cgc tgt gag ctg aac tgc ccg aaa ggc cag       1968
Ala Trp Arg Glu Pro Gly Arg Cys Glu Leu Asn Cys Pro Lys Gly Gln
                645                 650                 655

gtg tac ctg cag tgc ggg acc ccc tgc aac ctg acc tgc cgc tct ctc       2016
Val Tyr Leu Gln Cys Gly Thr Pro Cys Asn Leu Thr Cys Arg Ser Leu
            660                 665                 670

tct tac ccg gat gag gaa tgc aat gag gcc tgc ctg gag ggc tgc ttc       2064
Ser Tyr Pro Asp Glu Glu Cys Asn Glu Ala Cys Leu Glu Gly Cys Phe
        675                 680                 685

tgc ccc cca ggg ctc tac atg gat gag agg ggg gac tgc gtg ccc aag       2112
Cys Pro Pro Gly Leu Tyr Met Asp Glu Arg Gly Asp Cys Val Pro Lys
    690                 695                 700

gcc cag tgc ccc tgt tac tat gac ggt gag atc ttc cag cca gaa gac       2160
Ala Gln Cys Pro Cys Tyr Tyr Asp Gly Glu Ile Phe Gln Pro Glu Asp
705                 710                 715                 720

atc ttc tca gac cat cac acc atg tgc tac tgt gag gat ggc ttc atg       2208
Ile Phe Ser Asp His His Thr Met Cys Tyr Cys Glu Asp Gly Phe Met
                725                 730                 735

cac tgt acc atg agt gga gtc ccc gga agc ttg ctg cct gac gct gtc       2256
His Cys Thr Met Ser Gly Val Pro Gly Ser Leu Leu Pro Asp Ala Val
            740                 745                 750

ctc agc agt ccc ctg tct cat cgc agc aaa agg agc cta tcc tgt cgg       2304
Leu Ser Ser Pro Leu Ser His Arg Ser Lys Arg Ser Leu Ser Cys Arg
        755                 760                 765

ccc ccc atg gtc aag ctg gtg tgt ccc gct gac aac ctg cgg gct gaa       2352
Pro Pro Met Val Lys Leu Val Cys Pro Ala Asp Asn Leu Arg Ala Glu
```

```
    770                 775                 780

ggg ctc gag tgt acc aaa acg tgc cag aac tat gac ctg gag tgc atg       2400
Gly Leu Glu Cys Thr Lys Thr Cys Gln Asn Tyr Asp Leu Glu Cys Met
785                 790                 795                 800

agc atg ggc tgt gtc tct ggc tgc ctc tgc ccc ccg ggc atg gtc cgg       2448
Ser Met Gly Cys Val Ser Gly Cys Leu Cys Pro Pro Gly Met Val Arg
                805                 810                 815

cat gag aac aga tgt gtg gcc ctg gaa agg tgt ccc tgc ttc cat cag       2496
His Glu Asn Arg Cys Val Ala Leu Glu Arg Cys Pro Cys Phe His Gln
            820                 825                 830

ggc aag gag tat gcc cct gga gaa aca gtg aag att ggc tgc aac act       2544
Gly Lys Glu Tyr Ala Pro Gly Glu Thr Val Lys Ile Gly Cys Asn Thr
        835                 840                 845

tgt gtc tgt cgg gac cgg aag tgg aac tgc aca gac cat gtg tgt gat       2592
Cys Val Cys Arg Asp Arg Lys Trp Asn Cys Thr Asp His Val Cys Asp
    850                 855                 860

gcc acg tgc tcc acg atc ggc atg gcc cac tac ctc acc ttc gac ggg       2640
Ala Thr Cys Ser Thr Ile Gly Met Ala His Tyr Leu Thr Phe Asp Gly
865                 870                 875                 880

ctc aaa tac ctg ttc ccc ggg gag tgc cag tac gtt ctg gtg cag gat       2688
Leu Lys Tyr Leu Phe Pro Gly Glu Cys Gln Tyr Val Leu Val Gln Asp
                885                 890                 895

tac tgc ggc agt aac cct ggg acc ttt cgg atc cta gtg ggg aat aag       2736
Tyr Cys Gly Ser Asn Pro Gly Thr Phe Arg Ile Leu Val Gly Asn Lys
            900                 905                 910

gga tgc agc cac ccc tca gtg aaa tgc aag aaa cgg gtc acc atc ctg       2784
Gly Cys Ser His Pro Ser Val Lys Cys Lys Lys Arg Val Thr Ile Leu
        915                 920                 925

gtg gag gga gga gag att gag ctg ttt gac ggg gag gtg aat gtg aag       2832
Val Glu Gly Gly Glu Ile Glu Leu Phe Asp Gly Glu Val Asn Val Lys
    930                 935                 940

agg ccc atg aag gat gag act cac ttt gag gtg gtg gag tct ggc cgg       2880
Arg Pro Met Lys Asp Glu Thr His Phe Glu Val Val Glu Ser Gly Arg
945                 950                 955                 960

tac atc att ctg ctg ctg ggc aaa gcc ctc tcc gtg gtc tgg gac cgc       2928
Tyr Ile Ile Leu Leu Leu Gly Lys Ala Leu Ser Val Val Trp Asp Arg
                965                 970                 975

cac ctg agc atc tcc gtg gtc ctg aag cag aca tac cag gag aaa gtg       2976
His Leu Ser Ile Ser Val Val Leu Lys Gln Thr Tyr Gln Glu Lys Val
            980                 985                 990

tgt ggc ctg tgt ggg aat ttt gat  ggc atc cag aac aat  gac ctc acc     3024
Cys Gly Leu Cys Gly Asn Phe Asp  Gly Ile Gln Asn Asn  Asp Leu Thr
        995                 1000                1005

agc agc  aac ctc caa gtg gag  gaa gac cct gtg gac  ttt ggg aac        3069
Ser Ser  Asn Leu Gln Val Glu  Glu Asp Pro Val Asp  Phe Gly Asn
    1010                1015                1020

tcc tgg  aaa gtg agc tcg cag  tgt gct gac acc aga  aaa gtg cct        3114
Ser Trp  Lys Val Ser Ser Gln  Cys Ala Asp Thr Arg  Lys Val Pro
    1025                1030                1035

ctg gac  tca tcc cct gcc acc  tgc cat aac aac atc  atg aag cag        3159
Leu Asp  Ser Ser Pro Ala Thr  Cys His Asn Asn Ile  Met Lys Gln
```

```
    1040                1045                1050

acg atg  gtg gat tcc tcc tgt  aga atc ctt acc agt  gac gtc ttc        3204
Thr Met  Val Asp Ser Ser Cys  Arg Ile Leu Thr Ser  Asp Val Phe
    1055                1060                1065

cag gac  tgc aac aag ctg gtg  gac ccc gag cca tat  ctg gat gtc        3249
Gln Asp  Cys Asn Lys Leu Val  Asp Pro Glu Pro Tyr  Leu Asp Val
    1070                1075                1080

tgc att  tac gac acc tgc tcc  tgt gag tcc att ggg  gac tgc gcc        3294
Cys Ile  Tyr Asp Thr Cys Ser  Cys Glu Ser Ile Gly  Asp Cys Ala
    1085                1090                1095

tgc ttc  tgc gac acc att gct  gcc tat gcc cac gtg  tgt gcc cag        3339
Cys Phe  Cys Asp Thr Ile Ala  Ala Tyr Ala His Val  Cys Ala Gln
    1100                1105                1110

cat ggc  aag gtg gtg acc tgg  agg acg gcc aca ttg  tgc ccc cag        3384
His Gly  Lys Val Val Thr Trp  Arg Thr Ala Thr Leu  Cys Pro Gln
    1115                1120                1125

agc tgc  gag gag agg aat ctc  cgg gag aac ggg tat  gag tgt gag        3429
Ser Cys  Glu Glu Arg Asn Leu  Arg Glu Asn Gly Tyr  Glu Cys Glu
    1130                1135                1140

tgg cgc  tat aac agc tgt gca  cct gcc tgt caa gtc  acg tgt cag        3474
Trp Arg  Tyr Asn Ser Cys Ala  Pro Ala Cys Gln Val  Thr Cys Gln
    1145                1150                1155

cac cct  gag cca ctg gcc tgc  cct gtg cag tgt gtg  gag ggc tgc        3519
His Pro  Glu Pro Leu Ala Cys  Pro Val Gln Cys Val  Glu Gly Cys
    1160                1165                1170

cat gcc  cac tgc cct cca ggg  aaa atc ctg gat gag  ctt ttg cag        3564
His Ala  His Cys Pro Pro Gly  Lys Ile Leu Asp Glu  Leu Leu Gln
    1175                1180                1185

acc tgc  gtt gac cct gaa gac  tgt cca gtg tgt gag  gtg gct ggc        3609
Thr Cys  Val Asp Pro Glu Asp  Cys Pro Val Cys Glu  Val Ala Gly
    1190                1195                1200

cgg cgt  ttt gcc tca gga aag  aaa gtc acc ttg aat  ccc agt gac        3654
Arg Arg  Phe Ala Ser Gly Lys  Lys Val Thr Leu Asn  Pro Ser Asp
    1205                1210                1215

cct gag  cac tgc cag att tgc  cac tgt gat gtt gtc  aac ctc acc        3699
Pro Glu  His Cys Gln Ile Cys  His Cys Asp Val Val  Asn Leu Thr
    1220                1225                1230

tgt gaa  gcc tgc cag gag ccg  gga ggc ctg gtg gtg  cct ccc aca        3744
Cys Glu  Ala Cys Gln Glu Pro  Gly Gly Leu Val Val  Pro Pro Thr
    1235                1240                1245

gat gcc  ccg gtg agc ccc acc  act ctg tat gtg gag  gac atc tcg        3789
Asp Ala  Pro Val Ser Pro Thr  Thr Leu Tyr Val Glu  Asp Ile Ser
    1250                1255                1260

gaa ccg  ccg ttg cac gat ttc  tac tgc agc agg cta  ctg gac ctg        3834
Glu Pro  Pro Leu His Asp Phe  Tyr Cys Ser Arg Leu  Leu Asp Leu
    1265                1270                1275

gtc ttc  ctg ctg gat ggc tcc  tcc agg ctg tcc gag  gct gag ttt        3879
Val Phe  Leu Leu Asp Gly Ser  Ser Arg Leu Ser Glu  Ala Glu Phe
    1280                1285                1290

gaa gtg  ctg aag gcc ttt gtg  gtg gac atg atg gag  cgg ctg cgc        3924
Glu Val  Leu Lys Ala Phe Val  Val Asp Met Met Glu  Arg Leu Arg
```

```
    1295                1300                1305

atc tcc  cag aag tgg gtc cgc  gtg gcc gtg gtg gag  tac cac gac        3969
Ile Ser  Gln Lys Trp Val Arg  Val Ala Val Val Glu  Tyr His Asp
    1310                1315                1320

ggc tcc  cac gcc tac atc ggg  ctc aag gac cgg aag  cga ccg tca        4014
Gly Ser  His Ala Tyr Ile Gly  Leu Lys Asp Arg Lys  Arg Pro Ser
    1325                1330                1335

gag ctg  cgg cgc att gcc agc  cag gtg aag tat gcg  ggc agc cag        4059
Glu Leu  Arg Arg Ile Ala Ser  Gln Val Lys Tyr Ala  Gly Ser Gln
    1340                1345                1350

gtg gcc  tcc acc agc gag gtc  ttg aaa tac aca ctg  ttc caa atc        4104
Val Ala  Ser Thr Ser Glu Val  Leu Lys Tyr Thr Leu  Phe Gln Ile
    1355                1360                1365

ttc agc  aag atc gac cgc cct  gaa gcc tcc cgc atc  gcc ctg ctc        4149
Phe Ser  Lys Ile Asp Arg Pro  Glu Ala Ser Arg Ile  Ala Leu Leu
    1370                1375                1380

ctg atg  gcc agc cag gag ccc  caa cgg atg tcc cgg  aac ttt gtc        4194
Leu Met  Ala Ser Gln Glu Pro  Gln Arg Met Ser Arg  Asn Phe Val
    1385                1390                1395

cgc tac  gtc cag ggc ctg aag  aag aag aag gtc att  gtg atc ccg        4239
Arg Tyr  Val Gln Gly Leu Lys  Lys Lys Lys Val Ile  Val Ile Pro
    1400                1405                1410

gtg ggc  att ggg ccc cat gcc  aac ctc aag cag atc  cgc ctc atc        4284
Val Gly  Ile Gly Pro His Ala  Asn Leu Lys Gln Ile  Arg Leu Ile
    1415                1420                1425

gag aag  cag gcc cct gag aac  aag gcc ttc gtg ctg  agc agt gtg        4329
Glu Lys  Gln Ala Pro Glu Asn  Lys Ala Phe Val Leu  Ser Ser Val
    1430                1435                1440

gat gag  ctg gag cag caa agg  gac gag atc gtt agc  tac ctc tgt        4374
Asp Glu  Leu Glu Gln Gln Arg  Asp Glu Ile Val Ser  Tyr Leu Cys
    1445                1450                1455

gac ctt  gcc cct gaa gcc cct  cct cct act ctg ccc  ccc cac atg        4419
Asp Leu  Ala Pro Glu Ala Pro  Pro Pro Thr Leu Pro  Pro His Met
    1460                1465                1470

gca caa  gtc act gtg ggc ccg  ggg ctc ttg ggg gtt  tcg acc ctg        4464
Ala Gln  Val Thr Val Gly Pro  Gly Leu Leu Gly Val  Ser Thr Leu
    1475                1480                1485

ggg ccc  aag agg aac tcc atg  gtt ctg gat gtg gcg  ttc gtc ctg        4509
Gly Pro  Lys Arg Asn Ser Met  Val Leu Asp Val Ala  Phe Val Leu
    1490                1495                1500

gaa gga  tcg gac aaa att ggt  gaa gcc gac ttc aac  agg agc aag        4554
Glu Gly  Ser Asp Lys Ile Gly  Glu Ala Asp Phe Asn  Arg Ser Lys
    1505                1510                1515

gag ttc  atg gag gag gtg att  cag cgg atg gat gtg  ggc cag gac        4599
Glu Phe  Met Glu Glu Val Ile  Gln Arg Met Asp Val  Gly Gln Asp
    1520                1525                1530

agc atc  cac gtc acg gtg ctg  cag tac tcc tac atg  gtg acc gtg        4644
Ser Ile  His Val Thr Val Leu  Gln Tyr Ser Tyr Met  Val Thr Val
    1535                1540                1545

gag tac  ccc ttc agc gag gca  cag tcc aaa ggg gac  atc ctg cag        4689
Glu Tyr  Pro Phe Ser Glu Ala  Gln Ser Lys Gly Asp  Ile Leu Gln
```

```
    1550                1555                1560

cgg gtg  cga gag atc cgc tac  cag ggc ggc aac agg  acc aac act        4734
Arg Val  Arg Glu Ile Arg Tyr  Gln Gly Gly Asn Arg  Thr Asn Thr
    1565                1570                1575

ggg ctg  gcc ctg cgg tac ctc  tct gac cac agc ttc  ttg gtc agc        4779
Gly Leu  Ala Leu Arg Tyr Leu  Ser Asp His Ser Phe  Leu Val Ser
    1580                1585                1590

cag ggt  gac cgg gag cag gcg  ccc aac ctg gtc tac  atg gtc acc        4824
Gln Gly  Asp Arg Glu Gln Ala  Pro Asn Leu Val Tyr  Met Val Thr
    1595                1600                1605

gga aat  cct gcc tct gat gag  atc aag agg ctg cct  gga gac atc        4869
Gly Asn  Pro Ala Ser Asp Glu  Ile Lys Arg Leu Pro  Gly Asp Ile
    1610                1615                1620

cag gtg  gtg ccc att gga gtg  ggc cct aat gcc aac  gtg cag gag        4914
Gln Val  Val Pro Ile Gly Val  Gly Pro Asn Ala Asn  Val Gln Glu
    1625                1630                1635

ctg gag  agg att ggc tgg ccc  aat gcc cct atc ctc  atc cag gac        4959
Leu Glu  Arg Ile Gly Trp Pro  Asn Ala Pro Ile Leu  Ile Gln Asp
    1640                1645                1650

ttt gag  acg ctc ccc cga gag  gct cct gac ctg gtg  ctg cag agg        5004
Phe Glu  Thr Leu Pro Arg Glu  Ala Pro Asp Leu Val  Leu Gln Arg
    1655                1660                1665

tgc tgc  tcc gga gag ggg ctg  cag atc ccc acc ctc  tcc cct gca        5049
Cys Cys  Ser Gly Glu Gly Leu  Gln Ile Pro Thr Leu  Ser Pro Ala
    1670                1675                1680

cct gac  tgc agc cag ccc ctg  gac gtg atc ctt ctc  ctg gat ggc        5094
Pro Asp  Cys Ser Gln Pro Leu  Asp Val Ile Leu Leu  Leu Asp Gly
    1685                1690                1695

tcc tcc  agt ttc cca gct tct  tat ttt gat gaa atg  aag agt ttc        5139
Ser Ser  Ser Phe Pro Ala Ser  Tyr Phe Asp Glu Met  Lys Ser Phe
    1700                1705                1710

gcc aag  gct ttc att tca aaa  gcc aat ata ggg cct  cgt ctc act        5184
Ala Lys  Ala Phe Ile Ser Lys  Ala Asn Ile Gly Pro  Arg Leu Thr
    1715                1720                1725

cag gtg  tca gtg ctg cag tat  gga agc atc acc acc  att gac gtg        5229
Gln Val  Ser Val Leu Gln Tyr  Gly Ser Ile Thr Thr  Ile Asp Val
    1730                1735                1740

cca tgg  aac gtg gtc ccg gag  aaa gcc cat ttg ctg  agc ctt gtg        5274
Pro Trp  Asn Val Val Pro Glu  Lys Ala His Leu Leu  Ser Leu Val
    1745                1750                1755

gac gtc  atg cag cgg gag gga  ggc ccc agc caa atc  ggg gat gcc        5319
Asp Val  Met Gln Arg Glu Gly  Gly Pro Ser Gln Ile  Gly Asp Ala
    1760                1765                1770

ttg ggc  ttt gct gtg cga tac  ttg act tca gaa atg  cat ggg gcg        5364
Leu Gly  Phe Ala Val Arg Tyr  Leu Thr Ser Glu Met  His Gly Ala
    1775                1780                1785

cgc ccg  gga gcc tca aag gcg  gtg gtc atc ctg gtc  acg gac gtc        5409
Arg Pro  Gly Ala Ser Lys Ala  Val Val Ile Leu Val  Thr Asp Val
    1790                1795                1800

tct gtg  gat tca gtg gat gca  gca gct gat gcc gcc  agg tcc aac        5454
Ser Val  Asp Ser Val Asp Ala  Ala Ala Asp Ala Ala  Arg Ser Asn
```

```
    1805                1810                1815

aga gtg  aca gtg ttc cct att  gga att gga gat cgc  tac gat gca        5499
Arg Val  Thr Val Phe Pro Ile  Gly Ile Gly Asp Arg  Tyr Asp Ala
    1820                1825                1830

gcc cag  cta cgg atc ttg gca  ggc cca gca ggc gac  tcc aac gtg        5544
Ala Gln  Leu Arg Ile Leu Ala  Gly Pro Ala Gly Asp  Ser Asn Val
    1835                1840                1845

gtg aag  ctc cag cga atc gaa  gac ctc cct acc atg  gtc acc ttg        5589
Val Lys  Leu Gln Arg Ile Glu  Asp Leu Pro Thr Met  Val Thr Leu
    1850                1855                1860

ggc aat  tcc ttc ctc cac aaa  ctg tgc tct gga ttt  gtt agg att        5634
Gly Asn  Ser Phe Leu His Lys  Leu Cys Ser Gly Phe  Val Arg Ile
    1865                1870                1875

tgc atg  gat gag gat ggg aat  gag aag agg ccc ggg  gac gtc tgg        5679
Cys Met  Asp Glu Asp Gly Asn  Glu Lys Arg Pro Gly  Asp Val Trp
    1880                1885                1890

acc ttg  cca gac cag tgc cac  acc gtg act tgc cag  cca gat ggc        5724
Thr Leu  Pro Asp Gln Cys His  Thr Val Thr Cys Gln  Pro Asp Gly
    1895                1900                1905

cag acc  ttg ctg aag agt cat  cgg gtc aac tgt gac  cgg ggg ctg        5769
Gln Thr  Leu Leu Lys Ser His  Arg Val Asn Cys Asp  Arg Gly Leu
    1910                1915                1920

agg cct  tcg tgc cct aac agc  cag tcc cct gtt aaa  gtg gaa gag        5814
Arg Pro  Ser Cys Pro Asn Ser  Gln Ser Pro Val Lys  Val Glu Glu
    1925                1930                1935

acc tgt  ggc tgc cgc tgg acc  tgc ccc tgc gtg tgc  aca ggc agc        5859
Thr Cys  Gly Cys Arg Trp Thr  Cys Pro Cys Val Cys  Thr Gly Ser
    1940                1945                1950

tcc act  cgg cac atc gtg acc  ttt gat ggg cag aat  ttc aag ctg        5904
Ser Thr  Arg His Ile Val Thr  Phe Asp Gly Gln Asn  Phe Lys Leu
    1955                1960                1965

act ggc  agc tgt tct tat gtc  cta ttt caa aac aag  gag cag gac        5949
Thr Gly  Ser Cys Ser Tyr Val  Leu Phe Gln Asn Lys  Glu Gln Asp
    1970                1975                1980

ctg gag  gtg att ctc cat aat  ggt gcc tgc agc cct  gga gca agg        5994
Leu Glu  Val Ile Leu His Asn  Gly Ala Cys Ser Pro  Gly Ala Arg
    1985                1990                1995

cag ggc  tgc atg aaa tcc atc  gag gtg aag cac agt  gcc ctc tcc        6039
Gln Gly  Cys Met Lys Ser Ile  Glu Val Lys His Ser  Ala Leu Ser
    2000                2005                2010

gtc gag  ctg cac agt gac atg  gag gtg acg gtg aat  ggg aga ctg        6084
Val Glu  Leu His Ser Asp Met  Glu Val Thr Val Asn  Gly Arg Leu
    2015                2020                2025

gtc tct  gtt cct tac gtg ggt  ggg aac atg gaa gtc  aac gtt tat        6129
Val Ser  Val Pro Tyr Val Gly  Gly Asn Met Glu Val  Asn Val Tyr
    2030                2035                2040

ggt gcc  atc atg cat gag gtc  aga ttc aat cac ctt  ggt cac atc        6174
Gly Ala  Ile Met His Glu Val  Arg Phe Asn His Leu  Gly His Ile
    2045                2050                2055

ttc aca  ttc act cca caa aac  aat gag ttc caa ctg  cag ctc agc        6219
Phe Thr  Phe Thr Pro Gln Asn  Asn Glu Phe Gln Leu  Gln Leu Ser
```

```
    2060                2065                2070

ccc aag  act ttt gct tca aag  acg tat ggt ctg tgt  ggg atc tgt        6264
Pro Lys  Thr Phe Ala Ser Lys  Thr Tyr Gly Leu Cys  Gly Ile Cys
    2075                2080                2085

gat gag  aac gga gcc aat gac  ttc atg ctg agg gat  ggc aca gtc        6309
Asp Glu  Asn Gly Ala Asn Asp  Phe Met Leu Arg Asp  Gly Thr Val
    2090                2095                2100

acc aca  gac tgg aaa aca ctt  gtt cag gaa tgg act  gtg cag cgg        6354
Thr Thr  Asp Trp Lys Thr Leu  Val Gln Glu Trp Thr  Val Gln Arg
    2105                2110                2115

cca ggg  cag acg tgc cag ccc  atc ctg gag gag cag  tgt ctt gtc        6399
Pro Gly  Gln Thr Cys Gln Pro  Ile Leu Glu Glu Gln  Cys Leu Val
    2120                2125                2130

ccc gac  agc tcc cac tgc cag  gtc ctc ctc tta cca  ctg ttt gct        6444
Pro Asp  Ser Ser His Cys Gln  Val Leu Leu Leu Pro  Leu Phe Ala
    2135                2140                2145

gaa tgc  cac aag gtc ctg gct  cca gcc aca ttc tat  gcc atc tgc        6489
Glu Cys  His Lys Val Leu Ala  Pro Ala Thr Phe Tyr  Ala Ile Cys
    2150                2155                2160

cag cag  gac agt tgc cac cag  gag caa gtg tgt gag  gtg atc gcc        6534
Gln Gln  Asp Ser Cys His Gln  Glu Gln Val Cys Glu  Val Ile Ala
    2165                2170                2175

tct tat  gcc cac ctc tgt cgg  acc aac ggg gtc tgc  gtt gac tgg        6579
Ser Tyr  Ala His Leu Cys Arg  Thr Asn Gly Val Cys  Val Asp Trp
    2180                2185                2190

agg aca  cct gat ttc tgt gct  atg tca tgc cca cca  tct ctg gtt        6624
Arg Thr  Pro Asp Phe Cys Ala  Met Ser Cys Pro Pro  Ser Leu Val
    2195                2200                2205

tat aac  cac tgt gag cat ggc  tgt ccc cgg cac tgt  gat ggc aac        6669
Tyr Asn  His Cys Glu His Gly  Cys Pro Arg His Cys  Asp Gly Asn
    2210                2215                2220

gtg agc  tcc tgt ggg gac cat  ccc tcc gaa ggc tgt  ttc tgc cct        6714
Val Ser  Ser Cys Gly Asp His  Pro Ser Glu Gly Cys  Phe Cys Pro
    2225                2230                2235

cca gat  aaa gtc atg ttg gaa  ggc agc tgt gtc cct  gaa gag gcc        6759
Pro Asp  Lys Val Met Leu Glu  Gly Ser Cys Val Pro  Glu Glu Ala
    2240                2245                2250

tgc act  cag tgc att ggt gag  gat gga gtc cag cac  cag ttc ctg        6804
Cys Thr  Gln Cys Ile Gly Glu  Asp Gly Val Gln His  Gln Phe Leu
    2255                2260                2265

gaa gcc  tgg gtc ccg gac cac  cag ccc tgt cag atc  tgc aca tgc        6849
Glu Ala  Trp Val Pro Asp His  Gln Pro Cys Gln Ile  Cys Thr Cys
    2270                2275                2280

ctc agc  ggg cgg aag gtc aac  tgc aca acg cag ccc  tgc ccc acg        6894
Leu Ser  Gly Arg Lys Val Asn  Cys Thr Thr Gln Pro  Cys Pro Thr
    2285                2290                2295

gcc aaa  gct ccc acg tgt ggc  ctg tgt gaa gta gcc  cgc ctc cgc        6939
Ala Lys  Ala Pro Thr Cys Gly  Leu Cys Glu Val Ala  Arg Leu Arg
    2300                2305                2310

cag aat  gca gac cag tgc tgc  ccc gag tat gag tgt  gtg tgt gac        6984
Gln Asn  Ala Asp Gln Cys Cys  Pro Glu Tyr Glu Cys  Val Cys Asp
```

```
    2315                2320                2325

cca gtg  agc tgt gac ctg ccc  cca gtg cct cac tgt  gaa cgt ggc        7029
Pro Val  Ser Cys Asp Leu Pro  Pro Val Pro His Cys  Glu Arg Gly
    2330                2335                2340

ctc cag  ccc aca ctg acc aac  cct ggc gag tgc aga  ccc aac ttc        7074
Leu Gln  Pro Thr Leu Thr Asn  Pro Gly Glu Cys Arg  Pro Asn Phe
    2345                2350                2355

acc tgc  gcc tgc agg aag gag  gag tgc aaa aga gtg  tcc cca ccc        7119
Thr Cys  Ala Cys Arg Lys Glu  Glu Cys Lys Arg Val  Ser Pro Pro
    2360                2365                2370

tcc tgc  ccc ccg cac cgt ttg  ccc acc ctt cgg aag  acc cag tgc        7164
Ser Cys  Pro Pro His Arg Leu  Pro Thr Leu Arg Lys  Thr Gln Cys
    2375                2380                2385

tgt gat  gag tat gag tgt gcc  tgc aac tgt gtc aac  tcc aca gtg        7209
Cys Asp  Glu Tyr Glu Cys Ala  Cys Asn Cys Val Asn  Ser Thr Val
    2390                2395                2400

agc tgt  ccc ctt ggg tac ttg  gcc tca acc gcc acc  aat gac tgt        7254
Ser Cys  Pro Leu Gly Tyr Leu  Ala Ser Thr Ala Thr  Asn Asp Cys
    2405                2410                2415

ggc tgt  acc aca acc acc tgc  ctt ccc gac aag gtg  tgt gtc cac        7299
Gly Cys  Thr Thr Thr Thr Cys  Leu Pro Asp Lys Val  Cys Val His
    2420                2425                2430

cga agc  acc atc tac cct gtg  ggc cag ttc tgg gag  gag ggc tgc        7344
Arg Ser  Thr Ile Tyr Pro Val  Gly Gln Phe Trp Glu  Glu Gly Cys
    2435                2440                2445

gat gtg  tgc acc tgc acc gac  atg gag gat gcc gtg  atg ggc ctc        7389
Asp Val  Cys Thr Cys Thr Asp  Met Glu Asp Ala Val  Met Gly Leu
    2450                2455                2460

cgc gtg  gcc cag tgc tcc cag  aag ccc tgt gag gac  agc tgt cgg        7434
Arg Val  Ala Gln Cys Ser Gln  Lys Pro Cys Glu Asp  Ser Cys Arg
    2465                2470                2475

tcg ggc  ttc act tac gtt ctg  cat gaa ggc gag tgc  tgt gga agg        7479
Ser Gly  Phe Thr Tyr Val Leu  His Glu Gly Glu Cys  Cys Gly Arg
    2480                2485                2490

tgc ctg  cca tct gcc tgt gag  gtg gtg act ggc tca  ccg cgg ggg        7524
Cys Leu  Pro Ser Ala Cys Glu  Val Val Thr Gly Ser  Pro Arg Gly
    2495                2500                2505

gac tcc  cag tct tcc tgg aag  agt gtc ggc tcc cag  tgg gcc tcc        7569
Asp Ser  Gln Ser Ser Trp Lys  Ser Val Gly Ser Gln  Trp Ala Ser
    2510                2515                2520

ccg gag  aac ccc tgc ctc atc  aat gag tgt gtc cga  gtg aag gag        7614
Pro Glu  Asn Pro Cys Leu Ile  Asn Glu Cys Val Arg  Val Lys Glu
    2525                2530                2535

gag gtc  ttt ata caa caa agg  aac gtc tcc tgc ccc  cag ctg gag        7659
Glu Val  Phe Ile Gln Gln Arg  Asn Val Ser Cys Pro  Gln Leu Glu
    2540                2545                2550

gtc cct  gtc tgc ccc tcg ggc  ttt cag ctg agc tgt  aag acc tca        7704
Val Pro  Val Cys Pro Ser Gly  Phe Gln Leu Ser Cys  Lys Thr Ser
    2555                2560                2565

gcg tgc  tgc cca agc tgt cgc  tgt gag cgc atg gag  gcc tgc atg        7749
Ala Cys  Cys Pro Ser Cys Arg  Cys Glu Arg Met Glu  Ala Cys Met
```

```
    2570                2575                2580

ctc aat  ggc act gtc att ggg  ccc ggg aag act gtg  atg atc gat        7794
Leu Asn  Gly Thr Val Ile Gly  Pro Gly Lys Thr Val  Met Ile Asp
    2585                2590                2595

gtg tgc  acg acc tgc cgc tgc  atg gtg cag gtg ggg  gtc atc tct        7839
Val Cys  Thr Thr Cys Arg Cys  Met Val Gln Val Gly  Val Ile Ser
    2600                2605                2610

gga ttc  aag ctg gag tgc agg  aag acc acc tgc aac  ccc tgc ccc        7884
Gly Phe  Lys Leu Glu Cys Arg  Lys Thr Thr Cys Asn  Pro Cys Pro
    2615                2620                2625

ctg ggt  tac aag gaa gaa aat  aac aca ggt gaa tgt  tgt ggg aga        7929
Leu Gly  Tyr Lys Glu Glu Asn  Asn Thr Gly Glu Cys  Cys Gly Arg
    2630                2635                2640

tgt ttg  cct acg gct tgc acc  att cag cta aga gga  gga cag atc        7974
Cys Leu  Pro Thr Ala Cys Thr  Ile Gln Leu Arg Gly  Gly Gln Ile
    2645                2650                2655

atg aca  ctg aag cgt gat gag  acg ctc cag gat ggc  tgt gat act        8019
Met Thr  Leu Lys Arg Asp Glu  Thr Leu Gln Asp Gly  Cys Asp Thr
    2660                2665                2670

cac ttc  tgc aag gtc aat gag  aga gga gag tac ttc  tgg gag aag        8064
His Phe  Cys Lys Val Asn Glu  Arg Gly Glu Tyr Phe  Trp Glu Lys
    2675                2680                2685

agg gtc  aca ggc tgc cca ccc  ttt gat gaa cac aag  tgt ctg gct        8109
Arg Val  Thr Gly Cys Pro Pro  Phe Asp Glu His Lys  Cys Leu Ala
    2690                2695                2700

gag gga  ggt aaa att atg aaa  att cca ggc acc tgc  tgt gac aca        8154
Glu Gly  Gly Lys Ile Met Lys  Ile Pro Gly Thr Cys  Cys Asp Thr
    2705                2710                2715

tgt gag  gag cct gag tgc aac  gac atc act gcc agg  ctg cag tat        8199
Cys Glu  Glu Pro Glu Cys Asn  Asp Ile Thr Ala Arg  Leu Gln Tyr
    2720                2725                2730

gtc aag  gtg gga agc tgt aag  tct gaa gta gag gtg  gat atc cac        8244
Val Lys  Val Gly Ser Cys Lys  Ser Glu Val Glu Val  Asp Ile His
    2735                2740                2745

tac tgc  cag ggc aaa tgt gcc  agc aaa gcc atg tac  tcc att gac        8289
Tyr Cys  Gln Gly Lys Cys Ala  Ser Lys Ala Met Tyr  Ser Ile Asp
    2750                2755                2760

atc aac  gat gtg cag gac cag  tgc tcc tgc tgc tct  ccg aca cgg        8334
Ile Asn  Asp Val Gln Asp Gln  Cys Ser Cys Cys Ser  Pro Thr Arg
    2765                2770                2775

acg gag  ccc atg cag gtg gcc  ctg cac tgc acc aat  ggc tct gtt        8379
Thr Glu  Pro Met Gln Val Ala  Leu His Cys Thr Asn  Gly Ser Val
    2780                2785                2790

gtg tac  cat gag gtt ctc aat  gcc atg gag tgc aaa  tgc tcc ccc        8424
Val Tyr  His Glu Val Leu Asn  Ala Met Glu Cys Lys  Cys Ser Pro
    2795                2800                2805

agg aag  tgc agc aag tga                                           8442
Arg Lys  Cys Ser Lys
    2810
```

<210> 4

<211> 2813
<212> PRT
<213> Homo sapiens

<400> 4

```
Met Ile Pro Ala Arg Phe Ala Gly Val Leu Leu Ala Leu Ala Leu Ile
1               5                  10                  15

Leu Pro Gly Thr Leu Cys Ala Glu Gly Thr Arg Gly Arg Ser Ser Thr
            20                  25                  30

Ala Arg Cys Ser Leu Phe Gly Ser Asp Phe Val Asn Thr Phe Asp Gly
        35                  40                  45

Ser Met Tyr Ser Phe Ala Gly Tyr Cys Ser Tyr Leu Leu Ala Gly Gly
    50                  55                  60

Cys Gln Lys Arg Ser Phe Ser Ile Ile Gly Asp Phe Gln Asn Gly Lys
65                  70                  75                  80

Arg Val Ser Leu Ser Val Tyr Leu Gly Glu Phe Phe Asp Ile His Leu
                85                  90                  95

Phe Val Asn Gly Thr Val Thr Gln Gly Asp Gln Arg Val Ser Met Pro
            100                 105                 110

Tyr Ala Ser Lys Gly Leu Tyr Leu Glu Thr Glu Ala Gly Tyr Tyr Lys
        115                 120                 125

Leu Ser Gly Glu Ala Tyr Gly Phe Val Ala Arg Ile Asp Gly Ser Gly
    130                 135                 140

Asn Phe Gln Val Leu Leu Ser Asp Arg Tyr Phe Asn Lys Thr Cys Gly
145                 150                 155                 160

Leu Cys Gly Asn Phe Asn Ile Phe Ala Glu Asp Asp Phe Met Thr Gln
                165                 170                 175

Glu Gly Thr Leu Thr Ser Asp Pro Tyr Asp Phe Ala Asn Ser Trp Ala
            180                 185                 190

Leu Ser Ser Gly Glu Gln Trp Cys Glu Arg Ala Ser Pro Pro Ser Ser
        195                 200                 205

Ser Cys Asn Ile Ser Ser Gly Glu Met Gln Lys Gly Leu Trp Glu Gln
    210                 215                 220

Cys Gln Leu Leu Lys Ser Thr Ser Val Phe Ala Arg Cys His Pro Leu
225                 230                 235                 240

Val Asp Pro Glu Pro Phe Val Ala Leu Cys Glu Lys Thr Leu Cys Glu
                245                 250                 255
```

```
Cys Ala Gly Gly Leu Glu Cys Ala Cys Pro Ala Leu Leu Glu Tyr Ala
            260                 265                 270

Arg Thr Cys Ala Gln Glu Gly Met Val Leu Tyr Gly Trp Thr Asp His
        275                 280                 285

Ser Ala Cys Ser Pro Val Cys Pro Ala Gly Met Glu Tyr Arg Gln Cys
    290                 295                 300

Val Ser Pro Cys Ala Arg Thr Cys Gln Ser Leu His Ile Asn Glu Met
305                 310                 315                 320

Cys Gln Glu Arg Cys Val Asp Gly Cys Ser Cys Pro Glu Gly Gln Leu
                325                 330                 335

Leu Asp Glu Gly Leu Cys Val Glu Ser Thr Glu Cys Pro Cys Val His
            340                 345                 350

Ser Gly Lys Arg Tyr Pro Pro Gly Thr Ser Leu Ser Arg Asp Cys Asn
        355                 360                 365

Thr Cys Ile Cys Arg Asn Ser Gln Trp Ile Cys Ser Asn Glu Glu Cys
    370                 375                 380

Pro Gly Glu Cys Leu Val Thr Gly Gln Ser His Phe Lys Ser Phe Asp
385                 390                 395                 400

Asn Arg Tyr Phe Thr Phe Ser Gly Ile Cys Gln Tyr Leu Leu Ala Arg
                405                 410                 415

Asp Cys Gln Asp His Ser Phe Ser Ile Val Ile Glu Thr Val Gln Cys
            420                 425                 430

Ala Asp Asp Arg Asp Ala Val Cys Thr Arg Ser Val Thr Val Arg Leu
        435                 440                 445

Pro Gly Leu His Asn Ser Leu Val Lys Leu Lys His Gly Ala Gly Val
    450                 455                 460

Ala Met Asp Gly Gln Asp Val Gln Leu Pro Leu Leu Lys Gly Asp Leu
465                 470                 475                 480

Arg Ile Gln His Thr Val Thr Ala Ser Val Arg Leu Ser Tyr Gly Glu
                485                 490                 495

Asp Leu Gln Met Asp Trp Asp Gly Arg Gly Arg Leu Leu Val Lys Leu
            500                 505                 510

Ser Pro Val Tyr Ala Gly Lys Thr Cys Gly Leu Cys Gly Asn Tyr Asn
        515                 520                 525
```

```
Gly Asn Gln Gly Asp Asp Phe Leu Thr Pro Ser Gly Leu Ala Glu Pro
    530                 535                 540

Arg Val Glu Asp Phe Gly Asn Ala Trp Lys Leu His Gly Asp Cys Gln
545                 550                 555                 560

Asp Leu Gln Lys Gln His Ser Asp Pro Cys Ala Leu Asn Pro Arg Met
                565                 570                 575

Thr Arg Phe Ser Glu Glu Ala Cys Ala Val Leu Thr Ser Pro Thr Phe
            580                 585                 590

Glu Ala Cys His Arg Ala Val Ser Pro Leu Pro Tyr Leu Arg Asn Cys
        595                 600                 605

Arg Tyr Asp Val Cys Ser Cys Ser Asp Gly Arg Glu Cys Leu Cys Gly
    610                 615                 620

Ala Leu Ala Ser Tyr Ala Ala Ala Cys Ala Gly Arg Gly Val Arg Val
625                 630                 635                 640

Ala Trp Arg Glu Pro Gly Arg Cys Glu Leu Asn Cys Pro Lys Gly Gln
                645                 650                 655

Val Tyr Leu Gln Cys Gly Thr Pro Cys Asn Leu Thr Cys Arg Ser Leu
            660                 665                 670

Ser Tyr Pro Asp Glu Glu Cys Asn Glu Ala Cys Leu Glu Gly Cys Phe
        675                 680                 685

Cys Pro Pro Gly Leu Tyr Met Asp Glu Arg Gly Asp Cys Val Pro Lys
    690                 695                 700

Ala Gln Cys Pro Cys Tyr Tyr Asp Gly Glu Ile Phe Gln Pro Glu Asp
705                 710                 715                 720

Ile Phe Ser Asp His His Thr Met Cys Tyr Cys Glu Asp Gly Phe Met
                725                 730                 735

His Cys Thr Met Ser Gly Val Pro Gly Ser Leu Leu Pro Asp Ala Val
            740                 745                 750

Leu Ser Ser Pro Leu Ser His Arg Ser Lys Arg Ser Leu Ser Cys Arg
        755                 760                 765

Pro Pro Met Val Lys Leu Val Cys Pro Ala Asp Asn Leu Arg Ala Glu
    770                 775                 780

Gly Leu Glu Cys Thr Lys Thr Cys Gln Asn Tyr Asp Leu Glu Cys Met
785                 790                 795                 800
```

```
Ser Met Gly Cys Val Ser Gly Cys Leu Cys Pro Pro Gly Met Val Arg
                805                 810                 815

His Glu Asn Arg Cys Val Ala Leu Glu Arg Cys Pro Cys Phe His Gln
            820                 825                 830

Gly Lys Glu Tyr Ala Pro Gly Glu Thr Val Lys Ile Gly Cys Asn Thr
        835                 840                 845

Cys Val Cys Arg Asp Arg Lys Trp Asn Cys Thr Asp His Val Cys Asp
    850                 855                 860

Ala Thr Cys Ser Thr Ile Gly Met Ala His Tyr Leu Thr Phe Asp Gly
865                 870                 875                 880

Leu Lys Tyr Leu Phe Pro Gly Glu Cys Gln Tyr Val Leu Val Gln Asp
                885                 890                 895

Tyr Cys Gly Ser Asn Pro Gly Thr Phe Arg Ile Leu Val Gly Asn Lys
            900                 905                 910

Gly Cys Ser His Pro Ser Val Lys Cys Lys Lys Arg Val Thr Ile Leu
        915                 920                 925

Val Glu Gly Gly Glu Ile Glu Leu Phe Asp Gly Glu Val Asn Val Lys
    930                 935                 940

Arg Pro Met Lys Asp Glu Thr His Phe Glu Val Val Glu Ser Gly Arg
945                 950                 955                 960

Tyr Ile Ile Leu Leu Leu Gly Lys Ala Leu Ser Val Val Trp Asp Arg
                965                 970                 975

His Leu Ser Ile Ser Val Val Leu Lys Gln Thr Tyr Gln Glu Lys Val
            980                 985                 990

Cys Gly Leu Cys Gly Asn Phe Asp  Gly Ile Gln Asn Asn  Asp Leu Thr
        995                 1000                1005

Ser Ser  Asn Leu Gln Val Glu  Glu Asp Pro Val Asp  Phe Gly Asn
    1010                1015                1020

Ser Trp  Lys Val Ser Ser Gln  Cys Ala Asp Thr Arg  Lys Val Pro
    1025                1030                1035

Leu Asp  Ser Ser Pro Ala Thr  Cys His Asn Asn Ile  Met Lys Gln
    1040                1045                1050

Thr Met  Val Asp Ser Ser Cys  Arg Ile Leu Thr Ser  Asp Val Phe
    1055                1060                1065
```

```
Gln Asp  Cys Asn Lys Leu Val  Asp Pro Glu Pro Tyr  Leu Asp Val
    1070                1075                1080

Cys Ile  Tyr Asp Thr Cys Ser  Cys Glu Ser Ile Gly  Asp Cys Ala
    1085                1090                1095

Cys Phe  Cys Asp Thr Ile Ala  Ala Tyr Ala His Val  Cys Ala Gln
    1100                1105                1110

His Gly  Lys Val Val Thr Trp  Arg Thr Ala Thr Leu  Cys Pro Gln
    1115                1120                1125

Ser Cys  Glu Glu Arg Asn Leu  Arg Glu Asn Gly Tyr  Glu Cys Glu
    1130                1135                1140

Trp Arg  Tyr Asn Ser Cys Ala  Pro Ala Cys Gln Val  Thr Cys Gln
    1145                1150                1155

His Pro  Glu Pro Leu Ala Cys  Pro Val Gln Cys Val  Glu Gly Cys
    1160                1165                1170

His Ala  His Cys Pro Pro Gly  Lys Ile Leu Asp Glu  Leu Leu Gln
    1175                1180                1185

Thr Cys  Val Asp Pro Glu Asp  Cys Pro Val Cys Glu  Val Ala Gly
    1190                1195                1200

Arg Arg  Phe Ala Ser Gly Lys  Lys Val Thr Leu Asn  Pro Ser Asp
    1205                1210                1215

Pro Glu  His Cys Gln Ile Cys  His Cys Asp Val Val  Asn Leu Thr
    1220                1225                1230

Cys Glu  Ala Cys Gln Glu Pro  Gly Gly Leu Val Val  Pro Pro Thr
    1235                1240                1245

Asp Ala  Pro Val Ser Pro Thr  Thr Leu Tyr Val Glu  Asp Ile Ser
    1250                1255                1260

Glu Pro  Pro Leu His Asp Phe  Tyr Cys Ser Arg Leu  Leu Asp Leu
    1265                1270                1275

Val Phe  Leu Leu Asp Gly Ser  Ser Arg Leu Ser Glu  Ala Glu Phe
    1280                1285                1290

Glu Val  Leu Lys Ala Phe Val  Val Asp Met Met Glu  Arg Leu Arg
    1295                1300                1305

Ile Ser  Gln Lys Trp Val Arg  Val Ala Val Val Glu  Tyr His Asp
    1310                1315                1320
```

```
Gly Ser  His Ala Tyr Ile Gly  Leu Lys Asp Arg Lys  Arg Pro Ser
    1325                1330                1335

Glu Leu  Arg Arg Ile Ala Ser  Gln Val Lys Tyr Ala  Gly Ser Gln
    1340                1345                1350

Val Ala  Ser Thr Ser Glu Val  Leu Lys Tyr Thr Leu  Phe Gln Ile
    1355                1360                1365

Phe Ser  Lys Ile Asp Arg Pro  Glu Ala Ser Arg Ile  Ala Leu Leu
    1370                1375                1380

Leu Met  Ala Ser Gln Glu Pro  Gln Arg Met Ser Arg  Asn Phe Val
    1385                1390                1395

Arg Tyr  Val Gln Gly Leu Lys  Lys Lys Lys Val Ile  Val Ile Pro
    1400                1405                1410

Val Gly  Ile Gly Pro His Ala  Asn Leu Lys Gln Ile  Arg Leu Ile
    1415                1420                1425

Glu Lys  Gln Ala Pro Glu Asn  Lys Ala Phe Val Leu  Ser Ser Val
    1430                1435                1440

Asp Glu  Leu Glu Gln Gln Arg  Asp Glu Ile Val Ser  Tyr Leu Cys
    1445                1450                1455

Asp Leu  Ala Pro Glu Ala Pro  Pro Pro Thr Leu Pro  Pro His Met
    1460                1465                1470

Ala Gln  Val Thr Val Gly Pro  Gly Leu Leu Gly Val  Ser Thr Leu
    1475                1480                1485

Gly Pro  Lys Arg Asn Ser Met  Val Leu Asp Val Ala  Phe Val Leu
    1490                1495                1500

Glu Gly  Ser Asp Lys Ile Gly  Glu Ala Asp Phe Asn  Arg Ser Lys
    1505                1510                1515

Glu Phe  Met Glu Glu Val Ile  Gln Arg Met Asp Val  Gly Gln Asp
    1520                1525                1530

Ser Ile  His Val Thr Val Leu  Gln Tyr Ser Tyr Met  Val Thr Val
    1535                1540                1545

Glu Tyr  Pro Phe Ser Glu Ala  Gln Ser Lys Gly Asp  Ile Leu Gln
    1550                1555                1560

Arg Val  Arg Glu Ile Arg Tyr  Gln Gly Gly Asn Arg  Thr Asn Thr
    1565                1570                1575
```

```
Gly Leu  Ala Leu Arg Tyr Leu  Ser Asp His Ser Phe  Leu Val Ser
    1580                 1585                 1590

Gln Gly  Asp Arg Glu Gln Ala  Pro Asn Leu Val Tyr  Met Val Thr
    1595                 1600                 1605

Gly Asn  Pro Ala Ser Asp Glu  Ile Lys Arg Leu Pro  Gly Asp Ile
    1610                 1615                 1620

Gln Val  Val Pro Ile Gly Val  Gly Pro Asn Ala Asn  Val Gln Glu
    1625                 1630                 1635

Leu Glu  Arg Ile Gly Trp Pro  Asn Ala Pro Ile Leu  Ile Gln Asp
    1640                 1645                 1650

Phe Glu  Thr Leu Pro Arg Glu  Ala Pro Asp Leu Val  Leu Gln Arg
    1655                 1660                 1665

Cys Cys  Ser Gly Glu Gly Leu  Gln Ile Pro Thr Leu  Ser Pro Ala
    1670                 1675                 1680

Pro Asp  Cys Ser Gln Pro Leu  Asp Val Ile Leu Leu  Leu Asp Gly
    1685                 1690                 1695

Ser Ser  Ser Phe Pro Ala Ser  Tyr Phe Asp Glu Met  Lys Ser Phe
    1700                 1705                 1710

Ala Lys  Ala Phe Ile Ser Lys  Ala Asn Ile Gly Pro  Arg Leu Thr
    1715                 1720                 1725

Gln Val  Ser Val Leu Gln Tyr  Gly Ser Ile Thr Thr  Ile Asp Val
    1730                 1735                 1740

Pro Trp  Asn Val Val Pro Glu  Lys Ala His Leu Leu  Ser Leu Val
    1745                 1750                 1755

Asp Val  Met Gln Arg Glu Gly  Gly Pro Ser Gln Ile  Gly Asp Ala
    1760                 1765                 1770

Leu Gly  Phe Ala Val Arg Tyr  Leu Thr Ser Glu Met  His Gly Ala
    1775                 1780                 1785

Arg Pro  Gly Ala Ser Lys Ala  Val Val Ile Leu Val  Thr Asp Val
    1790                 1795                 1800

Ser Val  Asp Ser Val Asp Ala  Ala Ala Asp Ala Ala  Arg Ser Asn
    1805                 1810                 1815

Arg Val  Thr Val Phe Pro Ile  Gly Ile Gly Asp Arg  Tyr Asp Ala
    1820                 1825                 1830
```

```
Ala Gln  Leu Arg Ile Leu Ala  Gly Pro Ala Gly Asp  Ser Asn Val
    1835                 1840                 1845

Val Lys  Leu Gln Arg Ile Glu  Asp Leu Pro Thr Met  Val Thr Leu
    1850                 1855                 1860

Gly Asn  Ser Phe Leu His Lys  Leu Cys Ser Gly Phe  Val Arg Ile
    1865                 1870                 1875

Cys Met  Asp Glu Asp Gly Asn  Glu Lys Arg Pro Gly  Asp Val Trp
    1880                 1885                 1890

Thr Leu  Pro Asp Gln Cys His  Thr Val Thr Cys Gln  Pro Asp Gly
    1895                 1900                 1905

Gln Thr  Leu Leu Lys Ser His  Arg Val Asn Cys Asp  Arg Gly Leu
    1910                 1915                 1920

Arg Pro  Ser Cys Pro Asn Ser  Gln Ser Pro Val Lys  Val Glu Glu
    1925                 1930                 1935

Thr Cys  Gly Cys Arg Trp Thr  Cys Pro Cys Val Cys  Thr Gly Ser
    1940                 1945                 1950

Ser Thr  Arg His Ile Val Thr  Phe Asp Gly Gln Asn  Phe Lys Leu
    1955                 1960                 1965

Thr Gly  Ser Cys Ser Tyr Val  Leu Phe Gln Asn Lys  Glu Gln Asp
    1970                 1975                 1980

Leu Glu  Val Ile Leu His Asn  Gly Ala Cys Ser Pro  Gly Ala Arg
    1985                 1990                 1995

Gln Gly  Cys Met Lys Ser Ile  Glu Val Lys His Ser  Ala Leu Ser
    2000                 2005                 2010

Val Glu  Leu His Ser Asp Met  Glu Val Thr Val Asn  Gly Arg Leu
    2015                 2020                 2025

Val Ser  Val Pro Tyr Val Gly  Gly Asn Met Glu Val  Asn Val Tyr
    2030                 2035                 2040

Gly Ala  Ile Met His Glu Val  Arg Phe Asn His Leu  Gly His Ile
    2045                 2050                 2055

Phe Thr  Phe Thr Pro Gln Asn  Asn Glu Phe Gln Leu  Gln Leu Ser
    2060                 2065                 2070

Pro Lys  Thr Phe Ala Ser Lys  Thr Tyr Gly Leu Cys  Gly Ile Cys
    2075                 2080                 2085
```

```
Asp Glu  Asn Gly Ala Asn Asp  Phe Met Leu Arg Asp  Gly Thr Val
    2090                2095                2100

Thr Thr  Asp Trp Lys Thr Leu  Val Gln Glu Trp Thr  Val Gln Arg
    2105                2110                2115

Pro Gly  Gln Thr Cys Gln Pro  Ile Leu Glu Glu Gln  Cys Leu Val
    2120                2125                2130

Pro Asp  Ser Ser His Cys Gln  Val Leu Leu Leu Pro  Leu Phe Ala
    2135                2140                2145

Glu Cys  His Lys Val Leu Ala  Pro Ala Thr Phe Tyr  Ala Ile Cys
    2150                2155                2160

Gln Gln  Asp Ser Cys His Gln  Glu Gln Val Cys Glu  Val Ile Ala
    2165                2170                2175

Ser Tyr  Ala His Leu Cys Arg  Thr Asn Gly Val Cys  Val Asp Trp
    2180                2185                2190

Arg Thr  Pro Asp Phe Cys Ala  Met Ser Cys Pro Pro  Ser Leu Val
    2195                2200                2205

Tyr Asn  His Cys Glu His Gly  Cys Pro Arg His Cys  Asp Gly Asn
    2210                2215                2220

Val Ser  Ser Cys Gly Asp His  Pro Ser Glu Gly Cys  Phe Cys Pro
    2225                2230                2235

Pro Asp  Lys Val Met Leu Glu  Gly Ser Cys Val Pro  Glu Glu Ala
    2240                2245                2250

Cys Thr  Gln Cys Ile Gly Glu  Asp Gly Val Gln His  Gln Phe Leu
    2255                2260                2265

Glu Ala  Trp Val Pro Asp His  Gln Pro Cys Gln Ile  Cys Thr Cys
    2270                2275                2280

Leu Ser  Gly Arg Lys Val Asn  Cys Thr Thr Gln Pro  Cys Pro Thr
    2285                2290                2295

Ala Lys  Ala Pro Thr Cys Gly  Leu Cys Glu Val Ala  Arg Leu Arg
    2300                2305                2310

Gln Asn  Ala Asp Gln Cys Cys  Pro Glu Tyr Glu Cys  Val Cys Asp
    2315                2320                2325

Pro Val  Ser Cys Asp Leu Pro  Pro Val Pro His Cys  Glu Arg Gly
    2330                2335                2340
```

```
Leu Gln  Pro Thr Leu Thr Asn  Pro Gly Glu Cys Arg  Pro Asn Phe
    2345                 2350                 2355

Thr Cys  Ala Cys Arg Lys Glu  Glu Cys Lys Arg Val  Ser Pro Pro
    2360                 2365                 2370

Ser Cys  Pro Pro His Arg Leu  Pro Thr Leu Arg Lys  Thr Gln Cys
    2375                 2380                 2385

Cys Asp  Glu Tyr Glu Cys Ala  Cys Asn Cys Val Asn  Ser Thr Val
    2390                 2395                 2400

Ser Cys  Pro Leu Gly Tyr Leu  Ala Ser Thr Ala Thr  Asn Asp Cys
    2405                 2410                 2415

Gly Cys  Thr Thr Thr Thr Cys  Leu Pro Asp Lys Val  Cys Val His
    2420                 2425                 2430

Arg Ser  Thr Ile Tyr Pro Val  Gly Gln Phe Trp Glu  Glu Gly Cys
    2435                 2440                 2445

Asp Val  Cys Thr Cys Thr Asp  Met Glu Asp Ala Val  Met Gly Leu
    2450                 2455                 2460

Arg Val  Ala Gln Cys Ser Gln  Lys Pro Cys Glu Asp  Ser Cys Arg
    2465                 2470                 2475

Ser Gly  Phe Thr Tyr Val Leu  His Glu Gly Glu Cys  Cys Gly Arg
    2480                 2485                 2490

Cys Leu  Pro Ser Ala Cys Glu  Val Val Thr Gly Ser  Pro Arg Gly
    2495                 2500                 2505

Asp Ser  Gln Ser Ser Trp Lys  Ser Val Gly Ser Gln  Trp Ala Ser
    2510                 2515                 2520

Pro Glu  Asn Pro Cys Leu Ile  Asn Glu Cys Val Arg  Val Lys Glu
    2525                 2530                 2535

Glu Val  Phe Ile Gln Gln Arg  Asn Val Ser Cys Pro  Gln Leu Glu
    2540                 2545                 2550

Val Pro  Val Cys Pro Ser Gly  Phe Gln Leu Ser Cys  Lys Thr Ser
    2555                 2560                 2565

Ala Cys  Cys Pro Ser Cys Arg  Cys Glu Arg Met Glu  Ala Cys Met
    2570                 2575                 2580

Leu Asn  Gly Thr Val Ile Gly  Pro Gly Lys Thr Val  Met Ile Asp
    2585                 2590                 2595
```

Val Cys Thr Thr Cys Arg Cys Met Val Gln Val Gly Val Ile Ser
2600 2605 2610

Gly Phe Lys Leu Glu Cys Arg Lys Thr Thr Cys Asn Pro Cys Pro
2615 2620 2625

Leu Gly Tyr Lys Glu Glu Asn Asn Thr Gly Glu Cys Cys Gly Arg
2630 2635 2640

Cys Leu Pro Thr Ala Cys Thr Ile Gln Leu Arg Gly Gly Gln Ile
2645 2650 2655

Met Thr Leu Lys Arg Asp Glu Thr Leu Gln Asp Gly Cys Asp Thr
2660 2665 2670

His Phe Cys Lys Val Asn Glu Arg Gly Glu Tyr Phe Trp Glu Lys
2675 2680 2685

Arg Val Thr Gly Cys Pro Pro Phe Asp Glu His Lys Cys Leu Ala
2690 2695 2700

Glu Gly Gly Lys Ile Met Lys Ile Pro Gly Thr Cys Cys Asp Thr
2705 2710 2715

Cys Glu Glu Pro Glu Cys Asn Asp Ile Thr Ala Arg Leu Gln Tyr
2720 2725 2730

Val Lys Val Gly Ser Cys Lys Ser Glu Val Glu Val Asp Ile His
2735 2740 2745

Tyr Cys Gln Gly Lys Cys Ala Ser Lys Ala Met Tyr Ser Ile Asp
2750 2755 2760

Ile Asn Asp Val Gln Asp Gln Cys Ser Cys Cys Ser Pro Thr Arg
2765 2770 2775

Thr Glu Pro Met Gln Val Ala Leu His Cys Thr Asn Gly Ser Val
2780 2785 2790

Val Tyr His Glu Val Leu Asn Ala Met Glu Cys Lys Cys Ser Pro
2795 2800 2805

Arg Lys Cys Ser Lys
2810

<210> 5
<211> 1444
<212> PRT
<213> Artificial Sequence

<220>

<223> amino acid sequence of a single chain factor viii molecule

<400> 5

```
Ala Thr Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser Trp Asp Tyr
1               5                  10                  15

Met Gln Ser Asp Leu Gly Glu Leu Pro Val Asp Ala Arg Phe Pro Pro
            20                  25                  30

Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val Tyr Lys Lys
        35                  40                  45

Thr Leu Phe Val Glu Phe Thr Asp His Leu Phe Asn Ile Ala Lys Pro
    50                  55                  60

Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln Ala Glu Val
65                  70                  75                  80

Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser His Pro Val
                85                  90                  95

Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser Glu Gly Ala
            100                 105                 110

Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp Asp Lys Val
        115                 120                 125

Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu Lys Glu Asn
    130                 135                 140

Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser Tyr Leu Ser
145                 150                 155                 160

His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile Gly Ala Leu
                165                 170                 175

Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr Gln Thr Leu
            180                 185                 190

His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly Lys Ser Trp
        195                 200                 205

His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp Ala Ala Ser
    210                 215                 220

Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr Val Asn Arg
225                 230                 235                 240

Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val Tyr Trp His
                245                 250                 255
```

```
Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile Phe Leu Glu
            260                 265                 270

Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser Leu Glu Ile
        275                 280                 285

Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met Asp Leu Gly
    290                 295                 300

Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His Asp Gly Met
305                 310                 315                 320

Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro Gln Leu Arg
                325                 330                 335

Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp Leu Thr Asp
            340                 345                 350

Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser Pro Ser Phe
        355                 360                 365

Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr Trp Val His
    370                 375                 380

Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro Leu Val Leu
385                 390                 395                 400

Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn Asn Gly Pro
                405                 410                 415

Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met Ala Tyr Thr
            420                 425                 430

Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu Ser Gly Ile
        435                 440                 445

Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu Leu Ile Ile
    450                 455                 460

Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro His Gly Ile
465                 470                 475                 480

Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys Gly Val Lys
                485                 490                 495

His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe Lys Tyr Lys
            500                 505                 510

Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp Pro Arg Cys
        515                 520                 525
```

```
Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg Asp Leu Ala
    530                 535                 540

Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu Ser Val Asp
545                 550                 555                 560

Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val Ile Leu Phe
                565                 570                 575

Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu Asn Ile Gln
            580                 585                 590

Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp Pro Glu Phe
        595                 600                 605

Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val Phe Asp Ser
    610                 615                 620

Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp Tyr Ile Leu
625                 630                 635                 640

Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe Ser Gly Tyr
                645                 650                 655

Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr Leu Phe Pro
            660                 665                 670

Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro Gly Leu Trp
        675                 680                 685

Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly Met Thr Ala
    690                 695                 700

Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp Tyr Tyr Glu
705                 710                 715                 720

Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys Asn Asn Ala
                725                 730                 735

Ile Glu Pro Arg Ser Phe Ser Gln Asn Ser Arg His Pro Ser Thr Arg
            740                 745                 750

Gln Lys Gln Phe Asn Ala Thr Thr Ile Pro Glu Asn Thr Thr Leu Gln
        755                 760                 765

Ser Asp Gln Glu Glu Ile Asp Tyr Asp Asp Thr Ile Ser Val Glu Met
    770                 775                 780

Lys Lys Glu Asp Phe Asp Ile Tyr Asp Glu Asp Glu Asn Gln Ser Pro
785                 790                 795                 800
```

```
Arg Ser Phe Gln Lys Lys Thr Arg His Tyr Phe Ile Ala Ala Val Glu
                805                 810                 815

Arg Leu Trp Asp Tyr Gly Met Ser Ser Ser Pro His Val Leu Arg Asn
            820                 825                 830

Arg Ala Gln Ser Gly Ser Val Pro Gln Phe Lys Lys Val Val Phe Gln
        835                 840                 845

Glu Phe Thr Asp Gly Ser Phe Thr Gln Pro Leu Tyr Arg Gly Glu Leu
    850                 855                 860

Asn Glu His Leu Gly Leu Leu Gly Pro Tyr Ile Arg Ala Glu Val Glu
865                 870                 875                 880

Asp Asn Ile Met Val Thr Phe Arg Asn Gln Ala Ser Arg Pro Tyr Ser
                885                 890                 895

Phe Tyr Ser Ser Leu Ile Ser Tyr Glu Glu Asp Gln Arg Gln Gly Ala
            900                 905                 910

Glu Pro Arg Lys Asn Phe Val Lys Pro Asn Glu Thr Lys Thr Tyr Phe
        915                 920                 925

Trp Lys Val Gln His His Met Ala Pro Thr Lys Asp Glu Phe Asp Cys
    930                 935                 940

Lys Ala Trp Ala Tyr Phe Ser Asp Val Asp Leu Glu Lys Asp Val His
945                 950                 955                 960

Ser Gly Leu Ile Gly Pro Leu Leu Val Cys His Thr Asn Thr Leu Asn
                965                 970                 975

Pro Ala His Gly Arg Gln Val Thr Val Gln Glu Phe Ala Leu Phe Phe
            980                 985                 990

Thr Ile Phe Asp Glu Thr Lys Ser  Trp Tyr Phe Thr Glu  Asn Met Glu
        995                 1000                1005

Arg Asn  Cys Arg Ala Pro Cys  Asn Ile Gln Met Glu  Asp Pro Thr
    1010                1015                1020

Phe Lys  Glu Asn Tyr Arg Phe  His Ala Ile Asn Gly  Tyr Ile Met
    1025                1030                1035

Asp Thr  Leu Pro Gly Leu Val  Met Ala Gln Asp Gln  Arg Ile Arg
    1040                1045                1050

Trp Tyr  Leu Leu Ser Met Gly  Ser Asn Glu Asn Ile  His Ser Ile
    1055                1060                1065
```

```
His Phe  Ser Gly His Val Phe  Thr Val Arg Lys Lys  Glu Glu Tyr
    1070                1075                1080

Lys Met  Ala Leu Tyr Asn Leu  Tyr Pro Gly Val Phe  Glu Thr Val
    1085                1090                1095

Glu Met  Leu Pro Ser Lys Ala  Gly Ile Trp Arg Val  Glu Cys Leu
    1100                1105                1110

Ile Gly  Glu His Leu His Ala  Gly Met Ser Thr Leu  Phe Leu Val
    1115                1120                1125

Tyr Ser  Asn Lys Cys Gln Thr  Pro Leu Gly Met Ala  Ser Gly His
    1130                1135                1140

Ile Arg  Asp Phe Gln Ile Thr  Ala Ser Gly Gln Tyr  Gly Gln Trp
    1145                1150                1155

Ala Pro  Lys Leu Ala Arg Leu  His Tyr Ser Gly Ser  Ile Asn Ala
    1160                1165                1170

Trp Ser  Thr Lys Glu Pro Phe  Ser Trp Ile Lys Val  Asp Leu Leu
    1175                1180                1185

Ala Pro  Met Ile Ile His Gly  Ile Lys Thr Gln Gly  Ala Arg Gln
    1190                1195                1200

Lys Phe  Ser Ser Leu Tyr Ile  Ser Gln Phe Ile Ile  Met Tyr Ser
    1205                1210                1215

Leu Asp  Gly Lys Lys Trp Gln  Thr Tyr Arg Gly Asn  Ser Thr Gly
    1220                1225                1230

Thr Leu  Met Val Phe Phe Gly  Asn Val Asp Ser Ser  Gly Ile Lys
    1235                1240                1245

His Asn  Ile Phe Asn Pro Pro  Ile Ile Ala Arg Tyr  Ile Arg Leu
    1250                1255                1260

His Pro  Thr His Tyr Ser Ile  Arg Ser Thr Leu Arg  Met Glu Leu
    1265                1270                1275

Met Gly  Cys Asp Leu Asn Ser  Cys Ser Met Pro Leu  Gly Met Glu
    1280                1285                1290

Ser Lys  Ala Ile Ser Asp Ala  Gln Ile Thr Ala Ser  Ser Tyr Phe
    1295                1300                1305

Thr Asn  Met Phe Ala Thr Trp  Ser Pro Ser Lys Ala  Arg Leu His
    1310                1315                1320
```

```
Leu Gln  Gly Arg Ser Asn Ala  Trp Arg Pro Gln Val  Asn Asn Pro
    1325                1330                1335

Lys Glu  Trp Leu Gln Val Asp  Phe Gln Lys Thr Met  Lys Val Thr
    1340                1345                1350

Gly Val  Thr Thr Gln Gly Val  Lys Ser Leu Leu Thr  Ser Met Tyr
    1355                1360                1365

Val Lys  Glu Phe Leu Ile Ser  Ser Ser Gln Asp Gly  His Gln Trp
    1370                1375                1380

Thr Leu  Phe Phe Gln Asn Gly  Lys Val Lys Val Phe  Gln Gly Asn
    1385                1390                1395

Gln Asp  Ser Phe Thr Pro Val  Val Asn Ser Leu Asp  Pro Pro Leu
    1400                1405                1410

Leu Thr  Arg Tyr Leu Arg Ile  His Pro Gln Ser Trp  Val His Gln
    1415                1420                1425

Ile Ala  Leu Arg Met Glu Val  Leu Gly Cys Glu Ala  Gln Asp Leu
    1430                1435                1440

Tyr
```

<210> 6
<211> 585
<212> PRT
<213> Homo sapiens

<400> 6

```
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
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> 7
<211> 519
<212> PRT
<213> Artificial Sequence

<220>
<223> His-tagged D´D3

<220>
<221> MISC_FEATURE
<222> (1)..(479)
<223> Amino acid sequence of D´D3 - His8

<220>
<221> MISC_FEATURE
<222> (1)..(479)
<223> VWF D´D3 region (VWF amino acids 764 - 1242)

<220>
<221> MISC_FEATURE
<222> (480)..(511)
<223> glycine / serine linker

<220>
<221> MISC_FEATURE
<222> (512)..(519)
<223> polyhistidine tag

<400> 7

```
Ser Leu Ser Cys Arg Pro Pro Met Val Lys Leu Val Cys Pro Ala Asp
1               5                  10                  15

Asn Leu Arg Ala Glu Gly Leu Glu Cys Thr Lys Thr Cys Gln Asn Tyr
            20                  25                  30

Asp Leu Glu Cys Met Ser Met Gly Cys Val Ser Gly Cys Leu Cys Pro
        35                  40                  45

Pro Gly Met Val Arg His Glu Asn Arg Cys Val Ala Leu Glu Arg Cys
    50                  55                  60

Pro Cys Phe His Gln Gly Lys Glu Tyr Ala Pro Gly Glu Thr Val Lys
65                  70                  75                  80

Ile Gly Cys Asn Thr Cys Val Cys Arg Asp Arg Lys Trp Asn Cys Thr
                85                  90                  95

Asp His Val Cys Asp Ala Thr Cys Ser Thr Ile Gly Met Ala His Tyr
            100                 105                 110

Leu Thr Phe Asp Gly Leu Lys Tyr Leu Phe Pro Gly Glu Cys Gln Tyr
        115                 120                 125

Val Leu Val Gln Asp Tyr Cys Gly Ser Asn Pro Gly Thr Phe Arg Ile
    130                 135                 140

Leu Val Gly Asn Lys Gly Cys Ser His Pro Ser Val Lys Cys Lys Lys
145                 150                 155                 160

Arg Val Thr Ile Leu Val Glu Gly Gly Glu Ile Glu Leu Phe Asp Gly
                165                 170                 175

Glu Val Asn Val Lys Arg Pro Met Lys Asp Glu Thr His Phe Glu Val
            180                 185                 190

Val Glu Ser Gly Arg Tyr Ile Ile Leu Leu Leu Gly Lys Ala Leu Ser
        195                 200                 205
```

```
Val Val Trp Asp Arg His Leu Ser Ile Ser Val Val Leu Lys Gln Thr
    210                 215                 220

Tyr Gln Glu Lys Val Cys Gly Leu Cys Gly Asn Phe Asp Gly Ile Gln
225                 230                 235                 240

Asn Asn Asp Leu Thr Ser Ser Asn Leu Gln Val Glu Glu Asp Pro Val
                245                 250                 255

Asp Phe Gly Asn Ser Trp Lys Val Ser Ser Gln Cys Ala Asp Thr Arg
            260                 265                 270

Lys Val Pro Leu Asp Ser Ser Pro Ala Thr Cys His Asn Asn Ile Met
        275                 280                 285

Lys Gln Thr Met Val Asp Ser Ser Cys Arg Ile Leu Thr Ser Asp Val
    290                 295                 300

Phe Gln Asp Cys Asn Lys Leu Val Asp Pro Glu Pro Tyr Leu Asp Val
305                 310                 315                 320

Cys Ile Tyr Asp Thr Cys Ser Cys Glu Ser Ile Gly Asp Cys Ala Cys
                325                 330                 335

Phe Cys Asp Thr Ile Ala Ala Tyr Ala His Val Cys Ala Gln His Gly
            340                 345                 350

Lys Val Val Thr Trp Arg Thr Ala Thr Leu Cys Pro Gln Ser Cys Glu
        355                 360                 365

Glu Arg Asn Leu Arg Glu Asn Gly Tyr Glu Cys Glu Trp Arg Tyr Asn
    370                 375                 380

Ser Cys Ala Pro Ala Cys Gln Val Thr Cys Gln His Pro Glu Pro Leu
385                 390                 395                 400

Ala Cys Pro Val Gln Cys Val Glu Gly Cys His Ala His Cys Pro Pro
                405                 410                 415

Gly Lys Ile Leu Asp Glu Leu Leu Gln Thr Cys Val Asp Pro Glu Asp
            420                 425                 430

Cys Pro Val Cys Glu Val Ala Gly Arg Arg Phe Ala Ser Gly Lys Lys
        435                 440                 445

Val Thr Leu Asn Pro Ser Asp Pro Glu His Cys Gln Ile Cys His Cys
    450                 455                 460

Asp Val Val Asn Leu Thr Cys Glu Ala Cys Gln Glu Pro Gly Gly Ser
465                 470                 475                 480
```

Ser Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ser
485 490 495

Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ser His
500 505 510

His His His His His His His
515

<210> 8
<211> 584
<212> PRT
<213> Artificial sequence

<220>
<223> His-tagged CTP fusion protein

<220>
<221> MISC_FEATURE
<222> (1)..(479)
<223> VWF D´D3 region (VWF amino acids 764 - 1242)

<220>
<221> MISC_FEATURE
<222> (480)..(511)
<223> glycine / serine linker

<220>
<221> MISC_FEATURE
<222> (512)..(576)
<223> C-terminal peptide of human chorionic gonadotropin beta subunit

<220>
<221> MISC_FEATURE
<222> (577)..(584)
<223> Polyhistidine tag

<400> 8

Ser Leu Ser Cys Arg Pro Pro Met Val Lys Leu Val Cys Pro Ala Asp
1 5 10 15

Asn Leu Arg Ala Glu Gly Leu Glu Cys Thr Lys Thr Cys Gln Asn Tyr
20 25 30

Asp Leu Glu Cys Met Ser Met Gly Cys Val Ser Gly Cys Leu Cys Pro
35 40 45

Pro Gly Met Val Arg His Glu Asn Arg Cys Val Ala Leu Glu Arg Cys
50 55 60

Pro Cys Phe His Gln Gly Lys Glu Tyr Ala Pro Gly Glu Thr Val Lys
65 70 75 80

Ile Gly Cys Asn Thr Cys Val Cys Arg Asp Arg Lys Trp Asn Cys Thr
85 90 95

```
Asp His Val Cys Asp Ala Thr Cys Ser Thr Ile Gly Met Ala His Tyr
            100                 105                 110

Leu Thr Phe Asp Gly Leu Lys Tyr Leu Phe Pro Gly Glu Cys Gln Tyr
        115                 120                 125

Val Leu Val Gln Asp Tyr Cys Gly Ser Asn Pro Gly Thr Phe Arg Ile
    130                 135                 140

Leu Val Gly Asn Lys Gly Cys Ser His Pro Ser Val Lys Cys Lys Lys
145                 150                 155                 160

Arg Val Thr Ile Leu Val Glu Gly Gly Glu Ile Glu Leu Phe Asp Gly
                165                 170                 175

Glu Val Asn Val Lys Arg Pro Met Lys Asp Glu Thr His Phe Glu Val
            180                 185                 190

Val Glu Ser Gly Arg Tyr Ile Ile Leu Leu Leu Gly Lys Ala Leu Ser
        195                 200                 205

Val Val Trp Asp Arg His Leu Ser Ile Ser Val Val Leu Lys Gln Thr
    210                 215                 220

Tyr Gln Glu Lys Val Cys Gly Leu Cys Gly Asn Phe Asp Gly Ile Gln
225                 230                 235                 240

Asn Asn Asp Leu Thr Ser Ser Asn Leu Gln Val Glu Glu Asp Pro Val
                245                 250                 255

Asp Phe Gly Asn Ser Trp Lys Val Ser Ser Gln Cys Ala Asp Thr Arg
            260                 265                 270

Lys Val Pro Leu Asp Ser Ser Pro Ala Thr Cys His Asn Asn Ile Met
        275                 280                 285

Lys Gln Thr Met Val Asp Ser Ser Cys Arg Ile Leu Thr Ser Asp Val
    290                 295                 300

Phe Gln Asp Cys Asn Lys Leu Val Asp Pro Glu Pro Tyr Leu Asp Val
305                 310                 315                 320

Cys Ile Tyr Asp Thr Cys Ser Cys Glu Ser Ile Gly Asp Cys Ala Cys
                325                 330                 335

Phe Cys Asp Thr Ile Ala Ala Tyr Ala His Val Cys Ala Gln His Gly
            340                 345                 350

Lys Val Val Thr Trp Arg Thr Ala Thr Leu Cys Pro Gln Ser Cys Glu
        355                 360                 365
```

```
Glu Arg Asn Leu Arg Glu Asn Gly Tyr Glu Cys Glu Trp Arg Tyr Asn
    370                 375                 380

Ser Cys Ala Pro Ala Cys Gln Val Thr Cys Gln His Pro Glu Pro Leu
385                 390                 395                 400

Ala Cys Pro Val Gln Cys Val Glu Gly Cys His Ala His Cys Pro Pro
                405                 410                 415

Gly Lys Ile Leu Asp Glu Leu Leu Gln Thr Cys Val Asp Pro Glu Asp
            420                 425                 430

Cys Pro Val Cys Glu Val Ala Gly Arg Arg Phe Ala Ser Gly Lys Lys
        435                 440                 445

Val Thr Leu Asn Pro Ser Asp Pro Glu His Cys Gln Ile Cys His Cys
    450                 455                 460

Asp Val Val Asn Leu Thr Cys Glu Ala Cys Gln Glu Pro Gly Gly Ser
465                 470                 475                 480

Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly
                485                 490                 495

Gly Ser Gly Gly Ser Gly Gly Gly Ser Gly Gly Ser Gly Ser Ser Ala
            500                 505                 510

Ser Ser Ser Ser Lys Ala Pro Pro Pro Ser Leu Pro Ser Pro Ser Arg
        515                 520                 525

Leu Pro Gly Pro Ser Asp Thr Pro Ile Leu Pro Gln Ala Ser Ser Ser
    530                 535                 540

Ser Lys Ala Pro Pro Pro Ser Leu Pro Ser Pro Ser Arg Leu Pro Gly
545                 550                 555                 560

Pro Ser Asp Thr Pro Ile Leu Pro Gln Ala Gly Gly Ser Gly Gly Ser
                565                 570                 575

His His His His His His His His
            580
```