

SEQUENCE LISTING

<110> Saitama Medical University
Daiichi Sankyo Company, Limited

<120> Pharmaceutical Composition for Treatment or Prevention of
Ectopic Ossification

<130> PH-7730-PCT

<150> JP 2018-039066

<151> 2018-03-05

<160> 42

<170> PatentIn version 3.5

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<211> 509

<212> PRT

<213> Homo sapiens

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Thr Leu Leu Glu Cys Val Gly Lys Gly Arg Tyr Gly Glu Val Trp Arg
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Glu Val Leu Asp Glu Thr Ile Gln Val Asp Cys Phe Asp Ser Tyr Lys
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Arg Met Val Ser Asn Gly Ile Val Glu Asp Tyr Lys Pro Pro Phe Tyr
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Asp Val Val Pro Asn Asp Pro Ser Phe Glu Asp Met Arg Lys Val Val
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Cys Val Asp Gln Gln Arg Pro Asn Ile Pro Asn Arg Trp Phe Ser Asp
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$\langle 212 \rangle$	PRT
$\langle 213 \rangle$	Mus musculus

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Val Tyr Gln Lys Gly Cys Phe Gln Val Tyr Glu Gln Gly Lys Met Thr
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Cys Lys Thr Pro Pro Ser Pro Gly Gln Ala Val Glu Cys Cys Gln Gly
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Asp Trp Cys Asn Arg Asn Ile Thr Ala Gln Leu Pro Thr Lys Gly Lys
100 105 110

Ser Phe Pro Gly Thr Gln Asn Phe His Leu Glu Val Gly Leu Ile Ile
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Leu Ser Val Val Phe Ala Val Cys Leu Leu Ala Cys Ile Leu Gly Val
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Ala Leu Arg Lys Phe Lys Arg Arg Asn Gln Glu Arg Leu Asn Pro Arg
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Asp Val Glu Tyr Gly Thr Ile Glu Gly Leu Ile Thr Thr Asn Val Gly
165 170 175

Asp Ser Thr Leu Ala Glu Leu Leu Asp His Ser Cys Thr Ser Gly Ser
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Gly Ser Gly Leu Pro Phe Leu Val Gln Arg Thr Val Ala Arg Gln Ile
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Thr Leu Leu Glu Cys Val Gly Lys Gly Arg Tyr Gly Glu Val Trp Arg
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Gly Ser Trp Gln Gly Glu Asn Val Ala Val Lys Ile Phe Ser Ser Arg
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Asp Glu Lys Ser Trp Phe Arg Glu Thr Glu Leu Tyr Asn Thr Val Met
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Leu Arg His Glu Asn Ile Leu Gly Phe Ile Ala Ser Asp Met Thr Ser
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Arg His Ser Ser Thr Gln Leu Trp Leu Ile Thr His Tyr His Glu Met
275 280 285

Gly Ser Leu Tyr Asp Tyr Leu Gln Leu Thr Thr Leu Asp Thr Val Ser
290 295 300

Cys Leu Arg Ile Val Leu Ser Ile Ala Ser Gly Leu Ala His Leu His
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Glu Val Leu Asp Glu Thr Ile Gln Val Asp Cys Phe Asp Ser Tyr Lys
385 390 395 400

Arg Val Asp Ile Trp Ala Phe Gly Leu Val Leu Trp Glu Val Ala Arg
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Arg Met Val Ser Asn Gly Ile Val Glu Asp Tyr Lys Pro Pro Phe Tyr
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Asp Val Val Pro Asn Asp Pro Ser Phe Glu Asp Met Arg Lys Val Val
 435 440 445

Cys Val Asp Gln Gln Arg Pro Asn Ile Pro Asn Arg Trp Phe Ser Asp
 450 455 460

Pro Thr Leu Thr Ser Leu Ala Lys Leu Met Lys Glu Cys Trp Tyr Gln
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Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Arg Ala Asn Gln Gly
35 40 45

Val Ser Leu Ser Arg Tyr Asn Leu Met His Trp Tyr Gln Gln Lys Pro
50 55 60

Gly Gln Lys Pro Lys Leu Leu Ile Tyr Arg Ser Ser Asn Leu Ala Ser
65 70 75 80

Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
85 90 95

Leu Thr Ile Ser Ser Val Gln Ala Asp Asp Ile Ala Val Tyr Tyr Cys
100 105 110

Gln Gln Ser Arg Glu Ser Pro Phe Thr Phe Gly Gln Gly Thr Lys Leu
115 120 125

Glu Leu Lys Arg Ala Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro
130 135 140

Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu
145 150 155 160

Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn
165 170 175

Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser
180 185 190

Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala
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Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp
1 5 10 15

Val Leu Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
20 25 30

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Ser His Tyr Tyr Met Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ala Ser Ile Thr Asn Ser Gly Gly Ser Ile Asn Tyr Arg
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Ser
85 90 95

Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Thr
100 105 110

Tyr Tyr Cys Thr Arg Glu Gly Gly Glu Asn Tyr Gly Gly Tyr Pro Pro
115 120 125

Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser
130 135 140

Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr
145 150 155 160

Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro
165 170 175

Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val
180 185 190

His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser

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

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
370 375 380

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
385 390 395 400

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
405 410 415

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
420 425 430

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
435 440 445

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
450 455 460

Ser Leu Ser Leu Ser Pro Gly Lys
465 470

<210> 32

<211> 238

<212> PRT

<213> Artificial

<220>

<223> Amino acid sequence of humanized hA2-15A-L6

<220>

<221> SIGNAL

<222> (1).. (20)

<220>

<221> V_region

<222> (21).. (133)

<220>

<221> C_region

<222> (134).. (238)

<400> 32

Met Val Leu Gln Thr Gln Val Phe Ile Ser Leu Leu Leu Trp Ile Ser
1 5 10 15

Gly Ala Tyr Gly Asp Ile Val Leu Thr Gln Ser Pro Asp Ser Leu Ala
20 25 30

Val Ser Leu Gly Glu Arg Ala Thr Ile Asn Cys Arg Ala Asn Gln Gly
35 40 45

Val Ser Leu Ser Arg Tyr Asn Leu Met His Trp Tyr Gln Gln Lys Pro
50 55 60

Gly Gln Lys Pro Lys Leu Leu Ile Tyr Arg Ser Ser Asn Leu Ala Gln
65 70 75 80

Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
85 90 95

Leu Thr Ile Ser Ser Val Gln Ala Asp Asp Ile Ala Val Tyr Tyr Cys
100 105 110

Gln Gln Ser Arg Glu Ser Pro Phe Thr Phe Gly Gln Gly Thr Lys Leu
115 120 125

Glu Leu Lys Arg Ala Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro
130 135 140

Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu
145 150 155 160

Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn
165 170 175

Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser
180 185 190

Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala
195 200 205

Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly
210 215 220

Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
225 230 235

<210> 33

<211> 468

<212> PRT

<213> Artificial

<220>

<223> amino acid sequence of humanized hA2-15A-H4_IgG2 type

<400> 33

Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp
1 5 10 15

Val Leu Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
20 25 30

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
35 40 45

Ser His Tyr Tyr Met Ala Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ala Ser Ile Thr Asn Ser Gly Gly Ser Ile Asn Tyr Arg
65 70 75 80

Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Ser
85 90 95

Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Thr
100 105 110

Tyr Tyr Cys Thr Arg Glu Gly Gly Glu Asn Tyr Gly Gly Tyr Pro Pro
115 120 125

Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser
130 135 140

Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr
145 150 155 160

Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro
165 170 175

Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val
180 185 190

His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
195 200 205

Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr
210 215 220

Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val
225 230 235 240

Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val
245 250 255

Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
260 265 270

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
275 280 285

His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
290 295 300

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr
305 310 315 320

Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn
325 330 335

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro
340 345 350

Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln
355 360 365

Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val
370 375 380

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
385 390 395 400

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
405 410 415

Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
420 425 430

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
435 440 445

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
450 455 460

Ser Pro Gly Lys
465

<210> 34
<211> 470
<212> PRT
<213> Artificial

<220>
<223> Amino acid sequence of humanized hA2-27D-H2

<220>

<221> SIGNAL
<222> (1).. (19)

<220>
<221> V_region
<222> (20).. (140)

<220>
<221> C_region
<222> (141).. (470)

<400> 34

Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp
1 5 10 15

Val Leu Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
20 25 30

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Ser Thr Phe
35 40 45

Ser Asn Tyr Gly Met Lys Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ser Ser Ile Ser Arg Ser Ser Thr Tyr Ile Tyr Tyr Ala
65 70 75 80

Asp Thr Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Ala Ala Ile Ser Thr Pro Phe Tyr Trp Tyr Phe Asp

115		120		125
Phe Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys				
130		135		140
Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly				
145		150		155
				160
Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro				
	165		170	175
Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr				
	180		185	190
Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val				
195		200		205
Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn				
210		215		220
Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro				
225		230		235
				240
Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu				
	245		250	255
Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp				
	260		265	270
Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp				
275		280		285

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
290 295 300

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
305 310 315 320

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
325 330 335

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
340 345 350

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
355 360 365

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
370 375 380

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
385 390 395 400

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
405 410 415

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
420 425 430

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
435 440 445

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu

450

455

460

Ser Leu Ser Pro Gly Lys
 465 470

<210> 35

<211> 234

<212> PRT

<213> Artificial

<220>

<223> Amino acid sequence of humanized hA2-27D-L2

<220>

<221> SIGNAL

<222> (1).. (20)

<220>

<221> V_region

<222> (21).. (129)

<220>

<221> C_region

<222> (130).. (234)

<400> 35

Met Val Leu Gln Thr Gln Val Phe Ile Ser Leu Leu Leu Trp Ile Ser
 1 5 10 15

Gly Ala Tyr Gly Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser
 20 25 30

Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Leu Ala Ser Ser Ser
 35 40 45

Val Ser Tyr Met Thr Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Arg
50 55 60

Leu Trp Ile Tyr Gly Thr Ser Asn Leu Ala Ser Gly Val Pro Asp Arg
65 70 75 80

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg
85 90 95

Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Leu His Leu Thr Ser
100 105 110

Tyr Pro Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
115 120 125

Ala Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
130 135 140

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
145 150 155 160

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
165 170 175

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
180 185 190

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
195 200 205

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro

210

215

220

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys

225

230

<210> 36

<211> 470

<212> PRT

<213> Artificial

<220>

<223> Amino acid sequence of humanized hA2-27D-H3

<220>

<221> SIGNAL

<222> (1).. (19)

<220>

<221> V_region

<222> (20).. (140)

<220>

<221> C_region

<222> (141).. (470)

<400> 36

Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp

1

5

10

15

Val Leu Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln

20

25

30

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Ser Thr Phe

35

40

45

Ser Asn Tyr Gly Met Lys Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu
50 55 60

Glu Trp Val Ala Ser Ile Ser Arg Ser Ser Thr Tyr Ile Tyr Tyr Ala
65 70 75 80

Asp Thr Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
85 90 95

Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
100 105 110

Tyr Tyr Cys Ala Ala Ala Ile Ser Thr Pro Phe Tyr Trp Tyr Phe Asp
115 120 125

Phe Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys
130 135 140

Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
145 150 155 160

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
165 170 175

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
180 185 190

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
195 200 205

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
210 215 220

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
225 230 235 240

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
245 250 255

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
260 265 270

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
275 280 285

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
290 295 300

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
305 310 315 320

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
325 330 335

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
340 345 350

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
355 360 365

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn
370 375 380

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
385 390 395 400

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
405 410 415

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
420 425 430

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
435 440 445

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
450 455 460

Ser Leu Ser Pro Gly Lys
465 470

<210> 37
<211> 234
<212> PRT
<213> Artificial

<220>
<223> Amino acid sequence of humanized hA2-27D-L4

<220>
<221> SIGNAL
<222> (1).. (20)

<220>
<221> V_region
<222> (21).. (129)

<220>

<221> C_region

<222> (130)..(234)

<400> 37

Met Val Leu Gln Thr Gln Val Phe Ile Ser Leu Leu Leu Trp Ile Ser
1 5 10 15

Gly Ala Tyr Gly Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Met Ser
20 25 30

Ala Ser Pro Gly Glu Arg Val Thr Leu Ser Cys Leu Ala Ser Ser Ser
35 40 45

Val Ser Tyr Met Thr Trp Tyr Gln Gln Lys Pro Gly Ala Ser Pro Arg
50 55 60

Leu Trp Ile Tyr Gly Thr Ser Asn Leu Ala Ser Gly Val Pro Asp Arg
65 70 75 80

Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Arg
85 90 95

Met Glu Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Leu His Leu Thr Ser
100 105 110

Tyr Pro Pro Tyr Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys Arg
115 120 125

Ala Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
130 135 140

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr

145 150 155 160

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
165 170 175

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
180 185 190

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
195 200 205

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
210 215 220

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
225 230

<210> 38
<211> 470
<212> PRT
<213> Artificial

<220>
<223> amino acid sequence of humanized hA2-27D-H2_LALA

<400> 38

Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp
1 5 10 15

Val Leu Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln
20 25 30

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Ser Thr Phe

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

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
210 215 220

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
225 230 235 240

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
245 250 255

Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
260 265 270

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
275 280 285

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
290 295 300

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
305 310 315 320

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
325 330 335

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
340 345 350

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
355 360 365

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn

370

375

380

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
 385 390 395 400

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
 405 410 415

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
 420 425 430

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
 435 440 445

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
 450 455 460

Ser Leu Ser Pro Gly Lys
 465 470

<210> 39

<211> 470

<212> PRT

<213> Artificial

<220>

<223> amino acid sequence of humanized hA2-27D-H3_LALA

<400> 39

Met Lys His Leu Trp Phe Phe Leu Leu Leu Val Ala Ala Pro Arg Trp
 1 5 10 15

Val Leu Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln

20

25

30

Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Ser Thr Phe
 35 40 45

Ser Asn Tyr Gly Met Lys Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu
 50 55 60

Glu Trp Val Ala Ser Ile Ser Arg Ser Ser Thr Tyr Ile Tyr Tyr Ala
 65 70 75 80

Asp Thr Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
 85 90 95

Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
 100 105 110

Tyr Tyr Cys Ala Ala Ala Ile Ser Thr Pro Phe Tyr Trp Tyr Phe Asp
 115 120 125

Phe Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys
 130 135 140

Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
 145 150 155 160

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
 165 170 175

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
 180 185 190

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
195 200 205

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
210 215 220

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro
225 230 235 240

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
245 250 255

Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
260 265 270

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
275 280 285

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
290 295 300

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
305 310 315 320

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
325 330 335

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
340 345 350

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu

355		360		365
Pro Gln Val Tyr Thr Leu	Pro Pro Ser Arg Glu Glu Met Thr Lys Asn			
370	375	380		
Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile				
385	390	395		400
Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr				
	405	410		415
Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys				
	420	425		430
Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys				
435	440			445
Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu				
450	455			460
Ser Leu Ser Pro Gly Lys				
465	470			
<210>	40			
<211>	509			
<212>	PRT			
<213>	Macca mulatta			
<400>	40			
Met Val Asp Gly Val Met Ile Leu Pro Val Leu Ile Ile Ile Ala Leu				
1	5	10		15

Pro Ser Pro Ser Met Glu Asp Glu Lys Pro Lys Val Asn Pro Lys Leu
20 25 30

Tyr Met Cys Val Cys Glu Gly Leu Ser Cys Gly Asn Glu Asp His Cys
35 40 45

Glu Gly Gln Gln Cys Phe Ser Ser Leu Ser Ile Asn Asp Gly Phe His
50 55 60

Val Tyr Gln Lys Gly Cys Phe Gln Val Tyr Glu Gln Gly Lys Met Thr
65 70 75 80

Cys Lys Thr Pro Pro Ser Pro Gly Gln Ala Val Glu Cys Cys Gln Gly
85 90 95

Asp Trp Cys Asn Arg Asn Ile Thr Ala Gln Leu Pro Thr Lys Gly Lys
100 105 110

Ser Phe Pro Gly Thr Gln Asn Phe His Leu Glu Val Gly Leu Ile Ile
115 120 125

Leu Ser Val Val Phe Ala Val Cys Leu Leu Ala Cys Leu Leu Gly Val
130 135 140

Ala Leu Arg Lys Phe Lys Arg Arg Asn Gln Glu Arg Leu Asn Pro Arg
145 150 155 160

Asp Val Glu Tyr Gly Thr Ile Glu Gly Leu Ile Thr Thr Asn Val Gly
165 170 175

Asp Ser Thr Leu Ala Asp Leu Leu Asp His Ser Cys Thr Ser Gly Ser
180 185 190

Gly Ser Gly Leu Pro Phe Leu Val Gln Arg Thr Val Ala Arg Gln Ile
195 200 205

Thr Leu Leu Glu Cys Val Gly Lys Gly Arg Tyr Gly Glu Val Trp Arg
210 215 220

Gly Ser Trp Gln Gly Glu Asn Val Ala Val Lys Ile Phe Ser Ser Arg
225 230 235 240

Asp Glu Lys Ser Trp Phe Arg Glu Thr Glu Leu Tyr Asn Thr Val Met
245 250 255

Leu Arg His Glu Asn Ile Leu Gly Phe Ile Ala Ser Asp Met Thr Ser
260 265 270

Arg His Ser Ser Thr Gln Leu Trp Leu Ile Thr His Tyr His Glu Met
275 280 285

Gly Ser Leu Tyr Asp Tyr Leu Gln Leu Thr Thr Leu Asp Thr Val Ser
290 295 300

Cys Leu Arg Ile Val Leu Ser Ile Ala Ser Gly Leu Ala His Leu His
305 310 315 320

Ile Glu Ile Phe Gly Thr Gln Gly Lys Pro Ala Ile Ala His Arg Asp
325 330 335

Leu Lys Ser Lys Asn Ile Leu Val Lys Lys Asn Gly Gln Cys Cys Ile
340 345 350

Ala Asp Leu Gly Leu Ala Val Met His Ser Gln Ser Thr Asn Gln Leu
355 360 365

Asp Val Gly Asn Asn Pro Arg Val Gly Thr Lys Arg Tyr Met Ala Pro
370 375 380

Glu Val Leu Asp Glu Thr Ile Gln Val Asp Cys Phe Asp Ser Tyr Lys
385 390 395 400

Arg Val Asp Ile Trp Ala Phe Gly Leu Val Leu Trp Glu Val Ala Arg
405 410 415

Arg Met Val Ser Asn Gly Ile Val Glu Asp Tyr Lys Pro Pro Phe Tyr
420 425 430

Asp Val Val Pro Asn Asp Pro Ser Phe Glu Asp Met Arg Lys Val Val
435 440 445

Cys Val Asp Gln Gln Arg Pro Asn Ile Pro Asn Arg Trp Phe Ser Asp
450 455 460

Pro Thr Leu Thr Ser Leu Ala Lys Leu Met Lys Glu Cys Trp Tyr Gln
465 470 475 480

Asn Pro Ser Ala Arg Leu Thr Ala Leu Arg Ile Lys Lys Thr Leu Thr
485 490 495

Lys Ile Asp Asn Ser Leu Asp Lys Leu Lys Thr Asp Cys
500 505

<210> 41

<211> 509

<212> PRT

<213> Canis lupus

<400> 41

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

Pro	Ser	Pro	Ser	Met	Glu	Asp	Glu	Lys	Pro	Lys	Val	Asn	Pro	Lys	Leu
		20					25					30			

Tyr	Met	Cys	Val	Cys	Glu	Gly	Leu	Ser	Cys	Gly	Asn	Glu	Asp	His	Cys
	35					40					45				

Glu	Gly	Gln	Gln	Cys	Phe	Ser	Ser	Leu	Ser	Ile	Asn	Asp	Gly	Phe	His
	50				55					60					

Val	Tyr	Gln	Lys	Gly	Cys	Phe	Gln	Val	Tyr	Glu	Gln	Gly	Lys	Met	Thr
65				70					75					80	

Cys	Lys	Thr	Pro	Pro	Ser	Pro	Gly	Gln	Ala	Val	Glu	Cys	Cys	Gln	Gly
			85				90							95	

Asp	Trp	Cys	Asn	Arg	Asn	Ile	Thr	Ala	Gln	Leu	Pro	Thr	Lys	Gly	Lys
		100					105					110			

Ser	Phe	Pro	Glu	Thr	Gln	Asn	Phe	His	Leu	Glu	Val	Gly	Leu	Ile	Ile
	115					120					125				

Leu	Ser	Val	Val	Phe	Ala	Val	Cys	Leu	Leu	Ala	Cys	Leu	Leu	Gly	Val
	130				135					140					

Ala	Leu	Arg	Lys	Phe	Lys	Arg	Arg	Asn	Gln	Glu	Arg	Leu	Asn	Pro	Arg
-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----

145		150		155		160
Asp Val Glu Tyr Gly Thr Ile Glu Gly Leu Ile Thr Thr Asn Val Gly						
	165		170		175	
Asp Ser Thr Leu Ala Asp Leu Leu Asp His Ser Cys Thr Ser Gly Ser						
	180		185		190	
Gly Ser Gly Leu Pro Phe Leu Val Gln Arg Thr Val Ala Arg Gln Ile						
	195		200		205	
Thr Leu Leu Glu Cys Val Gly Lys Gly Arg Tyr Gly Glu Val Trp Arg						
	210		215		220	
Gly Ser Trp Gln Gly Glu Asn Val Ala Val Lys Ile Phe Ser Ser Arg						
225		230		235		240
Asp Glu Lys Ser Trp Phe Arg Glu Thr Glu Leu Tyr Asn Thr Val Met						
	245		250		255	
Leu Arg His Glu Asn Ile Leu Gly Phe Ile Ala Ser Asp Met Thr Ser						
	260		265		270	
Arg His Ser Ser Thr Gln Leu Trp Leu Ile Thr His Tyr His Glu Met						
	275		280		285	
Gly Ser Leu Tyr Asp Tyr Leu Gln Leu Thr Thr Leu Asp Thr Val Ser						
	290		295		300	
Cys Leu Arg Ile Val Leu Ser Ile Ala Ser Gly Leu Ala His Leu His						
305		310		315		320

Ile Glu Ile Phe Gly Thr Gln Gly Lys Pro Ala Ile Ala His Arg Asp
325 330 335

Leu Lys Ser Lys Asn Ile Leu Val Lys Lys Asn Gly Gln Cys Cys Ile
340 345 350

Ala Asp Leu Gly Leu Ala Val Met His Ser Gln Ser Thr Asn Gln Leu
355 360 365

Asp Val Gly Asn Asn Pro Arg Val Gly Thr Lys Arg Tyr Met Ala Pro
370 375 380

Glu Val Leu Asp Glu Thr Ile Gln Val Asp Cys Phe Asp Ser Tyr Lys
385 390 395 400

Arg Val Asp Ile Trp Ala Phe Gly Leu Val Leu Trp Glu Val Ala Arg
405 410 415

Arg Met Val Ser Asn Gly Ile Val Glu Asp Tyr Lys Pro Pro Phe Tyr
420 425 430

Asp Val Val Pro Asn Asp Pro Ser Phe Glu Asp Met Arg Lys Val Val
435 440 445

Cys Val Asp Gln Gln Arg Pro Asn Ile Pro Asn Arg Trp Phe Ser Asp
450 455 460

Pro Thr Leu Thr Ser Leu Ala Lys Leu Met Lys Glu Cys Trp Tyr Gln
465 470 475 480

Asn Pro Ser Ala Arg Leu Thr Ala Leu Arg Ile Lys Lys Thr Leu Thr

485

490

495

Lys Ile Asp Asn Ser Leu Asp Lys Leu Lys Thr Asp Cys
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<210> 42

<211> 509

<212> PRT

<213> Rattus norvegicus

<400> 42

Met Val Asp Gly Ala Met Ile Leu Ser Val Leu Met Met Met Ala Leu
 1 5 10 15

Pro Ser Pro Ser Met Glu Asp Glu Glu Pro Lys Val Asn Pro Lys Leu
 20 25 30

Tyr Met Cys Val Cys Glu Gly Leu Ser Cys Gly Asn Glu Asp His Cys
 35 40 45

Glu Gly Gln Gln Cys Phe Ser Ser Leu Ser Val Asn Asp Gly Phe Arg
 50 55 60

Val Tyr Gln Lys Gly Cys Phe Gln Val Tyr Glu Gln Gly Lys Met Thr
 65 70 75 80

Cys Lys Thr Pro Pro Ser Pro Gly Gln Ala Val Glu Cys Cys Gln Gly
 85 90 95

Asp Trp Cys Asn Arg Asn Val Thr Ala Arg Leu Pro Thr Lys Gly Lys
 100 105 110

Ser Phe Pro Gly Ser Gln Asn Phe His Leu Glu Val Gly Leu Ile Ile
115 120 125

Leu Ser Val Val Phe Ala Val Cys Leu Phe Ala Cys Ile Leu Gly Val
130 135 140

Ala Leu Arg Lys Phe Lys Arg Arg Asn Gln Glu Arg Leu Asn Pro Arg
145 150 155 160

Asp Val Glu Tyr Gly Thr Ile Glu Gly Leu Ile Thr Thr Asn Val Gly
165 170 175

Asp Ser Thr Leu Ala Glu Leu Leu Asp His Ser Cys Thr Ser Gly Ser
180 185 190

Gly Ser Gly Leu Pro Phe Leu Val Gln Arg Thr Val Ala Arg Gln Ile
195 200 205

Thr Leu Leu Glu Cys Val Gly Lys Gly Arg Tyr Gly Glu Val Trp Arg
210 215 220

Gly Ser Trp Gln Gly Glu Asn Val Ala Val Lys Ile Phe Ser Ser Arg
225 230 235 240

Asp Glu Lys Ser Trp Phe Arg Glu Thr Glu Leu Tyr Asn Thr Val Met
245 250 255

Leu Arg His Glu Asn Ile Leu Gly Phe Ile Ala Ser Asp Met Thr Ser
260 265 270

Arg His Ser Ser Thr Gln Leu Trp Leu Ile Thr His Tyr His Glu Met
275 280 285

Gly Ser Leu Tyr Asp Tyr Leu Gln Leu Thr Thr Leu Asp Thr Val Ser
290 295 300

Cys Leu Arg Ile Val Leu Ser Ile Ala Ser Gly Leu Ala His Leu His
305 310 315 320

Ile Glu Ile Phe Gly Thr Gln Gly Lys Ser Ala Ile Ala His Arg Asp
325 330 335

Leu Lys Ser Lys Asn Ile Leu Val Lys Lys Asn Gly Gln Cys Cys Ile
340 345 350

Ala Asp Leu Gly Leu Ala Val Met His Ser Gln Ser Thr Asn Gln Leu
355 360 365

Asp Val Gly Asn Asn Pro Arg Val Gly Thr Lys Arg Tyr Met Ala Pro
370 375 380

Glu Val Leu Asp Glu Thr Ile Gln Val Asp Cys Phe Asp Ser Tyr Lys
385 390 395 400

Arg Val Asp Ile Trp Ala Phe Gly Leu Val Leu Trp Glu Val Ala Arg
405 410 415

Arg Met Val Ser Asn Gly Ile Val Glu Asp Tyr Lys Pro Pro Phe Tyr
420 425 430

Asp Val Val Pro Asn Asp Pro Ser Phe Glu Asp Met Arg Lys Val Val
435 440 445

Cys Val Asp Gln Gln Arg Pro Asn Ile Pro Asn Arg Trp Phe Ser Asp
450 455 460

Pro Thr Leu Thr Ser Leu Ala Lys Leu Met Lys Glu Cys Trp Tyr Gln
465 470 475 480

Asn Pro Ser Ala Arg Leu Thr Ala Leu Arg Ile Lys Lys Thr Leu Thr
485 490 495

Lys Ile Asp Asn Ser Leu Asp Lys Leu Lys Thr Asp Cys
500 505