

SEQUENCE LISTING

<110> Bayer Pharma AG

<120> Novel antibodies against FXI and uses thereof

<130> BHC14 1 061

<160> 38

<170> PatentIn version 3.5

<210> 1

<211> 15

<212> PRT

<213> mouse

<400> 1

Lys	Ala	Ser	Gln	Ser	Val	Asp	Tyr	Asp	Gly	Asp	Ser	Tyr	Leu	Asn
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<210> 2

<211> 7

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<213> mouse

<400> 2

Ala	Ala	Ser	Asn	Leu	Glu	Ser
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<213> mouse

<400> 3

Gln	Gln	Ser	Asn	Gly	Asp	Pro
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<213> mouse

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Gly Phe Ser Leu Ser Thr Ser Gly Met Gly Val Gly
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<210> 5

<211> 12

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<213> mouse

<400> 5

His Ile Trp Trp Asp Asp Asp Lys Tyr Tyr Asn Pro
1 5 10

<210> 6

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Lys Arg Ser Ser Val Val Ala His Tyr Tyr Ala Met Asp
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<210> 7

<211> 625

<212> PRT

<213> human

<400> 7

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

Ser Gly Glu Cys Val Thr Gln Leu Leu Lys Asp Thr Cys Phe Glu Gly
20 25 30

Gly Asp Ile Thr Thr Val Phe Thr Pro Ser Ala Lys Tyr Cys Gln Val
35 40 45

Val Cys Thr Tyr His Pro Arg Cys Leu Leu Phe Thr Phe Thr Ala Glu
50 55 60

Ser Pro Ser Glu Asp Pro Thr Arg Trp Phe Thr Cys Val Leu Lys Asp
65 70 75 80

Ser Val Thr Glu Thr Leu Pro Arg Val Asn Arg Thr Ala Ala Ile Ser
85 90 95

Gly Tyr Ser Phe Lys Gln Cys Ser His Gln Ile Ser Ala Cys Asn Lys
100 105 110

Asp Ile Tyr Val Asp Leu Asp Met Lys Gly Ile Asn Tyr Asn Ser Ser
115 120 125

Val Ala Lys Ser Ala Gln Glu Cys Gln Glu Arg Cys Thr Asp Asp Val
130 135 140

His Cys His Phe Phe Thr Tyr Ala Thr Arg Gln Phe Pro Ser Leu Glu
145 150 155 160

His Arg Asn Ile Cys Leu Leu Lys His Thr Gln Thr Gly Thr Pro Thr
165 170 175

Arg Ile Thr Lys Leu Asp Lys Val Val Ser Gly Phe Ser Leu Lys Ser
180 185 190

Cys Ala Leu Ser Asn Leu Ala Cys Ile Arg Asp Ile Phe Pro Asn Thr
195 200 205

Val Phe Ala Asp Ser Asn Ile Asp Ser Val Met Ala Pro Asp Ala Phe
210 215 220

Val Cys Gly Arg Ile Cys Thr His His Pro Gly Cys Leu Phe Phe Thr
225 230 235 240

Phe Phe Ser Gln Glu Trp Pro Lys Glu Ser Gln Arg Asn Leu Cys Leu
245 250 255

Leu Lys Thr Ser Glu Ser Gly Leu Pro Ser Thr Arg Ile Lys Lys Ser

260

265

270

Lys Ala Leu Ser Gly Phe Ser Leu Gln Ser Cys Arg His Ser Ile Pro
 275 280 285

Val Phe Cys His Ser Ser Phe Tyr His Asp Thr Asp Phe Leu Gly Glu
 290 295 300

Glu Leu Asp Ile Val Ala Ala Lys Ser His Glu Ala Cys Gln Lys Leu
 305 310 315 320

Cys Thr Asn Ala Val Arg Cys Gln Phe Phe Thr Tyr Thr Pro Ala Gln
 325 330 335

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

Asn Gly Ser Pro Thr Lys Ile Leu His Gly Arg Gly Gly Ile Ser Gly
 355 360 365

Tyr Thr Leu Arg Leu Cys Lys Met Asp Asn Glu Cys Thr Thr Lys Ile
 370 375 380

Lys Pro Arg Ile Val Gly Gly Thr Ala Ser Val Arg Gly Glu Trp Pro
 385 390 395 400

Trp Gln Val Thr Leu His Thr Thr Ser Pro Thr Gln Arg His Leu Cys
 405 410 415

Gly Gly Ser Ile Ile Gly Asn Gln Trp Ile Leu Thr Ala Ala His Cys
 420 425 430

Phe Tyr Gly Val Glu Ser Pro Lys Ile Leu Arg Val Tyr Ser Gly Ile
 435 440 445

Leu Asn Gln Ser Glu Ile Lys Glu Asp Thr Ser Phe Phe Gly Val Gln
 450 455 460

Glu Ile Ile Ile His Asp Gln Tyr Lys Met Ala Glu Ser Gly Tyr Asp
465 470 475 480

Ile Ala Leu Leu Lys Leu Glu Thr Thr Val Asn Tyr Thr Asp Ser Gln
485 490 495

Arg Pro Ile Cys Leu Pro Ser Lys Gly Asp Arg Asn Val Ile Tyr Thr
500 505 510

Asp Cys Trp Val Thr Gly Trp Gly Tyr Arg Lys Leu Arg Asp Lys Ile
515 520 525

Gln Asn Thr Leu Gln Lys Ala Lys Ile Pro Leu Val Thr Asn Glu Glu
530 535 540

Cys Gln Lys Arg Tyr Arg Gly His Lys Ile Thr His Lys Met Ile Cys
545 550 555 560

Ala Gly Tyr Arg Glu Gly Gly Lys Asp Ala Cys Lys Gly Asp Ser Gly
565 570 575

Gly Pro Leu Ser Cys Lys His Asn Glu Val Trp His Leu Val Gly Ile
580 585 590

Thr Ser Trp Gly Glu Gly Cys Ala Gln Arg Glu Arg Pro Gly Val Tyr
595 600 605

Thr Asn Val Val Glu Tyr Val Asp Trp Ile Leu Glu Lys Thr Gln Ala
610 615 620

Val
625

<210> 8
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<212> PRT
<213> artificial

<220>

<223> Humanized

<400> 8

Lys Ala Ser Gln Ser Val Leu Tyr Ser Gly Asp Asn Tyr Leu Asn
1 5 10 15

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<211> 7

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<220>

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<400> 9

Ala Ala Ser Thr Leu Glu Ser
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<210> 10

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<220>

<223> humanized

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Gln Gln Tyr Asn Gly Asp Pro Trp Thr
1 5

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<211> 7

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<213> artificial

<220>

<223> humanized

<400> 11

Thr Ser Gly Met Gly Val Gly
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<213> artificial

<220>
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<400> 12

His Ile Asp Trp Asp Asp Asp Lys Tyr Tyr Ser Pro Ser Leu Lys Ser
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<210> 13
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<212> PRT
<213> artificial

<220>
<223> humanized

<400> 13

Ile Arg Ser Ser Val Tyr Ala His Tyr Tyr Gly Met Asp Tyr
1 5 10

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<220>
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<400> 14

Lys Ser Ser Gln Ser Val Leu Tyr Ser Gly Asp Asn Tyr Leu Asn
1 5 10 15

<210> 15
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<400> 15

His Ile Asp Trp Asp Asp Asp Lys Tyr Tyr Ser Thr
1 5 10

<210> 16

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<213> artificial

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<223> humanized

<400> 16

Ile Arg Ser Ser Val Tyr Ala His Tyr Tyr Gly Met Asp Val
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<210> 17

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<212> PRT

<213> artificial

<220>

<223> humanized

<400> 17

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

Glu Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Leu Tyr Ser
20 25 30

Gly Asp Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser Thr Leu Glu Ser Gly Ile Pro Asp
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65 70 75 80

Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Tyr Asn
85 90 95

Gly Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 18
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<220>
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<400> 18

Glu Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln
1 5 10 15

Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser
20 25 30

Gly Met Gly Val Gly Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu
35 40 45

Trp Leu Ala His Ile Asp Trp Asp Asp Asp Lys Tyr Tyr Ser Pro Ser
50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val
65 70 75 80

Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
85 90 95

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

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 19
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<213> artificial

<220>
<223> humanized

<400> 19

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

Glu Arg Ala Thr Ile Ser Cys Lys Ser Ser Gln Ser Val Leu Tyr Ser
20 25 30

Gly Asp Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser Thr Leu Glu Ser Gly Ile Pro Asp
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65 70 75 80

Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Tyr Asn
85 90 95

Gly Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

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<220>
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Glu Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln

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

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<220>
 <223> humanized

<400> 21

Asp	Ile	Val	Met	Thr	Gln	Ser	Pro	Asp	Ser	Leu	Ala	Val	Ser	Leu	Gly
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Glu	Arg	Ala	Thr	Ile	Ser	Cys	Lys	Ala	Ser	Gln	Ser	Val	Leu	Tyr	Ser
		20						25					30		

Gly Asp Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro

35

40

45

Lys Leu Leu Ile Tyr Ala Ala Ser Thr Leu Glu Ser Gly Ile Pro Asp
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
 65 70 75 80

Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Tyr Asn
 85 90 95

Gly Thr Pro Trp Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 100 105 110

<210> 22

<211> 124

<212> PRT

<213> artificial

<220>

<223> humanized

<400> 22

Glu Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln
 1 5 10 15

Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser
 20 25 30

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

Trp Leu Ala His Ile Asp Trp Asp Asp Asp Lys Tyr Tyr Ser Thr Ser
 50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val
 65 70 75 80

Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr

85

90

95

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

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 115 120

<210> 23
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<220>
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<400> 23

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

Glu Arg Ala Thr Ile Ser Cys Lys Ser Ser Gln Ser Val Leu Tyr Ser
 20 25 30

Ser Asn Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser Thr Leu Glu Ser Gly Ile Pro Asp
 50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
 65 70 75 80

Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Tyr Tyr
 85 90 95

Ser Thr Pro Trp Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 100 105 110

<210> 24

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<400> 24

Glu Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln
1 5 10 15

Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser
20 25 30

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

Trp Leu Ala His Ile Asp Trp Asp Asp Asp Lys Tyr Tyr Ser Thr Ser
50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val
65 70 75 80

Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
85 90 95

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

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 25
<211> 111
<212> PRT
<213> mouse

<400> 25

Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Gln Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His
65 70 75 80

Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Ser Asn
85 90 95

Gly Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 26
<211> 124
<212> PRT
<213> mouse

<400> 26

Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser Thr Ser
20 25 30

Gly Met Gly Val Gly Trp Ile Arg Gln Pro Ser Gly Lys Gly Leu Glu
35 40 45

Trp Leu Ala His Ile Trp Trp Asp Asp Asp Lys Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Gln Leu Thr Ile Ser Lys Asp Thr Ser Arg Asn Gln Val

65		70		75		80									
Phe	Leu	Lys	Ile	Thr	Ser	Val	Asp	Ala	Ala	Asp	Thr	Ala	Thr	Tyr	Tyr
			85						90					95	
Cys	Ala	Arg	Lys	Arg	Ser	Ser	Val	Val	Ala	His	Tyr	Tyr	Ala	Met	Asp
			100					105					110		
Tyr	Trp	Gly	Gln	Gly	Thr	Ser	Val	Thr	Val	Ser	Ser				
		115					120								
<210> 27															
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<400> 27															
Asp	Ile	Val	Met	Thr	Gln	Ser	Pro	Asp	Ser	Leu	Ala	Val	Ser	Leu	Gly
1				5					10					15	
Glu	Arg	Ala	Thr	Ile	Ser	Cys	Lys	Ala	Ser	Gln	Ser	Val	Leu	Tyr	Ser
			20					25					30		
Gly	Asp	Asn	Tyr	Leu	Asn	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Pro	Pro
		35					40					45			
Lys	Leu	Leu	Ile	Tyr	Ala	Ala	Ser	Thr	Leu	Glu	Ser	Gly	Ile	Pro	Asp
	50					55					60				
Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser
65					70					75				80	
Ser	Leu	Gln	Ala	Glu	Asp	Val	Ala	Val	Tyr	Tyr	Cys	Gln	Gln	Tyr	Asn
			85						90					95	
Gly	Asp	Pro	Trp	Thr	Phe	Gly	Gly	Gly	Thr	Lys	Val	Glu	Ile	Lys	Arg

100

105

110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
 115 120 125

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
 130 135 140

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
 145 150 155 160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
 165 170 175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
 180 185 190

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
 195 200 205

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
 210 215

<210> 28
 <211> 453
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<220>
 <223> humanized

<400> 28

Glu Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln
 1 5 10 15

Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser
 20 25 30

Gly Met Gly Val Gly Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu

35

40

45

Trp Leu Ala His Ile Asp Trp Asp Asp Asp Lys Tyr Tyr Ser Pro Ser
 50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val
 65 70 75 80

Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
 85 90 95

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

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
 115 120 125

Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
 130 135 140

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
 145 150 155 160

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
 165 170 175

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
 180 185 190

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
 195 200 205

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro
 210 215 220

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
 225 230 235 240

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
245 250 255

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
260 265 270

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
275 280 285

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
290 295 300

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
305 310 315 320

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
325 330 335

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
340 345 350

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
355 360 365

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
370 375 380

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
385 390 395 400

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
405 410 415

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
420 425 430

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

435

440

445

Ser Leu Ser Pro Gly
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<210> 29

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<213> artificial

<220>

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<400> 29

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

Glu Arg Ala Thr Ile Ser Cys Lys Ser Ser Gln Ser Val Leu Tyr Ser
20 25 30

Gly Asp Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser Thr Leu Glu Ser Gly Ile Pro Asp
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65 70 75 80

Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Tyr Asn
85 90 95

Gly Asp Pro Trp Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
100 105 110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
115 120 125

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

130

135

140

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
 145 150 155 160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
 165 170 175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
 180 185 190

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
 195 200 205

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
 210 215

<210> 30
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<220>
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<400> 30

Glu Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln
 1 5 10 15

Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser
 20 25 30

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

Trp Leu Ala His Ile Asp Trp Asp Asp Asp Lys Tyr Tyr Ser Thr Ser
 50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val

65		70		75		80									
Val	Leu	Thr	Met	Thr	Asn	Met	Asp	Pro	Val	Asp	Thr	Ala	Thr	Tyr	Tyr
			85						90					95	
Cys	Ala	Arg	Ile	Arg	Ser	Ser	Val	Tyr	Ala	His	Tyr	Tyr	Gly	Met	Asp
			100					105					110		
Val	Trp	Gly	Gln	Gly	Thr	Thr	Val	Thr	Val	Ser	Ser	Ala	Ser	Thr	Lys
		115					120					125			
Gly	Pro	Ser	Val	Phe	Pro	Leu	Ala	Pro	Ser	Ser	Lys	Ser	Thr	Ser	Gly
	130					135					140				
Gly	Thr	Ala	Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe	Pro	Glu	Pro
145					150					155					160
Val	Thr	Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly	Val	His	Thr
				165					170					175	
Phe	Pro	Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu	Ser	Ser	Val
			180					185					190		
Val	Thr	Val	Pro	Ser	Ser	Ser	Leu	Gly	Thr	Gln	Thr	Tyr	Ile	Cys	Asn
		195					200					205			
Val	Asn	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Lys	Lys	Val	Glu	Pro
	210					215					220				
Lys	Ser	Cys	Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys	Pro	Ala	Pro	Glu
225					230					235					240
Leu	Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys	Pro	Lys	Asp
				245					250					255	
Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val	Val	Val	Asp
			260					265					270		

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
275 280 285

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
290 295 300

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
305 310 315 320

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
325 330 335

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
340 345 350

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
355 360 365

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
370 375 380

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
385 390 395 400

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
405 410 415

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
420 425 430

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
435 440 445

Ser Leu Ser Pro Gly
450

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cagcagaaac cgggccagcc gccgaaactg ctgatttatg cggcgagcac cctggaaagc 180
ggcattccgg atcgcttttag cggcagcggc agcggcaccg attttacctt gaccattagc 240
agcctgcagg cggaagatgt ggcggtgtat tattgccagc agtataacgg cgatccgtgg 300
acctttggcg gcggcaccaa agtggaaatt aaa 333

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<223> humanized

<400> 32
gaagtgaccc tgcgcgaaaag cggcccggcg ctggtgaaac cgacccagac cctgaccctg 60
acctgcacct ttagcggctt tagcctgagc accagcggca tgggcgtggg ctggattcgc 120
cagccgccgg gcaaagcgct ggaatggctg gcgcatattg attgggatga tgataaatat 180
tatagcccga gcctgaaaag ccgcctgacc attagcaaag ataccagcaa aaaccaggtg 240
gtgctgacca tgaccaacat ggatccgggtg gataccgcga cctattattg cgcgcgcat 300
cgcagcagcg tgtatgcgca ttattatggc atggattatt ggggccaggg caccaccgtg 360
accgtgagca gc 372

<210> 33
<211> 333
<212> DNA
<213> artificial

<220>

<223> humanized

<400> 33

gatattgtga tgacccagag cccggatagc ctggcgggtga gcctgggcga acgcgcgacc	60
attagctgca aaagcagcca gagcgtgctg tatagcggcg ataactatct gaactggtat	120
cagcagaaac cgggccagcc gccgaaactg ctgatttatg cggcgagcac cctggaaagc	180
ggcattccgg atcgcttttag cggcagcggc agcggcaccg attttaccct gaccattagc	240
agcctgcagg cggaagatgt ggcggtgtat tattgccagc agtataacgg cgatccgtgg	300
acctttggcg gcggcaccaa agtggaaatt aaa	333

<210> 34

<211> 372

<212> DNA

<213> artificial

<220>

<223> humanized

<400> 34

gaagtgaccc tgcgcgaaag cggcccggcg ctggtgaaac cgacccagac cctgaccctg	60
acctgcacct ttagcggctt tagcctgagc accagcggca tgtgcgtggg ctggattcgc	120
cagccgccgg gcaaagcgct ggaatggctg gcgcatattg attgggatga tgataaatat	180
tatagcacca gcctgaaaag ccgcctgacc attagcaaag ataccagcaa aaaccaggtg	240
gtgctgacca tgaccaacat ggatccgggtg gataccgcga cctattattg cgcgcgatt	300
cgcagcagcg tgtatgcgca ttattatggc atggatgtgt ggggccaggg caccaccgtg	360
accgtgagca gc	372

<210> 35

<211> 218

<212> PRT

<213> artificial

<220>

<223> humanized

<400> 35

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

Glu Arg Ala Thr Ile Ser Cys Lys Ala Ser Gln Ser Val Leu Tyr Ser
20 25 30

Gly Asp Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser Thr Leu Glu Ser Gly Ile Pro Asp
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65 70 75 80

Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Tyr Asn
85 90 95

Gly Thr Pro Trp Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
100 105 110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
115 120 125

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
130 135 140

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145 150 155 160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
165 170 175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
180 185 190

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

195

200

205

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
 210 215

<210> 36
 <211> 453
 <212> PRT
 <213> artificial

<220>
 <223> humanized

<400> 36

Glu Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln
 1 5 10 15

Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser
 20 25 30

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

Trp Leu Ala His Ile Asp Trp Asp Asp Asp Lys Tyr Tyr Ser Thr Ser
 50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val
 65 70 75 80

Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
 85 90 95

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

Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
 115 120 125

Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly

130

135

140

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
 145 150 155 160

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
 165 170 175

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
 180 185 190

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
 195 200 205

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro
 210 215 220

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
 225 230 235 240

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
 245 250 255

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
 260 265 270

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
 275 280 285

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
 290 295 300

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
 305 310 315 320

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
 325 330 335

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
340 345 350

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
355 360 365

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
370 375 380

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
385 390 395 400

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
405 410 415

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
420 425 430

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
435 440 445

Ser Leu Ser Pro Gly
450

<210> 37
<211> 218
<212> PRT
<213> artificial

<220>
<223> humanized

<400> 37

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

Glu Arg Ala Thr Ile Ser Cys Lys Ser Ser Gln Ser Val Leu Tyr Ser
20 25 30

Ser Asn Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Ala Ala Ser Thr Leu Glu Ser Gly Ile Pro Asp
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65 70 75 80

Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Tyr Tyr
85 90 95

Ser Thr Pro Trp Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
100 105 110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
115 120 125

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
130 135 140

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145 150 155 160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
165 170 175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
180 185 190

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
195 200 205

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 38

<211> 453
<212> PRT
<213> artificial

<220>
<223> humanized

<400> 38

Glu Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln
1 5 10 15

Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Ser Thr Ser
20 25 30

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

Trp Leu Ala His Ile Asp Trp Asp Asp Asp Lys Tyr Tyr Ser Thr Ser
50 55 60

Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val
65 70 75 80

Val Leu Thr Met Thr Asn Met Asp Pro Val Asp Thr Ala Thr Tyr Tyr
85 90 95

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

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys
115 120 125

Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
130 135 140

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
145 150 155 160

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr

165

170

175

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
 180 185 190

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
 195 200 205

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro
 210 215 220

Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
 225 230 235 240

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
 245 250 255

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
 260 265 270

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
 275 280 285

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
 290 295 300

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
 305 310 315 320

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
 325 330 335

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
 340 345 350

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
 355 360 365

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
370 375 380

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
385 390 395 400

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
405 410 415

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
420 425 430

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
435 440 445

Ser Leu Ser Pro Gly
450