

SEQUENCE LISTING

<110> Juno Therapeutics, INC.

<120> CELLS EXPRESSING A CHIMERIC RECEPTOR
FROM A MODIFIED CD247 LOCUS, RELATED POLYNUCLEOTIDES AND
METHODS

<130> 735042015840

<140> Not yet assigned

<141> Concurrently herewith

<150> 62/841,578

<151> 2019-05-01

<160> 131

<170> FastSEQ for Windows Version 4.0

<210> 1

<211> 12

<212> PRT

<213> Homo sapiens

<220>

<223> spacer (IgG4hinge)

<400> 1

Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro

1

5

10

<210> 2

<211> 36

<212> DNA

<213> Homo sapiens

<220>

<223> spacer (IgG4hinge)

<400> 2

gaatctaagt acggaccgcc ctgccccct tgcctt

36

<210> 3

<211> 119

<212> PRT

<213> Homo sapiens

<220>

<223> Hinge-CH3 spacer

<400> 3

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

<210> 4

<211> 229

<212> PRT

<213> Homo sapiens

<220>

<223> Hinge-CH2-CH3 spacer

<400> 4

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

210 215 220
 Leu Ser Leu Gly Lys
 225

<210> 5
 <211> 282
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> IgD-hinge-Fc

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

<210> 6
 <211> 24

<212> PRT
<213> Artificial Sequence

<220>
<223> T2A

<400> 6
Leu Glu Gly Gly Gly Glu Gly Arg Gly Ser Leu Leu Thr Cys Gly Asp
1 5 10 15
Val Glu Glu Asn Pro Gly Pro Arg
20

<210> 7
<211> 357
<212> PRT
<213> Artificial Sequence

<220>
<223> tEGFR

<400> 7
Met Leu Leu Leu Val Thr Ser Leu Leu Leu Cys Glu Leu Pro His Pro
1 5 10 15
Ala Phe Leu Leu Ile Pro Arg Lys Val Cys Asn Gly Ile Gly Ile Gly
20 25 30
Glu Phe Lys Asp Ser Leu Ser Ile Asn Ala Thr Asn Ile Lys His Phe
35 40 45
Lys Asn Cys Thr Ser Ile Ser Gly Asp Leu His Ile Leu Pro Val Ala
50 55 60
Phe Arg Gly Asp Ser Phe Thr His Thr Pro Pro Leu Asp Pro Gln Glu
65 70 75 80
Leu Asp Ile Leu Lys Thr Val Lys Glu Ile Thr Gly Phe Leu Leu Ile
85 90 95
Gln Ala Trp Pro Glu Asn Arg Thr Asp Leu His Ala Phe Glu Asn Leu
100 105 110
Glu Ile Ile Arg Gly Arg Thr Lys Gln His Gly Gln Phe Ser Leu Ala
115 120 125
Val Val Ser Leu Asn Ile Thr Ser Leu Gly Leu Arg Ser Leu Lys Glu
130 135 140
Ile Ser Asp Gly Asp Val Ile Ile Ser Gly Asn Lys Asn Leu Cys Tyr
145 150 155 160
Ala Asn Thr Ile Asn Trp Lys Lys Leu Phe Gly Thr Ser Gly Gln Lys
165 170 175
Thr Lys Ile Ile Ser Asn Arg Gly Glu Asn Ser Cys Lys Ala Thr Gly
180 185 190
Gln Val Cys His Ala Leu Cys Ser Pro Glu Gly Cys Trp Gly Pro Glu
195 200 205
Pro Arg Asp Cys Val Ser Cys Arg Asn Val Ser Arg Gly Arg Glu Cys
210 215 220
Val Asp Lys Cys Asn Leu Leu Glu Gly Glu Pro Arg Glu Phe Val Glu
225 230 235 240
Asn Ser Glu Cys Ile Gln Cys His Pro Glu Cys Leu Pro Gln Ala Met
245 250 255

Asn	Ile	Thr	Cys	Thr	Gly	Arg	Gly	Pro	Asp	Asn	Cys	Ile	Gln	Cys	Ala
			260					265					270		
His	Tyr	Ile	Asp	Gly	Pro	His	Cys	Val	Lys	Thr	Cys	Pro	Ala	Gly	Val
		275					280					285			
Met	Gly	Glu	Asn	Asn	Thr	Leu	Val	Trp	Lys	Tyr	Ala	Asp	Ala	Gly	His
	290					295					300				
Val	Cys	His	Leu	Cys	His	Pro	Asn	Cys	Thr	Tyr	Gly	Cys	Thr	Gly	Pro
305					310					315					320
Gly	Leu	Glu	Gly	Cys	Pro	Thr	Asn	Gly	Pro	Lys	Ile	Pro	Ser	Ile	Ala
			325					330						335	
Thr	Gly	Met	Val	Gly	Ala	Leu	Leu	Leu	Leu	Leu	Val	Val	Ala	Leu	Gly
		340						345					350		
Ile	Gly	Leu	Phe	Met											
		355													

<210> 8
 <211> 27
 <212> PRT
 <213> Homo sapiens

<220>
 <223> CD28

<300>
 <308> Uniprot P10747
 <309> 1989-07-01

Phe	Trp	Val	Leu	Val	Val	Val	Gly	Gly	Val	Leu	Ala	Cys	Tyr	Ser	Leu
1				5					10					15	
Leu	Val	Thr	Val	Ala	Phe	Ile	Ile	Phe	Trp	Val					
			20					25							

<210> 9
 <211> 66
 <212> PRT
 <213> Homo sapiens

<220>
 <223> CD28

<300>
 <308> Uniprot P10747
 <309> 1989-07-01

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

Val Leu Ala Cys Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile Phe
50 55 60
Trp Val
65

<210> 10
<211> 41
<212> PRT
<213> Homo sapiens

<220>
<223> CD28

<300>
<308> Uniprot P10747
<309> 1989-07-01

<400> 10
Arg Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr
1 5 10 15
Pro Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro
20 25 30
Pro Arg Asp Phe Ala Ala Tyr Arg Ser
35 40

<210> 11
<211> 41
<212> PRT
<213> Homo sapiens

<220>
<223> CD28 (LL to GG)

<400> 11
Arg Ser Lys Arg Ser Arg Gly Gly His Ser Asp Tyr Met Asn Met Thr
1 5 10 15
Pro Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro
20 25 30
Pro Arg Asp Phe Ala Ala Tyr Arg Ser
35 40

<210> 12
<211> 42
<212> PRT
<213> Homo sapiens

<220>
<223> 4-1BB

<300>
<308> Uniprot Q07011.1

<309> 1995-02-01

<400> 12

Lys	Arg	Gly	Arg	Lys	Lys	Leu	Leu	Tyr	Ile	Phe	Lys	Gln	Pro	Phe	Met
1				5				10					15		
Arg	Pro	Val	Gln	Thr	Thr	Gln	Glu	Glu	Asp	Gly	Cys	Ser	Cys	Arg	Phe
			20					25					30		
Pro	Glu	Glu	Glu	Glu	Gly	Gly	Cys	Glu	Leu						
		35					40								

<210> 13

<211> 112

<212> PRT

<213> Homo sapiens

<220>

<223> CD3 zeta

<400> 13

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

<210> 14

<211> 112

<212> PRT

<213> hmo sapiens

<220>

<223> CD3 zeta

<400> 14

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

65					70					75					80
Arg	Arg	Gly	Lys	Gly	His	Asp	Gly	Leu	Tyr	Gln	Gly	Leu	Ser	Thr	Ala
				85					90					95	
Thr	Lys	Asp	Thr	Tyr	Asp	Ala	Leu	His	Met	Gln	Ala	Leu	Pro	Pro	Arg
			100					105					110		

<210> 15
 <211> 112
 <212> PRT
 <213> Homo sapiens

<220>
 <223> CD3 zeta

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

<210> 16
 <211> 335
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> tEGFR

<400> 16															
Arg	Lys	Val	Cys	Asn	Gly	Ile	Gly	Ile	Gly	Glu	Phe	Lys	Asp	Ser	Leu
1				5					10					15	
Ser	Ile	Asn	Ala	Thr	Asn	Ile	Lys	His	Phe	Lys	Asn	Cys	Thr	Ser	Ile
		20					25						30		
Ser	Gly	Asp	Leu	His	Ile	Leu	Pro	Val	Ala	Phe	Arg	Gly	Asp	Ser	Phe
		35					40					45			
Thr	His	Thr	Pro	Pro	Leu	Asp	Pro	Gln	Glu	Leu	Asp	Ile	Leu	Lys	Thr
	50					55					60				
Val	Lys	Glu	Ile	Thr	Gly	Phe	Leu	Leu	Ile	Gln	Ala	Trp	Pro	Glu	Asn
65					70					75					80
Arg	Thr	Asp	Leu	His	Ala	Phe	Glu	Asn	Leu	Glu	Ile	Ile	Arg	Gly	Arg
			85					90						95	
Thr	Lys	Gln	His	Gly	Gln	Phe	Ser	Leu	Ala	Val	Val	Ser	Leu	Asn	Ile

<400> 18

Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val
1 5 10 15
Glu Glu Asn Pro Gly Pro
20

<210> 19

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> P2A

<400> 19

Ala Thr Asn Phe Ser Leu Leu Lys Gln Ala Gly Asp Val Glu Glu Asn
1 5 10 15
Pro Gly Pro

<210> 20

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> E2A

<400> 20

Gln Cys Thr Asn Tyr Ala Leu Leu Lys Leu Ala Gly Asp Val Glu Ser
1 5 10 15
Asn Pro Gly Pro
20

<210> 21

<211> 22

<212> PRT

<213> Artificial Sequence

<220>

<223> F2A

<400> 21

Val Lys Gln Thr Leu Asn Phe Asp Leu Leu Lys Leu Ala Gly Asp Val
1 5 10 15
Glu Ser Asn Pro Gly Pro
20

<210> 22

<211> 10

<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<220>
<221> REPEAT
<222> (5)...(9)
<223> SGGGG is repeated 5 times

<400> 22
Pro Gly Gly Gly Ser Gly Gly Gly Gly Pro
1 5 10

<210> 23
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Linker

<400> 23
Gly Ser Ala Asp Asp Ala Lys Lys Asp Ala Ala Lys Lys Asp Gly Lys
1 5 10 15
Ser

<210> 24
<211> 66
<212> DNA
<213> Artificial Sequence

<220>
<223> GMCSFR alpha chain signal sequence

<400> 24
atgcttctcc tgggtgacaag ccttctgctc tgtgagttac cacaccagc attcctcctg 60
atccca 66

<210> 25
<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<223> GMCSFR alpha chain signal sequence

<400> 25
Met Leu Leu Leu Val Thr Ser Leu Leu Leu Cys Glu Leu Pro His Pro
1 5 10 15

Ala Phe Leu Leu Ile Pro
20

<210> 26
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> CD8 alpha signal peptide

<400> 26
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15
His Ala

<210> 27
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Hinge

<400> 27
Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro
1 5 10 15

<210> 28
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> Hinge

<400> 28
Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro
1 5 10

<210> 29
<211> 61
<212> PRT
<213> Artificial Sequence

<220>
<223> Hinge

<400> 29

Glu	Leu	Lys	Thr	Pro	Leu	Gly	Asp	Thr	His	Thr	Cys	Pro	Arg	Cys	Pro
1				5					10					15	
Glu	Pro	Lys	Ser	Cys	Asp	Thr	Pro	Pro	Pro	Cys	Pro	Arg	Cys	Pro	Glu
			20				25						30		
Pro	Lys	Ser	Cys	Asp	Thr	Pro	Pro	Pro	Cys	Pro	Arg	Cys	Pro	Glu	Pro
		35					40					45			
Lys	Ser	Cys	Asp	Thr	Pro	Pro	Pro	Cys	Pro	Arg	Cys	Pro			
	50					55					60				

<210> 30
 <211> 12
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Hinge

Glu	Ser	Lys	Tyr	Gly	Pro	Pro	Cys	Pro	Ser	Cys	Pro
1				5					10		

<210> 31
 <211> 5
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Hinge

<220>
 <221> VARIANT
 <222> (1)...(1)
 <223> Xaa is glycine, cysteine or arginine

<220>
 <221> VARIANT
 <222> (4)...(4)
 <223> Xaa is cysteine or threonine

Xaa	Pro	Pro	Xaa	Pro
1			5	

<210> 32
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Hinge

<400> 32
Tyr Gly Pro Pro Cys Pro Pro Cys Pro
1 5

<210> 33
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Hinge

<400> 33
Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro
1 5 10

<210> 34
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> Hinge

<400> 34
Glu Val Val Val Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro
1 5 10

<210> 35
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR L1

<400> 35
Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn
1 5 10

<210> 36
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR L2

<400> 36
Ser Arg Leu His Ser Gly Val

1 5

<210> 37
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR L3

<400> 37
Gly Asn Thr Leu Pro Tyr Thr Phe Gly
1 5

<210> 38
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR H1

<400> 38
Asp Tyr Gly Val Ser
1 5

<210> 39
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR H2

<400> 39
Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser
1 5 10 15

<210> 40
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR H3

<400> 40
Tyr Ala Met Asp Tyr Trp Gly
1 5

<210> 41
 <211> 120
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> VH

<400> 41
 Glu Val Lys Leu Gln Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln
 1 5 10 15
 Ser Leu Ser Val Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr
 20 25 30
 Gly Val Ser Trp Ile Arg Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu
 35 40 45
 Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys
 50 55 60
 Ser Arg Leu Thr Ile Ile Lys Asp Asn Ser Lys Ser Gln Val Phe Leu
 65 70 75 80
 Lys Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala
 85 90 95
 Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln
 100 105 110
 Gly Thr Ser Val Thr Val Ser Ser
 115 120

<210> 42
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> VL

<400> 42
 Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
 1 5 10 15
 Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
 20 25 30
 Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
 35 40 45
 Tyr His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60
 Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
 65 70 75 80
 Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
 85 90 95
 Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr
 100 105

<210> 43

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

<220>
<223> scFv

<400> 43
Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15
Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
20 25 30
Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
35 40 45
Tyr His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65 70 75 80
Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Ser Thr Ser Gly
100 105 110
Ser Gly Lys Pro Gly Ser Gly Glu Gly Ser Thr Lys Gly Glu Val Lys
115 120 125
Leu Gln Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser
130 135 140
Val Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser
145 150 155 160
Trp Ile Arg Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile
165 170 175
Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu
180 185 190
Thr Ile Ile Lys Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn
195 200 205
Ser Leu Gln Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr
210 215 220
Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
225 230 235 240
Val Thr Val Ser Ser
245

<210> 44
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR L1

<400> 44
Lys Ala Ser Gln Asn Val Gly Thr Asn Val Ala
1 5 10

<210> 45
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR L2

<400> 45
Ser Ala Thr Tyr Arg Asn Ser
1 5

<210> 46
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR L3

<400> 46
Gln Gln Tyr Asn Arg Tyr Pro Tyr Thr
1 5

<210> 47
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR H1

<400> 47
Ser Tyr Trp Met Asn
1 5

<210> 48
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR H2

<400> 48
Gln Ile Tyr Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe Lys
1 5 10 15
Gly

<210> 49
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR H3

<400> 49
Lys Thr Ile Ser Ser Val Val Asp Phe Tyr Phe Asp Tyr
1 5 10

<210> 50
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<223> VH

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

<210> 51
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> VL

<400> 51
Asp Ile Glu Leu Thr Gln Ser Pro Lys Phe Met Ser Thr Ser Val Gly
1 5 10 15
Asp Arg Val Ser Val Thr Cys Lys Ala Ser Gln Asn Val Gly Thr Asn
20 25 30

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

<210> 52
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> linker

<400> 52
 Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 1 5 10 15

<210> 53
 <211> 245
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> scFv

<400> 53
 Glu Val Lys Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ser
 1 5 10 15
 Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Tyr
 20 25 30
 Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45
 Gly Gln Ile Tyr Pro Gly Asp Gly Asp Thr Asn Tyr Asn Gly Lys Phe
 50 55 60
 Lys Gly Gln Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
 65 70 75 80
 Met Gln Leu Ser Gly Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
 85 90 95
 Ala Arg Lys Thr Ile Ser Ser Val Val Asp Phe Tyr Phe Asp Tyr Trp
 100 105 110
 Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
 115 120 125
 Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Glu Leu Thr Gln Ser
 130 135 140
 Pro Lys Phe Met Ser Thr Ser Val Gly Asp Arg Val Ser Val Thr Cys
 145 150 155 160

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

<210> 54
 <211> 12
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> HC-CDR3

<400> 54
 His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr
 1 5 10

<210> 55
 <211> 7
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> LC-CDR2

<400> 55
 His Thr Ser Arg Leu His Ser
 1 5

<210> 56
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> LC-CDR3

<400> 56
 Gln Gln Gly Asn Thr Leu Pro Tyr Thr
 1 5

<210> 57

<211> 735
<212> DNA
<213> Artificial Sequence

<220>
<223> Sequence encoding scFv

<400> 57
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gacggcaccg tcaagctgct gatctaccac accagccggc tgcacagcgg cgtgcccagc 180
cggtttagcg gcagcggctc cggcaccgac tacagccta ccatctcaa cctggaacag 240
gaagatatcg ccacctactt ttgccagcag ggcaacacac tgccctacac ctttggcggc 300
ggaacaaagc tggaaatcac cggcagcacc tccggcagcg gcaagcctgg cagcggcgag 360
ggcagcacca agggcgaggt gaagctgcag gaaagcggcc ctggcctggt ggcccccagc 420
cagagccta gcgtgacctg caccgtgagc ggcgtagacc tgcccgacta cggcgtagc 480
tggatccggc agccccccag gaagggcctg gaatggctgg gcgtgatctg gggcagcgag 540
accacctact acaacagcgc cctgaagagc cggctgacca tcatcaagga caacagcaag 600
agccaggtgt tcctgaagat gaacagcctg cagaccgacg acaccgccat ctactactgc 660
gccaagcact actactacgg cggcagctac gccatggact actggggcca gggcaccagc 720
gtgaccgtga gcagc 735

<210> 58
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<223> linker

<400> 58
Gly Ser Thr Ser Gly Ser Gly Lys Pro Gly Ser Gly Glu Gly Ser Thr
1 5 10 15
Lys Gly

<210> 59
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> CD247 (CD3z) target sequence 1

<400> 59
caccttcact ctcaggaaca 20

<210> 60
<211> 20
<212> DNA
<213> Artificial Sequence

<220>

<223> CD247 (CD3z) target sequence 2

<400> 60
gaatgacacc atagatgaag 20

<210> 61
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> CD247 (CD3z) target sequence 3

<400> 61
tgaagaggat tccatccagc 20

<210> 62
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> CD247 (CD3z) target sequence 4

<400> 62
tccagcaggt agcagagttt 20

<210> 63
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> CD247 (CD3z) target sequence + PAM 1

<400> 63
caccttcact ctcaggaaca gg 22

<210> 64
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> CD247 (CD3z) target sequence + PAM 2

<400> 64
gaatgacacc atagatgaag agg 23

<210> 65
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
 <223> CD247 (CD3z) target sequence + PAM 3

 <400> 65
 tgaagaggat tccatccagc agg 23

 <210> 66
 <211> 23
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> CD247 (CD3z) target sequence + PAM 4

 <400> 66
 tccagcaggt agcagagttt ggg 23

 <210> 67
 <211> 20
 <212> DNA
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 <220>
 <223> CD247 (CD3z) target sequence 5

 <400> 67
 agacgcccc gcgtaccagc 20

 <210> 68
 <211> 20
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> CD247 (CD3z) target sequence 6

 <400> 68
 gctgacttac gttatagagc 20

 <210> 69
 <211> 20
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> CD247 (CD3z) target sequence 7

 <400> 69
 tttcaccgcg gccatcctgc 20

 <210> 70
 <211> 20
 <212> DNA
 <213> Artificial Sequence

<220>

<223> CD247 (CD3z) target sequence 8

<400> 70

taatcggcaa ctgtgcctgc

20

<210> 71

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> CD247 (CD3z) target sequence 9

<400> 71

cggaggccta cagtgcgatt

20

<210> 72

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> CD247 (CD3z) target sequence 10

<400> 72

tggtagccac cttcactctc

20

<210> 73

<211> 164

<212> PRT

<213> Homo sapiens

<220>

<223> CD247 isoform 1 precursor protein sequence

<300>

<308> NP_932170.1

<309> 2020-03-28

<400> 73

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

Gly	Gly	Lys	Pro	Gln	Arg	Arg	Lys	Asn	Pro	Gln	Glu	Gly	Leu	Tyr	Asn
			100					105					110		
Glu	Leu	Gln	Lys	Asp	Lys	Met	Ala	Glu	Ala	Tyr	Ser	Glu	Ile	Gly	Met
		115					120					125			
Lys	Gly	Glu	Arg	Arg	Arg	Gly	Lys	Gly	His	Asp	Gly	Leu	Tyr	Gln	Gly
	130					135					140				
Leu	Ser	Thr	Ala	Thr	Lys	Asp	Thr	Tyr	Asp	Ala	Leu	His	Met	Gln	Ala
145					150					155					160
Leu	Pro	Pro	Arg												

<210> 74
 <211> 1690
 <212> DNA
 <213> Homo sapiens

<220>
 <223> CD247 isoform 1 precursor mRNA sequence

<300>
 <308> NM_198053.2
 <309> 2020-01-13

<400> 74

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gcctctttct	gagggaaagg	acaagatgaa	gtggaaggcg	cttttcaccg	cggccatcct	180
gcaggcacag	ttgccgatta	cagaggcaca	gagctttggc	ctgctggatc	ccaaactctg	240
ctacctgctg	gatggaatcc	tcttcatcta	tggtgtcatt	ctcactgcct	tgttcctgag	300
agtgaagttc	agcaggagcg	cagacgcccc	cgcgtaccag	cagggccaga	accagctcta	360
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ggaccctgag	atggggggaa	agccgcagag	aaggaagaac	cctcaggaag	gcctgtacaa	480
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ccggaggggc	aaggggcacg	atggccttta	ccagggtctc	agtacagcca	ccaaggacac	600
ctacgacgcc	cttcacatgc	aggccctgcc	ccctcgctaa	cagccagggg	atttcaccac	660
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tgagtctgtt	ttgtaaagtc	cccagagaaa	gcgcagatgc	tagcacatgc	cctaattgtc	1020
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tcacctcctt	tcaaggtaac	tgtactgggc	catgtttgtc	ctccctgggt	agagggccgg	1140
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aaaaaaaaaa						1690

<210> 75
 <211> 163
 <212> PRT
 <213> Homo sapiens

 <220>
 <223> CD247 isoform 2 precursor protein sequence

 <300>
 <308> NO_000725.1
 <309> 2020-02-20

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

<210> 76
 <211> 1687
 <212> DNA
 <213> Homo sapiens

<220>
 <223> CD247 isoform 2 precursor mRNA sequence

<400> 76
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 gcctctttct gagggaaagg acaagatgaa gtggaaggcg cttttcaccg cggccatcct 180
 gcaggcacag ttgccgatta cagaggcaca gagctttggc ctgctggatc ccaaactctg 240
 ctacctgctg gatggaatcc tcttcatcta tgggtgtcatt ctcactgcct tgttcctgag 300
 agtgaagttc agcaggagcg cagacgcccc cgcgtaccag cagggccaga accagctcta 360
 taacgagctc aatctaggac gaagagagga gtacgatgtt ttggacaaga gacgtggccg 420

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aaggccagac	ctgcagacgc	ccagattatg	agacacagga	tgaagcattt	acaacccggt	720
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aaaaaaa						1687

<210> 77

<211> 1189

<212> DNA

<213> Homo sapiens

<220>

<223> EF1alpha promoter

<300>

<308> J04617.1

<309> 1994-11-07

<400> 77

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gaattacttc	cacgcccctg	gctgcagtac	gtgattcttg	atcccagagct	tcgggttgga	360
agtgggtggg	agagttcgag	gccttgcgct	taaggagccc	cttcgcctcg	tgcttgagtt	420
gaggcctggc	ctgggcgctg	gggccgccgc	gtgcgaatct	ggtggcacct	tcgcgcctgt	480
ctcgtgctt	tcgataagtc	tctagccatt	taaaattht	gatgacctgc	tcgacgctt	540
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cacctcgatt	agttctcgag	cttttgaggt	acgtcgtctt	taggttgggg	ggaggggttt	1020
tatgcgatgg	agtttcccca	cactgagtgg	gtggagactg	aagttaggcc	agcttggcac	1080

ttgatgtaat tctccttgga atttgccctt tttgagtttg gatcttggtt cattctcaag 1140
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<210> 78
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> human HBB splice acceptor site

<400> 78
ctgacctctt ctcttcctcc cacag 25

<210> 79
<211> 13
<212> DNA
<213> Artificial Sequence

<220>
<223> Human IgG splice acceptor site

<400> 79
tttctctcca cag 13

<210> 80
<211> 600
<212> DNA
<213> Artificial Sequence

<220>
<223> 5' homology arm

<400> 80
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ccatcatttg acctattgtc tccctgtggg taggcctcag agccacacac ctcaggccag 180
gagtaccatt catccagacg tgaacatctt cccgaggctt ccagagttct tggttcacac 240
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ctcatctgct cgccttgttt ccacctccc tcccattgcc ccaggttctt tggccccaca 360
gcggccacat ctgccgttgg tgccaatagg tttccagga gctggttgag gtgggaggga 420
gggagagggt tgtgatcagg ctgaggcatg gggattggat atagtctccg tgtcatgatt 480
tatttgggtca gtcagtccta gtgccaccct ggggtaatgg ggatgtgttc tcgtcacctt 540
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<210> 81
<211> 600
<212> DNA
<213> Artificial Sequence

<220>
<223> 3' homology arm

<400> 81
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atccaggagc aaagcaagga ccagccaagt gtgtgccttg agtgggctga ggaggaggtg 180
gcagtgtctg gctgagatgg acagggtagg agggagagcc tgggtgctagg cacctccatg 240
acaagccgta caaatgtgtg cacatcagag tgtcccaggg aaggcgatgc tactggtgac 300
aaaggggctt acactcaggc agaggtcctt ctttccaagt gtgaatgaag gccatgttag 360
cctttctctt gaaaaggccc tttcctcatc tgtaactggg gagctgacca gagcgtgggt 420
ttttcacttg gtgccttgca gaccctggat ttcttcgtgg ggctggtcat ggtgtgggca 480
gagattggaa gaatttagga gtaaagggga gaatccagtc ccagtcatca cttcagtgtc 540
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<220>
<223> FKBP

<400> 82
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Lys Arg Gly Gln Thr Cys Val Val His Tyr Thr Gly Met Leu Glu Asp
20 25 30
Gly Lys Lys Met Asp Ser Ser Arg Asp Arg Asn Lys Pro Phe Lys Phe
35 40 45
Met Leu Gly Lys Gln Glu Val Ile Arg Gly Trp Glu Glu Gly Val Ala
50 55 60
Gln Met Ser Val Gly Gln Arg Ala Lys Leu Thr Ile Ser Pro Asp Tyr
65 70 75 80
Ala Tyr Gly Ala Thr Gly His Pro Gly Ile Ile Pro Pro His Ala Thr
85 90 95
Leu Val Phe Asp Val Glu Leu Leu Lys Leu Glu
100 105

<210> 83
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> FKBP12v36

<400> 83
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35 40 45
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Cys Ala Ala Xaa
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<210> 87
<211> 20
<212> RNA
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<220>
<223> CD247 (CD3z) targeting domain 1

<400> 87
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<210> 88
<211> 20
<212> RNA
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<220>
<223> CD247 (CD3z) targeting domain 2

<400> 88
gaaugacacc auagaugaag 20

<210> 89
<211> 20
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<220>
<223> CD247 (CD3z) targeting domain 3

<400> 89
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<210> 90
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<220>
<223> CD247 (CD3z) targeting domain 4

<400> 90
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<210> 91
<211> 20
<212> RNA
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<220>

<223> CD247 (CD3z) targeting domain 5

<400> 91

agacgcccc gcguaccagc

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<210> 92

<211> 20

<212> RNA

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<223> CD247 (CD3z) targeting domain 6

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<210> 93

<211> 20

<212> RNA

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<223> CD247 (CD3z) targeting domain 7

<400> 93

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<210> 94

<211> 20

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<223> CD247 (CD3z) targeting domain 8

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<210> 95

<211> 20

<212> RNA

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<220>

<223> CD247 (CD3z) targeting domain 9

<400> 95

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<210> 96

<211> 20

<212> RNA

<213> Artificial Sequence

<220>
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<400> 96
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<210> 97
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aaggcuaguc cguuaucaac uugaaaaagu ggcaccgagu cggugc 106

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cguaaucaac uugaaaaagu ggcaccgagu cggugc 96

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cguaaucaac uugaaaaagu ggcaccgagu cggugc 96

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<212> RNA
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 <210> 105
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 <220>
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 <210> 106
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 <210> 107
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 <210> 108
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 <212> RNA
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 <220>
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 aaggcuaguc cguuauca 18

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<211> 12
<212> RNA
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<220>
<223> exemplary proximal and tail domain

<400> 109
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<210> 110
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aaaugccgug uuuaucucgu caacuuguug gcgagauuuu uu 102

<210> 112
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 <213> Streptococcus mutans

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<400> 112
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 Trp Ala Val Val Thr Asp Asp Tyr Lys Val Pro Ala Lys Lys Met Lys
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 Val Leu Gly Asn Thr Asp Lys Ser His Ile Glu Lys Asn Leu Leu Gly
 35 40 45
 Ala Leu Leu Phe Asp Ser Gly Asn Thr Ala Glu Asp Arg Arg Leu Lys
 50 55 60
 Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Arg Asn Arg Ile Leu Tyr
 65 70 75 80
 Leu Gln Glu Ile Phe Ser Glu Glu Met Gly Lys Val Asp Asp Ser Phe
 85 90 95
 Phe His Arg Leu Glu Asp Ser Phe Leu Val Thr Glu Asp Lys Arg Gly
 100 105 110
 Glu Arg His Pro Ile Phe Gly Asn Leu Glu Glu Glu Val Lys Tyr His
 115 120 125
 Glu Asn Phe Pro Thr Ile Tyr His Leu Arg Gln Tyr Leu Ala Asp Asn
 130 135 140
 Pro Glu Lys Val Asp Leu Arg Leu Val Tyr Leu Ala Leu Ala His Ile
 145 150 155 160
 Ile Lys Phe Arg Gly His Phe Leu Ile Glu Gly Lys Phe Asp Thr Arg
 165 170 175
 Asn Asn Asp Val Gln Arg Leu Phe Gln Glu Phe Leu Ala Val Tyr Asp
 180 185 190
 Asn Thr Phe Glu Asn Ser Ser Leu Gln Glu Gln Asn Val Gln Val Glu
 195 200 205
 Glu Ile Leu Thr Asp Lys Ile Ser Lys Ser Ala Lys Lys Asp Arg Val
 210 215 220
 Leu Lys Leu Phe Pro Asn Glu Lys Ser Asn Gly Arg Phe Ala Glu Phe
 225 230 235 240
 Leu Lys Leu Ile Val Gly Asn Gln Ala Asp Phe Lys Lys His Phe Glu
 245 250 255
 Leu Glu Glu Lys Ala Pro Leu Gln Phe Ser Lys Asp Thr Tyr Glu Glu
 260 265 270
 Glu Leu Glu Val Leu Leu Ala Gln Ile Gly Asp Asn Tyr Ala Glu Leu
 275 280 285
 Phe Leu Ser Ala Lys Lys Leu Tyr Asp Ser Ile Leu Leu Ser Gly Ile
 290 295 300
 Leu Thr Val Thr Asp Val Gly Thr Lys Ala Pro Leu Ser Ala Ser Met
 305 310 315 320
 Ile Gln Arg Tyr Asn Glu His Gln Met Asp Leu Ala Gln Leu Lys Gln
 325 330 335
 Phe Ile Arg Gln Lys Leu Ser Asp Lys Tyr Asn Glu Val Phe Ser Asp
 340 345 350
 Val Ser Lys Asp Gly Tyr Ala Gly Tyr Ile Asp Gly Lys Thr Asn Gln

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Glu	Ala	Phe	Tyr	Lys	Tyr	Leu	Lys	Gly	Leu	Leu	Asn	Lys	Ile	Glu	Gly
	370					375					380				
Ser	Gly	Tyr	Phe	Leu	Asp	Lys	Ile	Glu	Arg	Glu	Asp	Phe	Leu	Arg	Lys
385					390					395					400
Gln	Arg	Thr	Phe	Asp	Asn	Gly	Ser	Ile	Pro	His	Gln	Ile	His	Leu	Gln
				405					410					415	
Glu	Met	Arg	Ala	Ile	Ile	Arg	Arg	Gln	Ala	Glu	Phe	Tyr	Pro	Phe	Leu
			420					425					430		
Ala	Asp	Asn	Gln	Asp	Arg	Ile	Glu	Lys	Leu	Leu	Thr	Phe	Arg	Ile	Pro
		435					440					445			
Tyr	Tyr	Val	Gly	Pro	Leu	Ala	Arg	Gly	Lys	Ser	Asp	Phe	Ala	Trp	Leu
	450					455					460				
Ser	Arg	Lys	Ser	Ala	Asp	Lys	Ile	Thr	Pro	Trp	Asn	Phe	Asp	Glu	Ile
465					470					475					480
Val	Asp	Lys	Glu	Ser	Ser	Ala	Glu	Ala	Phe	Ile	Asn	Arg	Met	Thr	Asn
				485					490					495	
Tyr	Asp	Leu	Tyr	Leu	Pro	Asn	Gln	Lys	Val	Leu	Pro	Lys	His	Ser	Leu
			500					505					510		
Leu	Tyr	Glu	Lys	Phe	Thr	Val	Tyr	Asn	Glu	Leu	Thr	Lys	Val	Lys	Tyr
		515					520					525			
Lys	Thr	Glu	Gln	Gly	Lys	Thr	Ala	Phe	Phe	Asp	Ala	Asn	Met	Lys	Gln
	530					535					540				
Glu	Ile	Phe	Asp	Gly	Val	Phe	Lys	Val	Tyr	Arg	Lys	Val	Thr	Lys	Asp
545					550					555					560
Lys	Leu	Met	Asp	Phe	Leu	Glu	Lys	Glu	Phe	Asp	Glu	Phe	Arg	Ile	Val
				565					570					575	
Asp	Leu	Thr	Gly	Leu	Asp	Lys	Glu	Asn	Lys	Val	Phe	Asn	Ala	Ser	Tyr
			580					585					590		
Gly	Thr	Tyr	His	Asp	Leu	Cys	Lys	Ile	Leu	Asp	Lys	Asp	Phe	Leu	Asp
		595					600					605			
Asn	Ser	Lys	Asn	Glu	Lys	Ile	Leu	Glu	Asp	Ile	Val	Leu	Thr	Leu	Thr
	610					615					620				
Leu	Phe	Glu	Asp	Arg	Glu	Met	Ile	Arg	Lys	Arg	Leu	Glu	Asn	Tyr	Ser
625					630					635					640
Asp	Leu	Leu	Thr	Lys	Glu	Gln	Val	Lys	Lys	Leu	Glu	Arg	Arg	His	Tyr
				645					650					655	
Thr	Gly	Trp	Gly	Arg	Leu	Ser	Ala	Glu	Leu	Ile	His	Gly	Ile	Arg	Asn
			660					665					670		
Lys	Glu	Ser	Arg	Lys	Thr	Ile	Leu	Asp	Tyr	Leu	Ile	Asp	Asp	Gly	Asn
		675					680					685			
Ser	Asn	Arg	Asn	Phe	Met	Gln	Leu	Ile	Asn	Asp	Asp	Ala	Leu	Ser	Phe
	690					695					700				
Lys	Glu	Glu	Ile	Ala	Lys	Ala	Gln	Val	Ile	Gly	Glu	Thr	Asp	Asn	Leu
705															

785					790					795					800
Glu	Asn	Ser	Gln	Leu	Gln	Asn	Asp	Arg	Leu	Phe	Leu	Tyr	Tyr	Leu	Gln
				805					810					815	
Asn	Gly	Arg	Asp	Met	Tyr	Thr	Gly	Glu	Glu	Leu	Asp	Ile	Asp	Tyr	Leu
			820					825					830		
Ser	Gln	Tyr	Asp	Ile	Asp	His	Ile	Ile	Pro	Gln	Ala	Phe	Ile	Lys	Asp
			835				840						845		
Asn	Ser	Ile	Asp	Asn	Arg	Val	Leu	Thr	Ser	Ser	Lys	Glu	Asn	Arg	Gly
	850				855						860				
Lys	Ser	Asp	Asp	Val	Pro	Ser	Lys	Asp	Val	Val	Arg	Lys	Met	Lys	Ser
865					870				875						880
Tyr	Trp	Ser	Lys	Leu	Leu	Ser	Ala	Lys	Leu	Ile	Thr	Gln	Arg	Lys	Phe
				885					890						895
Asp	Asn	Leu	Thr	Lys	Ala	Glu	Arg	Gly	Gly	Leu	Thr	Asp	Asp	Asp	Lys
			900					905					910		
Ala	Gly	Phe	Ile	Lys	Arg	Gln	Leu	Val	Glu	Thr	Arg	Gln	Ile	Thr	Lys
	915						920					925			
His	Val	Ala	Arg	Ile	Leu	Asp	Glu	Arg	Phe	Asn	Thr	Glu	Thr	Asp	Glu
	930					935					940				
Asn	Asn	Lys	Lys	Ile	Arg	Gln	Val	Lys	Ile	Val	Thr	Leu	Lys	Ser	Asn
945					950					955					960
Leu	Val	Ser	Asn	Phe	Arg	Lys	Glu	Phe	Glu	Leu	Tyr	Lys	Val	Arg	Glu
				965					970						975
Ile	Asn	Asp	Tyr	His	His	Ala	His	Asp	Ala	Tyr	Leu	Asn	Ala	Val	Ile
			980					985					990		
Gly	Lys	Ala	Leu	Leu	Gly	Val	Tyr	Pro	Gln	Leu	Glu	Pro	Glu	Phe	Val
	995						1000					1005			
Tyr	Gly	Asp	Tyr	Pro	His	Phe	His	Gly	His	Lys	Glu	Asn	Lys	Ala	Thr
	1010					1015					1020				
Ala	Lys	Lys	Phe	Phe	Tyr	Ser	Asn	Ile	Met	Asn	Phe	Phe	Lys	Lys	Asp
1025					1030					1035					1040
Asp	Val	Arg	Thr	Asp	Lys	Asn	Gly	Glu	Ile	Ile	Trp	Lys	Lys	Asp	Glu
				1045					1050					1055	
His	Ile	Ser	Asn	Ile	Lys	Lys	Val	Leu	Ser	Tyr	Pro	Gln	Val	Asn	Ile
			1060					1065					1070		
Val	Lys	Lys	Val	Glu	Glu	Gln	Thr	Gly	Gly	Phe	Ser	Lys	Glu	Ser	Ile
	1075						1080					1085			
Leu	Pro	Lys	Gly	Asn	Ser	Asp	Lys	Leu	Ile	Pro	Arg	Lys	Thr	Lys	Lys
	1090					1095					1100				
Phe	Tyr	Trp	Asp	Thr	Lys	Lys	Tyr	Gly	Gly	Phe	Asp	Ser	Pro	Ile	Val
1105					1110					1115					1120
Ala	Tyr	Ser	Ile	Leu	Val	Ile	Ala	Asp	Ile	Glu	Lys	Gly	Lys	Ser	Lys
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Lys	Leu	Lys	Thr	Val	Lys	Ala	Leu	Val	Gly	Val	Thr	Ile	Met	Glu	Lys
	1140							1145					1150		
Met	Thr	Phe	Glu	Arg	Asp	Pro	Val	Ala	Phe	Leu	Glu	Arg	Lys	Gly	Tyr
	1155						1160					1165			
Arg	Asn	Val	Gln	Glu	Glu	Asn	Ile	Ile	Lys	Leu	Pro	Lys	Tyr	Ser	Leu
	1170					1175					1180				
Phe	Lys	Leu	Glu	Asn	Gly	Arg	Lys	Arg	Leu	Leu	Ala	Ser	Ala	Arg	Glu
1185					1190					1195					1200
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				1205					1210					1215	
Leu	Tyr	His	Ala	Lys	Asn	Ile	His	Lys	Val	Asp	Glu	Pro	Lys	His	Leu

Ile	Ala	Gln	Leu	Pro	Gly	Glu	Lys	Lys	Asn	Gly	Leu	Phe	Gly	Asn	Leu	225	230	235	240
Ile	Ala	Leu	Ser	Leu	Gly	Leu	Thr	Pro	Asn	Phe	Lys	Ser	Asn	Phe	Asp	245	250	255	
Leu	Ala	Glu	Asp	Ala	Lys	Leu	Gln	Leu	Ser	Lys	Asp	Thr	Tyr	Asp	Asp	260	265	270	
Asp	Leu	Asp	Asn	Leu	Leu	Ala	Gln	Ile	Gly	Asp	Gln	Tyr	Ala	Asp	Leu	275	280	285	
Phe	Leu	Ala	Ala	Lys	Asn	Leu	Ser	Asp	Ala	Ile	Leu	Ser	Asp	Ile		290	295	300	
Leu	Arg	Val	Asn	Thr	Glu	Ile	Thr	Lys	Ala	Pro	Leu	Ser	Ala	Ser	Met	305	310	315	320
Ile	Lys	Arg	Tyr	Asp	Glu	His	His	Gln	Asp	Leu	Thr	Leu	Leu	Lys	Ala	325	330	335	
Leu	Val	Arg	Gln	Gln	Leu	Pro	Glu	Lys	Tyr	Lys	Glu	Ile	Phe	Phe	Asp	340	345	350	
Gln	Ser	Lys	Asn	Gly	Tyr	Ala	Gly	Tyr	Ile	Asp	Gly	Gly	Ala	Ser	Gln	355	360	365	
Glu	Glu	Phe	Tyr	Lys	Phe	Ile	Lys	Pro	Ile	Leu	Glu	Lys	Met	Asp	Gly	370	375	380	
Thr	Glu	Glu	Leu	Leu	Val	Lys	Leu	Asn	Arg	Glu	Asp	Leu	Leu	Arg	Lys	385	390	395	400
Gln	Arg	Thr	Phe	Asp	Asn	Gly	Ser	Ile	Pro	His	Gln	Ile	His	Leu	Gly	405	410	415	
Glu	Leu	His	Ala	Ile	Leu	Arg	Arg	Gln	Glu	Asp	Phe	Tyr	Pro	Phe	Leu	420	425	430	
Lys	Asp	Asn	Arg	Glu	Lys	Ile	Glu	Lys	Ile	Leu	Thr	Phe	Arg	Ile	Pro	435	440	445	
Tyr	Tyr	Val	Gly	Pro	Leu	Ala	Arg	Gly	Asn	Ser	Arg	Phe	Ala	Trp	Met	450	455	460	
Thr	Arg	Lys	Ser	Glu	Glu	Thr	Ile	Thr	Pro	Trp	Asn	Phe	Glu	Glu	Val	465	470	475	480
Val	Asp	Lys	Gly	Ala	Ser	Ala	Gln	Ser	Phe	Ile	Glu	Arg	Met	Thr	Asn	485	490	495	
Phe	Asp	Lys	Asn	Leu	Pro	Asn	Glu	Lys	Val	Leu	Pro	Lys	His	Ser	Leu	500	505	510	
Leu	Tyr	Glu	Tyr	Phe	Thr	Val	Tyr	Asn	Glu	Leu	Thr	Lys	Val	Lys	Tyr	515	520	525	
Val	Thr	Glu	Gly	Met	Arg	Lys	Pro	Ala	Phe	Leu	Ser	Gly	Glu	Gln	Lys	530	535	540	
Lys	Ala	Ile	Val	Asp	Leu	Leu	Phe	Lys	Thr	Asn	Arg	Lys	Val	Thr	Val	545	550	555	560
Lys	Gln	Leu	Lys	Glu	Asp	Tyr	Phe	Lys	Lys	Ile	Glu	Cys	Phe	Asp	Ser	565	570	575	
Val	Glu	Ile	Ser	Gly	Val	Glu	Asp	Arg	Phe	Asn	Ala	Ser	Leu	Gly	Thr	580	585	590	
Tyr	His	Asp	Leu	Leu	Lys	Ile	Ile	Lys	Asp	Lys	Asp	Phe	Leu	Asp	Asn	595	600	605	
Glu	Glu	Asn	Glu	Asp	Ile	Leu	Glu	Asp	Ile	Val	Leu	Thr	Leu	Thr	Leu	610	615	620	
Phe	Glu	Asp	Arg	Glu	Met	Ile	Glu	Glu	Arg	Leu	Lys	Thr	Tyr	Ala	His	625	630	635	640
Leu	Phe	Asp	Asp	Lys	Val	Met	Lys	Gln	Leu	Lys	Arg	Arg	Arg	Tyr	Thr	645	650	655	

Gly 660	Trp	Gly 665	Arg 670	Leu 675	Ser 680	Arg 685	Lys 690	Leu 695	Ile 700	Asn 705	Gly 710	Ile 715	Arg 720	Asp 725	Lys 730
Gln 675	Ser	Gly 680	Lys 685	Thr 690	Ile 695	Leu 700	Asp 705	Phe 710	Leu 715	Lys 720	Ser 725	Asp 730	Gly 735	Phe 740	Ala 745
Asn 690	Arg	Asn 695	Phe 700	Met 705	Gln 710	Leu 715	Ile 720	His 725	Asp 730	Asp 735	Ser 740	Leu 745	Thr 750	Phe 755	Lys 760
Glu 705	Asp	Ile 710	Gln 715	Lys 720	Ala 725	Gln 730	Val 735	Ser 740	Gly 745	Gln 750	Gly 755	Asp 760	Ser 765	Leu 770	His 775
Glu 715	His	Ile 720	Ala 725	Asn 730	Leu 735	Ala 740	Gly 745	Ser 750	Pro 755	Ala 760	Ile 765	Lys 770	Lys 775	Gly 780	Ile 785
Leu 725	Gln	Thr 730	Val 735	Lys 740	Val 745	Val 750	Asp 755	Glu 760	Leu 765	Val 770	Lys 775	Val 780	Met 785	Gly 790	Arg 795
His 735	Lys	Pro 740	Glu 745	Asn 750	Ile 755	Val 760	Ile 765	Glu 770	Met 775	Ala 780	Arg 785	Glu 790	Asn 795	Gln 800	Thr 805
Thr 745	Gln	Lys 750	Gly 755	Gln 760	Lys 765	Asn 770	Ser 775	Arg 780	Glu 785	Arg 790	Met 795	Lys 800	Arg 805	Ile 810	Glu 815
Glu 755	Gly	Ile 760	Lys 765	Glu 770	Leu 775	Gly 780	Ser 785	Gln 790	Ile 795	Leu 800	Lys 805	Glu 810	His 815	Pro 820	Val 825
Glu 765	Asn	Thr 770	Gln 775	Leu 780	Gln 785	Asn 790	Glu 795	Lys 800	Leu 805	Tyr 810	Leu 815	Tyr 820	Tyr 825	Leu 830	Gln 835
Asn 775	Gly	Arg 780	Asp 785	Met 790	Tyr 795	Val 800	Asp 805	Gln 810	Glu 815	Leu 820	Asp 825	Ile 830	Asn 835	Arg 840	Leu 845
Ser 785	Asp	Tyr 790	Asp 795	Val 800	Asp 805	His 810	Ile 815	Val 820	Pro 825	Gln 830	Ser 835	Phe 840	Leu 845	Lys 850	Asp 855
Asp 795	Ser	Ile 800	Asp 805	Asn 810	Lys 815	Val 820	Leu 825	Thr 830	Arg 835	Ser 840	Asp 845	Lys 850	Asn 855	Arg 860	Gly 865
Lys 805	Ser	Asp 810	Asn 815	Val 820	Pro 825	Ser 830	Glu 835	Glu 840	Val 845	Val 850	Lys 855	Lys 860	Met 865	Lys 870	Asn 875
Tyr 815	Trp	Arg 820	Gln 825	Leu 830	Leu 835	Asn 840	Ala 845	Lys 850	Leu 855	Ile 860	Thr 865	Gln 870	Arg 875	Lys 880	Phe 885
Asp 825	Asn	Leu 830	Thr 835	Lys 840	Ala 845	Glu 850	Arg 855	Gly 860	Gly 865	Leu 870	Ser 875	Glu 880	Leu 885	Asp 890	Lys 895
Ala 835	Gly	Phe 840	Ile 845	Lys 850	Arg 855	Gln 860	Leu 865	Val 870	Glu 875	Thr 880	Arg 885	Gln 890	Ile 895	Thr 900	Lys 905
His 845	Val	Ala 850	Gln 855	Ile 860	Leu 865	Asp 870	Ser 875	Arg 880	Met 885	Asn 890	Thr 895	Lys 900	Tyr 905	Asp 910	Glu 915
Asn 855	Asp	Lys 860	Leu 865	Ile 870	Arg 875	Glu 880	Val 885	Lys 890	Val 895	Ile 900	Thr 905	Leu 910	Lys 915	Ser 920	Lys 925
Leu 865	Val	Ser 870	Asp 875	Phe 880	Arg 885	Lys 890	Asp 895	Phe 900	Gln 905	Phe 910	Tyr 915	Lys 920	Val 925	Arg 930	Glu 935
Ile 875	Asn	Asn 880	Tyr 885	His 890	His 895	Ala 900	His 905	Asp 910	Ala 915	Tyr 920	Leu 925	Asn 930	Ala 935	Val 940	Val 945
Gly 885	Thr	Ala 890	Leu 895	Ile 900	Lys 905	Lys 910	Tyr 915	Pro 920	Lys 925	Leu 930	Glu 935	Ser 940	Glu 945	Phe 950	Val 955
Tyr 895	Gly	Asp 900	Tyr 905	Lys 910	Val 915	Tyr 920	Asp 925	Val 930	Arg 935	Lys 940	Met 945	Ile 950	Ala 955	Lys 960	Ser 965
Glu 905	Gln	Glu 910	Ile 915	Gly 920	Lys 925	Ala 930	Thr 935	Ala 940	Lys 945	Tyr 950	Phe 955	Phe 960	Tyr 965	Ser 970	Asn 975
Ile 915	Met	Asn 920	Phe 925	Phe 930	Lys 935	Thr 940	Glu 945	Ile 950	Thr 955	Leu 960	Ala 965	Asn 970	Gly 975	Glu 980	

Pro	Gln	Val	Asn	Ile	Val	Lys	Lys	Thr	Glu	Val	Gln	Thr	Gly	Gly	Phe
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Ser	Lys	Glu	Ser	Ile	Leu	Pro	Lys	Arg	Asn	Ser	Asp	Lys	Leu	Ile	Ala
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Arg	Lys	Lys	Asp	Trp	Asp	Pro	Lys	Lys	Tyr	Gly	Gly	Phe	Asp	Ser	Pro
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Thr	Val	Ala	Tyr	Ser	Val	Leu	Val	Val	Ala	Lys	Val	Glu	Lys	Gly	Lys
			1140						1145					1150	
Ser	Lys	Lys	Leu	Lys	Ser	Val	Lys	Glu	Leu	Leu	Gly	Ile	Thr	Ile	Met
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Glu	Arg	Ser	Ser	Phe	Glu	Lys	Asn	Pro	Ile	Asp	Phe	Leu	Glu	Ala	Lys
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Gly	Tyr	Lys	Glu	Val	Lys	Lys	Asp	Leu	Ile	Ile	Lys	Leu	Pro	Lys	Tyr
1185					1190					1195					1200
Ser	Leu	Phe	Glu	Leu	Glu	Asn	Gly	Arg	Lys	Arg	Met	Leu	Ala	Ser	Ala
				1205					1210						1215
Gly	Glu	Leu	Gln	Lys	Gly	Asn	Glu	Leu	Ala	Leu	Pro	Ser	Lys	Tyr	Val
			1220					1225						1230	
Asn	Phe	Leu	Tyr	Leu	Ala	Ser	His	Tyr	Glu	Lys	Leu	Lys	Gly	Ser	Pro
		1235					1240						1245		
Glu	Asp	Asn	Glu	Gln	Lys	Gln	Leu	Phe	Val	Glu	Gln	His	Lys	His	Tyr
	1250					1255					1260				
Leu	Asp	Glu	Ile	Ile	Glu	Gln	Ile	Ser	Glu	Phe	Ser	Lys	Arg	Val	Ile
1265					1270					1275					1280
Leu	Ala	Asp	Ala	Asn	Leu	Asp	Lys	Val	Leu	Ser	Ala	Tyr	Asn	Lys	His
				1285					1290					1295	
Arg	Asp	Lys	Pro	Ile	Arg	Glu	Gln	Ala	Glu	Asn	Ile	Ile	His	Leu	Phe
			1300					1305					1310		
Thr	Leu	Thr	Asn	Leu	Gly	Ala	Pro	Ala	Ala	Phe	Lys	Tyr	Phe	Asp	Thr
		1315					1320						1325		
Thr	Ile	Asp	Arg	Lys	Arg	Tyr	Thr	Ser	Thr	Lys	Glu	Val	Leu	Asp	Ala
	1330					1335					1340				
Thr	Leu	Ile	His	Gln	Ser	Ile	Thr	Gly	Leu	Tyr	Glu	Thr	Arg	Ile	Asp
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Leu	Ser	Gln	Leu	Gly	Gly	Asp									
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<212> PRT

<213> Streptococcus thermophilus

<220>

<223> Cas9

<400> 114

Thr	Lys	Pro	Tyr	Ser	Ile	Gly	Leu	Asp	Ile	Gly	Thr	Asn	Ser	Val	Gly
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Trp	Ala	Val	Thr	Thr	Asp	Asn	Tyr	Lys	Val	Pro	Ser	Lys	Lys	Met	Lys
			20					25					30		
Val	Leu	Gly	Asn	Thr	Ser	Lys	Lys	Tyr	Ile	Lys	Lys	Asn	Leu	Leu	Gly
	35					40						45			
Val	Leu	Leu	Phe	Asp	Ser	Gly	Ile	Thr	Ala	Glu	Gly	Arg	Arg	Leu	Lys

50	55	60			
Arg Thr Ala Arg Arg Arg Tyr Thr Arg Arg Arg Asn Arg Ile Leu Tyr					
65	70	75	80		
Leu Gln Glu Ile Phe Ser Thr Glu Met Ala Thr Leu Asp Asp Ala Phe					
	85	90	95		
Phe Gln Arg Leu Asp Asp Ser Phe Leu Val Pro Asp Asp Lys Arg Asp					
	100	105	110		
Ser Lys Tyr Pro Ile Phe Gly Asn Leu Val Glu Glu Lys Ala Tyr His					
	115	120	125		
Asp Glu Phe Pro Thr Ile Tyr His Leu Arg Lys Tyr Leu Ala Asp Ser					
	130	135	140		
Thr Lys Lys Ala Asp Leu Arg Leu Val Tyr Leu Ala Leu Ala His Met					
	145	150	155		
Ile Lys Tyr Arg Gly His Phe Leu Ile Glu Gly Glu Phe Asn Ser Lys					
	165	170	175		
Asn Asn Asp Ile Gln Lys Asn Phe Gln Asp Phe Leu Asp Thr Tyr Asn					
	180	185	190		
Ala Ile Phe Glu Ser Asp Leu Ser Leu Glu Asn Ser Lys Gln Leu Glu					
	195	200	205		
Glu Ile Val Lys Asp Lys Ile Ser Lys Leu Glu Lys Lys Asp Arg Ile					
	210	215	220		
Leu Lys Leu Phe Pro Gly Glu Lys Asn Ser Gly Ile Phe Ser Glu Phe					
	225	230	235		
Leu Lys Leu Ile Val Gly Asn Gln Ala Asp Phe Arg Lys Cys Phe Asn					
	245	250	255		
Leu Asp Glu Lys Ala Ser Leu His Phe Ser Lys Glu Ser Tyr Asp Glu					
	260	265	270		
Asp Leu Glu Thr Leu Leu Gly Tyr Ile Gly Asp Asp Tyr Ser Asp Val					
	275	280	285		
Phe Leu Lys Ala Lys Lys Leu Tyr Asp Ala Ile Leu Leu Ser Gly Phe					
	290	295	300		
Leu Thr Val Thr Asp Asn Glu Thr Glu Ala Pro Leu Ser Ser Ala Met					
	305	310	315		
Ile Lys Arg Tyr Asn Glu His Lys Glu Asp Leu Ala Leu Leu Lys Glu					
	325	330	335		
Tyr Ile Arg Asn Ile Ser Leu Lys Thr Tyr Asn Glu Val Phe Lys Asp					
	340	345	350		
Asp Thr Lys Asn Gly Tyr Ala Gly Tyr Ile Asp Gly Lys Thr Asn Gln					
	355	360	365		
Glu Asp Phe Tyr Val Tyr Leu Lys Lys Leu Leu Ala Glu Phe Glu Gly					
	370	375	380		
Ala Asp Tyr Phe Leu Glu Lys Ile Asp Arg Glu Asp Phe Leu Arg Lys					
	385	390	395		
Gln Arg Thr Phe Asp Asn Gly Ser Ile Pro Tyr Gln Ile His Leu Gln					
	405	410	415		
Glu Met Arg Ala Ile Leu Asp Lys Gln Ala Lys Phe Tyr Pro Phe Leu					
	420	425	430		
Ala Lys Asn Lys Glu Arg Ile Glu Lys Ile Leu Thr Phe Arg Ile Pro					
	435	440	445		
Tyr Tyr Val Gly Pro Leu Ala Arg Gly Asn Ser Asp Phe Ala Trp Ser					
	450	455	460		
Ile Arg Lys Arg Asn Glu Lys Ile Thr Pro Trp Asn Phe Glu Asp Val					
	465	470	475		
Ile Asp Lys Glu Ser Ser Ala Glu Ala Phe Ile Asn Arg Met Thr Ser					

				485				490					495			
Phe	Asp	Leu	Tyr	Leu	Pro	Glu	Glu	Lys	Val	Leu	Pro	Lys	His	Ser	Leu	
			500					505					510			
Leu	Tyr	Glu	Thr	Phe	Asn	Val	Tyr	Asn	Glu	Leu	Thr	Lys	Val	Arg	Phe	
		515					520					525				
Ile	Ala	Glu	Ser	Met	Arg	Asp	Tyr	Gln	Phe	Leu	Asp	Ser	Lys	Gln	Lys	
	530					535					540					
Lys	Asp	Ile	Val	Arg	Leu	Tyr	Phe	Lys	Asp	Lys	Arg	Lys	Val	Thr	Asp	
545					550				555						560	
Lys	Asp	Ile	Ile	Glu	Tyr	Leu	His	Ala	Ile	Tyr	Gly	Tyr	Asp	Gly	Ile	
				565				570						575		
Glu	Leu	Lys	Gly	Ile	Glu	Lys	Gln	Phe	Asn	Ser	Ser	Leu	Ser	Thr	Tyr	
			580					585						590		
His	Asp	Leu	Leu	Asn	Ile	Ile	Asn	Asp	Lys	Glu	Phe	Leu	Asp	Asp	Ser	
		595					600					605				
Ser	Asn	Glu	Ala	Ile	Ile	Glu	Glu	Ile	Ile	His	Thr	Leu	Thr	Ile	Phe	
	610					615					620					
Glu	Asp	Arg	Glu	Met	Ile	Lys	Gln	Arg	Leu	Ser	Lys	Phe	Glu	Asn	Ile	
625					630					635					640	
Phe	Asp	Lys	Ser	Val	Leu	Lys	Lys	Leu	Ser	Arg	Arg	His	Tyr	Thr	Gly	
				645				650							655	
Trp	Gly	Lys	Leu	Ser	Ala	Lys	Leu	Ile	Asn	Gly	Ile	Arg	Asp	Glu	Lys	
		660					665						670			
Ser	Gly	Asn	Thr	Ile	Leu	Asp	Tyr	Leu	Ile	Asp	Asp	Gly	Ile	Ser	Asn	
		675				680						685				
Arg	Asn	Phe	Met	Gln	Leu	Ile	His	Asp	Asp	Ala	Leu	Ser	Phe	Lys	Lys	
	690					695				700						
Lys	Ile	Gln	Lys	Ala	Gln	Ile	Ile	Gly	Asp	Glu	Asp	Lys	Gly	Asn	Ile	
705					710				715						720	
Lys	Glu	Val	Val	Lys	Ser	Leu	Pro	Gly	Ser	Pro	Ala	Ile	Lys	Lys	Gly	
				725				730							735	
Ile	Leu	Gln	Ser	Ile	Lys	Ile	Val	Asp	Glu	Leu	Val	Lys	Val	Met	Gly	
			740					745						750		
Gly	Arg	Lys	Pro	Glu	Ser	Ile	Val	Val	Glu	Met	Ala	Arg	Glu	Asn	Gln	
		755					760					765				
Tyr	Thr	Asn	Gln	Gly	Lys	Ser	Asn	Ser	Gln	Gln	Arg	Leu	Lys	Arg	Leu	
	770				775						780					
Glu	Lys	Ser	Leu	Lys	Glu	Leu	Gly	Ser	Lys	Ile	Leu	Lys	Glu	Asn	Ile	
785					790				795						800	
Pro	Ala	Lys	Leu	Ser	Lys	Ile	Asp	Asn	Asn	Ala	Leu	Gln	Asn	Asp	Arg	
				805				810						815		
Leu	Tyr	Leu	Tyr	Tyr	Leu	Gln	Asn	Gly	Lys	Asp	Met	Tyr	Thr	Gly	Asp	
			820					825						830		
Asp	Leu	Asp	Ile	Asp	Arg	Leu	Ser	Asn	Tyr	Asp	Ile	Asp	His	Ile	Ile	
	835						840					845				
Pro	Gln	Ala	Phe	Leu	Lys	Asp	Asn	Ser	Ile	Asp	Asn	Lys	Val	Leu	Val	
	850					855					860					
Ser	Ser	Ala	Ser	Asn	Arg	Gly	Lys	Ser	Asp	Asp	Val	Pro	Ser	Leu	Glu	
865					870					875					880	
Val	Val	Lys	Lys	Arg	Lys	Thr	Phe	Trp	Tyr	Gln	Leu	Leu	Lys	Ser	Lys	
				885				890							895	
Leu	Ile	Ser	Gln	Arg	Lys	Phe	Asp	Asn	Leu	Thr	Lys	Ala	Glu	Arg	Gly	
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Gly	Leu	Ser	Pro	Glu	Asp	Lys	Ala	Gly	Phe	Ile	Gln	Arg	Gln	Leu	Val	

	915					920					925				
Glu Thr	Arg	Gln	Ile	Thr	Lys	His	Val	Ala	Arg	Leu	Leu	Asp	Glu	Lys	
930					935					940					
Phe Asn	Asn	Lys	Lys	Asp	Glu	Asn	Asn	Arg	Ala	Val	Arg	Thr	Val	Lys	
945					950					955					
Ile Ile	Thr	Leu	Lys	Ser	Thr	Leu	Val	Ser	Gln	Phe	Arg	Lys	Asp	Phe	
965					970					975					
Glu Leu	Tyr	Lys	Val	Arg	Glu	Ile	Asn	Asp	Phe	His	His	Ala	His	Asp	
980					985					990					
Ala Tyr	Leu	Asn	Ala	Val	Val	Ala	Ser	Ala	Leu	Leu	Lys	Lys	Tyr	Pro	
995					1000					1005					
Lys Leu	Glu	Pro	Glu	Phe	Val	Tyr	Gly	Asp	Tyr	Pro	Lys	Tyr	Asn	Ser	
1010					1015					1020					
Phe Arg	Glu	Arg	Lys	Ser	Ala	Thr	Glu	Lys	Val	Tyr	Phe	Tyr	Ser	Asn	
1025					1030					1035					
Ile Met	Asn	Ile	Phe	Lys	Lys	Ser	Ile	Ser	Leu	Ala	Asp	Gly	Arg	Val	
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Ile Glu	Arg	Pro	Leu	Ile	Glu	Val	Asn	Glu	Glu	Thr	Gly	Glu	Ser	Val	
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Trp Asn	Lys	Glu	Ser	Asp	Leu	Ala	Thr	Val	Arg	Arg	Val	Leu	Ser	Tyr	
1075					1080					1085					
Pro Gln	Val	Asn	Val	Val	Lys	Lys	Val	Glu	Glu	Gln	Asn	His	Gly	Leu	
1090					1095					1100					
Asp Arg	Gly	Lys	Pro	Lys	Gly	Leu	Phe	Asn	Ala	Asn	Leu	Ser	Ser	Lys	
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Pro Lys	Pro	Asn	Ser	Asn	Glu	Asn	Leu	Val	Gly	Ala	Lys	Glu	Tyr	Leu	
1125					1130					1135					
Asp Pro	Lys	Lys	Tyr	Gly	Gly	Tyr	Ala	Gly	Ile	Ser	Asn	Ser	Phe	Thr	
1140					1145					1150					
Val Leu	Val	Lys	Gly	Thr	Ile	Glu	Lys	Gly	Ala	Lys	Lys	Lys	Ile	Thr	
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Asn Val	Leu	Glu	Phe	Gln	Gly	Ile	Ser	Ile	Leu	Asp	Arg	Ile	Asn	Tyr	
1170					1175					1180					
Arg Lys	Asp	Lys	Leu	Asn	Phe	Leu	Leu	Glu	Lys	Gly	Tyr	Lys	Asp	Ile	
1185					1190					1195					
Glu Leu	Ile	Ile	Glu	Leu	Pro	Lys	Tyr	Ser	Leu	Phe	Glu	Leu	Ser	Asp	
1205					1210					1215					
Gly Ser	Arg	Arg	Met	Leu	Ala	Ser	Ile	Leu	Ser	Thr	Asn	Asn	Lys	Arg	
1220					1225					1230					
Gly Glu	Ile	His	Lys	Gly	Asn	Gln	Ile	Phe	Leu	Ser	Gln	Lys	Phe	Val	
1235					1240					1245					
Lys Leu	Leu	Tyr	His	Ala	Lys	Arg	Ile	Ser	Asn	Thr	Ile	Asn	Glu	Asn	
1250					1255					1260					
His Arg	Lys	Tyr	Val	Glu	Asn	His	Lys	Lys	Glu	Phe	Glu	Glu	Leu	Phe	
1265					1270					1275					
Tyr Tyr	Ile	Leu	Glu	Phe	Asn	Glu	Asn	Tyr	Val	Gly	Ala	Lys	Lys	Asn	
1285					1290					1295					
Gly Lys	Leu	Leu	Asn	Ser	Ala	Phe	Gln	Ser	Trp	Gln	Asn	His	Ser	Ile	
1300					1305					1310					
Asp Glu	Leu	Cys	Ser	Ser	Phe	Ile	Gly	Pro	Thr	Gly	Ser	Glu	Arg	Lys	
1315					1320					1325					
Gly Leu	Phe	Glu	Leu	Thr	Ser	Arg	Gly	Ser	Ala	Ala	Asp	Phe	Glu	Phe	
1330					1335					1340					
Leu Gly	Val	Lys	Ile	Pro	Arg	Tyr	Arg	Asp	Tyr	Thr	Pro	Ser	Ser	Leu	

1345		1350		1355		1360									
Leu	Lys	Asp	Ala	Thr	Leu	Ile	His	Gln	Ser	Val	Thr	Gly	Leu	Tyr	Glu
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Thr	Arg	Ile	Asp	Leu	Ala	Lys	Leu	Gly	Glu	Gly					
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<220>
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Ile	Ala	Gly	Asp	Ser	Glu	Lys	Lys	Gln	Ile	Lys	Lys	Asn	Phe	Trp	Gly
		35				40						45			
Val	Arg	Leu	Phe	Asp	Glu	Gly	Gln	Thr	Ala	Ala	Asp	Arg	Arg	Met	Ala
	50				55					60					
Arg	Thr	Ala	Arg	Arg	Arg	Ile	Glu	Arg	Arg	Arg	Asn	Arg	Ile	Ser	Tyr
65				70					75					80	
Leu	Gln	Gly	Ile	Phe	Ala	Glu	Glu	Met	Ser	Lys	Thr	Asp	Ala	Asn	Phe
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Phe	Cys	Arg	Leu	Ser	Asp	Ser	Phe	Tyr	Val	Asp	Asn	Glu	Lys	Arg	Asn
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Ser	Arg	His	Pro	Phe	Phe	Ala	Thr	Ile	Glu	Glu	Glu	Val	Glu	Tyr	His
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Lys	Asn	Tyr	Pro	Thr	Ile	Tyr	His	Leu	Arg	Glu	Glu	Leu	Val	Asn	Ser
	130					135					140				
Ser	Glu	Lys	Ala	Asp	Leu	Arg	Leu	Val	Tyr	Leu	Ala	Leu	Ala	His	Ile
145				150					155					160	
Ile	Lys	Tyr	Arg	Gly	Asn	Phe	Leu	Ile	Glu	Gly	Ala	Leu	Asp	Thr	Gln
			165					170					175		
Asn	Thr	Ser	Val	Asp	Gly	Ile	Tyr	Lys	Gln	Phe	Ile	Gln	Thr	Tyr	Asn
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Gln	Val	Phe	Ala	Ser	Gly	Ile	Glu	Asp	Gly	Ser	Leu	Lys	Lys	Leu	Glu
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Asp	Asn	Lys	Asp	Val	Ala	Lys	Ile	Leu	Val	Glu	Lys	Val	Thr	Arg	Lys
	210				215					220					
Glu	Lys	Leu	Glu	Arg	Ile	Leu	Lys	Leu	Tyr	Pro	Gly	Glu	Lys	Ser	Ala
225				230					235					240	
Gly	Met	Phe	Ala	Gln	Phe	Ile	Ser	Leu	Ile	Val	Gly	Ser	Lys	Gly	Asn
			245					250					255		
Phe	Gln	Lys	Pro	Phe	Asp	Leu	Ile	Glu	Lys	Ser	Asp	Ile	Glu	Cys	Ala
			260				265						270		
Lys	Asp	Ser	Tyr	Glu	Glu	Asp	Leu	Glu	Ser	Leu	Leu	Ala	Leu	Ile	Gly
	275					280						285			
Asp	Glu	Tyr	Ala	Glu	Leu	Phe	Val	Ala	Ala	Lys	Asn	Ala	Tyr	Ser	Ala
	290					295					300				

Val	Val	Leu	Ser	Ser	Ile	Ile	Thr	Val	Ala	Glu	Thr	Glu	Thr	Asn	Ala	305	310	315	320
Lys	Leu	Ser	Ala	Ser	Met	Ile	Glu	Arg	Phe	Asp	Thr	His	Glu	Glu	Asp	325	330	335	
Leu	Gly	Glu	Leu	Lys	Ala	Phe	Ile	Lys	Leu	His	Leu	Pro	Lys	His	Tyr	340	345	350	
Glu	Glu	Ile	Phe	Ser	Asn	Thr	Glu	Lys	His	Gly	Tyr	Ala	Gly	Tyr	Ile	355	360	365	
Asp	Gly	Lys	Thr	Lys	Gln	Ala	Asp	Phe	Tyr	Lys	Tyr	Met	Lys	Met	Thr	370	375	380	
Leu	Glu	Asn	Ile	Glu	Gly	Ala	Asp	Tyr	Phe	Ile	Ala	Lys	Ile	Glu	Lys	385	390	395	400
Glu	Asn	Phe	Leu	Arg	Lys	Gln	Arg	Thr	Phe	Asp	Asn	Gly	Ala	Ile	Pro	405	410		415
His	Gln	Leu	His	Leu	Glu	Glu	Leu	Glu	Ala	Ile	Leu	His	Gln	Gln	Ala	420	425	430	
Lys	Tyr	Tyr	Pro	Phe	Leu	Lys	Glu	Asn	Tyr	Asp	Lys	Ile	Lys	Ser	Leu	435	440	445	
Val	Thr	Phe	Arg	Ile	Pro	Tyr	Phe	Val	Gly	Pro	Leu	Ala	Asn	Gly	Gln	450	455	460	
Ser	Glu	Phe	Ala	Trp	Leu	Thr	Arg	Lys	Ala	Asp	Gly	Glu	Ile	Arg	Pro	465	470	475	480
Trp	Asn	Ile	Glu	Glu	Lys	Val	Asp	Phe	Gly	Lys	Ser	Ala	Val	Asp	Phe	485	490		495
Ile	Glu	Lys	Met	Thr	Asn	Lys	Asp	Thr	Tyr	Leu	Pro	Lys	Glu	Asn	Val	500	505	510	
Leu	Pro	Lys	His	Ser	Leu	Cys	Tyr	Gln	Lys	Tyr	Leu	Val	Tyr	Asn	Glu	515	520	525	
Leu	Thr	Lys	Val	Arg	Tyr	Ile	Asn	Asp	Gln	Gly	Lys	Thr	Ser	Tyr	Phe	530	535	540	
Ser	Gly	Gln	Glu	Lys	Glu	Gln	Ile	Phe	Asn	Asp	Leu	Phe	Lys	Gln	Lys	545	550	555	560
Arg	Lys	Val	Lys	Lys	Lys	Asp	Leu	Glu	Leu	Phe	Leu	Arg	Asn	Met	Ser	565	570		575
His	Val	Glu	Ser	Pro	Thr	Ile	Glu	Gly	Leu	Glu	Asp	Ser	Phe	Asn	Ser	580	585	590	
Ser	Tyr	Ser	Thr	Tyr	His	Asp	Leu	Lys	Val	Gly	Ile	Lys	Gln	Glu		595	600	605	
Ile	Leu	Asp	Asn	Pro	Val	Asn	Thr	Glu	Met	Leu	Glu	Asn	Ile	Val	Lys	610	615	620	
Ile	Leu	Thr	Val	Phe	Glu	Asp	Lys	Arg	Met	Ile	Lys	Glu	Gln	Leu	Gln	625	630	635	640
Gln	Phe	Ser	Asp	Val	Leu	Asp	Gly	Val	Val	Leu	Lys	Lys	Leu	Glu	Arg	645	650		655
Arg	His	Tyr	Thr	Gly	Trp	Gly	Arg	Leu	Ser	Ala	Lys	Leu	Leu	Met	Gly	660	665	670	
Ile	Arg	Asp	Lys	Gln	Ser	His	Leu	Thr	Ile	Leu	Asp	Tyr	Leu	Met	Asn	675	680	685	
Asp	Asp	Gly	Leu	Asn	Arg	Asn	Leu	Met	Gln	Leu	Ile	Asn	Asp	Ser	Asn	690	695	700	
Leu	Ser	Phe	Lys	Ser	Ile	Ile	Glu	Lys	Glu	Gln	Val	Thr	Thr	Ala	Asp	705	710	715	720
Lys	Asp	Ile	Gln	Ser	Ile	Val	Ala	Asp	Leu	Ala	Gly	Ser	Pro	Ala	Ile	725	730		735

Lys	Lys	Gly	Ile	Leu	Gln	Ser	Leu	Lys	Ile	Val	Asp	Glu	Leu	Val	Ser		
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Val	Met	Gly	Tyr	Pro	Pro	Gln	Thr	Ile	Val	Val	Glu	Met	Ala	Arg	Glu		
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Asn	Gln	Thr	Thr	Gly	Lys	Gly	Lys	Asn	Asn	Ser	Arg	Pro	Arg	Tyr	Lys		
	770					775					780						
Ser	Leu	Glu	Lys	Ala	Ile	Lys	Glu	Phe	Gly	Ser	Gln	Ile	Leu	Lys	Glu		
785					790				795						800		
His	Pro	Thr	Asp	Asn	Gln	Glu	Leu	Arg	Asn	Arg	Leu	Tyr	Leu	Tyr			
			805					810						815			
Tyr	Leu	Gln	Asn	Gly	Lys	Asp	Met	Tyr	Thr	Gly	Gln	Asp	Leu	Asp	Ile		
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His	Asn	Leu	Ser	Asn	Tyr	Asp	Ile	Asp	His	Ile	Val	Pro	Gln	Ser	Phe		
		835					840					845					
Ile	Thr	Asp	Asn	Ser	Ile	Asp	Asn	Leu	Val	Leu	Thr	Ser	Ser	Ala	Gly		
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Arg	Lys	Val	Phe	Trp	Glu	Lys	Leu	Tyr	Gln	Gly	Asn	Leu	Met	Ser	Lys		
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Ile	Thr	Lys	Asn	Val	Ala	Asn	Ile	Leu	His	Gln	Arg	Phe	Asn	Tyr	Glu		
	930					935					940						
Lys	Asp	Asp	His	Gly	Asn	Thr	Met	Lys	Gln	Val	Arg	Ile	Val	Thr	Leu		
945					950					955					960		
Lys	Ser	Ala	Leu	Val	Ser	Gln	Phe	Arg	Lys	Gln	Phe	Gln	Leu	Tyr	Lys		
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Val	Arg	Asp	Val	Asn	Asp	Tyr	His	His	Ala	His	Asp	Ala	Tyr	Leu	Asn		
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		995					1000					1005					
Glu	Phe	Val	Tyr	Gly	Asp	Tyr	His	Gln	Phe	Asp	Trp	Phe	Lys	Ala	Asn		
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Lys	Ala	Thr	Ala	Lys	Lys	Gln	Phe	Tyr	Thr	Asn	Ile	Met	Leu	Phe	Phe		
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Ala	Gln	Lys	Asp	Arg	Ile	Ile	Asp	Glu	Asn	Gly	Glu	Ile	Leu	Trp	Asp		
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Lys	Lys	Tyr	Leu	Asp	Thr	Val	Lys	Lys	Val	Met	Ser	Tyr	Arg	Gln	Met		
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Asn	Ile	Val	Lys	Lys	Thr	Glu	Ile	Gln	Lys	Gly	Glu	Phe	Ser	Lys	Ala		
	1075						1080					1085					
Thr	Ile	Lys	Pro	Lys	Gly	Asn	Ser	Ser	Lys	Leu	Ile	Pro	Arg	Lys	Thr		
	1090					1095						1100					
Asn	Trp	Asp	Pro	Met	Lys	Tyr	Gly	Gly	Leu	Asp	Ser	Pro	Asn	Met	Ala		
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Tyr	Ala	Val	Val	Ile	Glu	Tyr	Ala	Lys	Gly	Lys	Asn	Lys	Leu	Val	Phe		
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Glu	Lys	Lys	Ile	Ile	Arg	Val	Thr	Ile	Met	Glu	Arg	Lys	Ala	Phe	Glu		
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Lys	Asp	Glu	Lys	Ala	Phe	Leu	Glu	Glu	Gln	Gly	Tyr	Arg	Gln	Pro	Lys		
		1155					1160					1165					

Val	Leu	Ala	Lys	Leu	Pro	Lys	Tyr	Thr	Leu	Tyr	Glu	Cys	Glu	Glu	Gly
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Arg	Arg	Arg	Met	Leu	Ala	Ser	Ala	Asn	Glu	Ala	Gln	Lys	Gly	Asn	Gln
1185					1190					1195					1200
Gln	Val	Leu	Pro	Asn	His	Leu	Val	Thr	Leu	Leu	His	His	Ala	Ala	Asn
				1205					1210						1215
Cys	Glu	Val	Ser	Asp	Gly	Lys	Ser	Leu	Asp	Tyr	Ile	Glu	Ser	Asn	Arg
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Glu	Met	Phe	Ala	Glu	Leu	Leu	Ala	His	Val	Ser	Glu	Phe	Ala	Lys	Arg
		1235					1240					1245			
Tyr	Thr	Leu	Ala	Glu	Ala	Asn	Leu	Asn	Lys	Ile	Asn	Gln	Leu	Phe	Glu
	1250					1255					1260				
Gln	Asn	Lys	Glu	Gly	Asp	Ile	Lys	Ala	Ile	Ala	Gln	Ser	Phe	Val	Asp
1265					1270					1275					1280
Leu	Met	Ala	Phe	Asn	Ala	Met	Gly	Ala	Pro	Ala	Ser	Phe	Lys	Phe	Phe
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Glu	Thr	Thr	Ile	Glu	Arg	Lys	Arg	Tyr	Asn	Asn	Leu	Lys	Glu	Leu	Leu
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Asn	Ser	Thr	Ile	Ile	Tyr	Gln	Ser	Ile	Thr	Gly	Leu	Tyr	Glu	Ser	Arg
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Lys	Arg	Leu	Asp	Asp											
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<211> 1082

<212> PRT

<213> Neisseria meningitidis

<220>

<223> Cas9

<400> 116

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			20					25					30		
Glu	Asn	Pro	Ile	Arg	Leu	Ile	Asp	Leu	Gly	Val	Arg	Val	Phe	Glu	Arg
		35					40					45			
Ala	Glu	Val	Pro	Lys	Thr	Gly	Asp	Ser	Leu	Ala	Met	Ala	Arg	Arg	Leu
		50				55					60				
Ala	Arg	Ser	Val	Arg	Arg	Leu	Thr	Arg	Arg	Arg	Ala	His	Arg	Leu	Leu
65					70					75					80
Arg	Thr	Arg	Arg	Leu	Leu	Lys	Arg	Glu	Gly	Val	Leu	Gln	Ala	Ala	Asn
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Phe	Asp	Glu	Asn	Gly	Leu	Ile	Lys	Ser	Leu	Pro	Asn	Thr	Pro	Trp	Gln
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Leu	Arg	Ala	Ala	Ala	Leu	Asp	Arg	Lys	Leu	Thr	Pro	Leu	Glu	Trp	Ser
		115					120					125			
Ala	Val	Leu	Leu	His	Leu	Ile	Lys	His	Arg	Gly	Tyr	Leu	Ser	Gln	Arg
		130				135					140				
Lys	Asn	Glu	Gly	Glu	Thr	Ala	Asp	Lys	Glu	Leu	Gly	Ala	Leu	Leu	Lys
145					150					155					160
Gly	Val	Ala	Gly	Asn	Ala	His	Ala	Leu	Gln	Thr	Gly	Asp	Phe	Arg	Thr

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

		595					600					605				
Ser	Glu	Asn	Gln	Asn	Lys	Gly	Asn	Gln	Thr	Pro	Tyr	Glu	Tyr	Phe	Asn	
	610					615					620					
Gly	Lys	Asp	Asn	Ser	Arg	Glu	Trp	Gln	Glu	Phe	Lys	Ala	Arg	Val	Glu	
625					630					635					640	
Thr	Ser	Arg	Phe	Pro	Arg	Ser	Lys	Lys	Gln	Arg	Ile	Leu	Leu	Gln	Lys	
				645					650					655		
Phe	Asp	Glu	Asp	Gly	Phe	Lys	Glu	Arg	Asn	Leu	Asn	Asp	Thr	Arg	Tyr	
			660					665					670			
Val	Asn	Arg	Phe	Leu	Cys	Gln	Phe	Val	Ala	Asp	Arg	Met	Arg	Leu	Thr	
		675					680					685				
Gly	Lys	Gly	Lys	Lys	Arg	Val	Phe	Ala	Ser	Asn	Gly	Gln	Ile	Thr	Asn	
	690				695						700					
Leu	Leu	Arg	Gly	Phe	Trp	Gly	Leu	Arg	Lys	Val	Arg	Ala	Glu	Asn	Asp	
705					710					715					720	
Arg	His	His	Ala	Leu	Asp	Ala	Val	Val	Val	Ala	Cys	Ser	Thr	Val	Ala	
			725						730					735		
Met	Gln	Gln	Lys	Ile	Thr	Arg	Phe	Val	Arg	Tyr	Lys	Glu	Met	Asn	Ala	
			740				745						750			
Phe	Asp	Gly	Lys	Thr	Ile	Asp	Lys	Glu	Thr	Gly	Glu	Val	Leu	His	Gln	
		755				760					765					
Lys	Thr	His	Phe	Pro	Gln	Pro	Trp	Glu	Phe	Phe	Ala	Gln	Glu	Val	Met	
	770				775						780					
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Asp	Thr	Leu	Glu	Lys	Leu	Arg	Thr	Leu	Leu	Ala	Glu	Lys	Leu	Ser	Ser	
				805					810					815		
Arg	Pro	Glu	Ala	Val	His	Glu	Tyr	Val	Thr	Pro	Leu	Phe	Val	Ser	Arg	
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Ala	Pro	Asn	Arg	Lys	Met	Ser	Gly	Gln	Gly	His	Met	Glu	Thr	Val	Lys	
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Ser	Ala	Lys	Arg	Leu	Asp	Glu	Gly	Val	Ser	Val	Leu	Arg	Val	Pro	Leu	
	850				855						860					
Thr	Gln	Leu	Lys	Leu	Lys	Asp	Leu	Glu	Lys	Met	Val	Asn	Arg	Glu	Arg	
865					870					875					880	
Glu	Pro	Lys	Leu	Tyr	Glu	Ala	Leu	Lys	Ala	Arg	Leu	Glu	Ala	His	Lys	
				885					890					895		
Asp	Asp	Pro	Ala	Lys	Ala	Phe	Ala	Glu	Pro	Phe	Tyr	Lys	Tyr	Asp	Lys	
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Ala	Gly	Asn	Arg	Thr	Gln	Gln	Val	Lys	Ala	Val	Arg	Val	Glu	Gln	Val	
		915					920					925				
Gln	Lys	Thr	Gly	Val	Trp	Val	Arg	Asn	His	Asn	Gly	Ile	Ala	Asp	Asn	
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Ala	Thr	Met	Val	Arg	Val	Asp	Val	Phe	Glu	Lys	Gly	Asp	Lys	Tyr	Tyr	
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Leu 290	Phe	Leu	Ala	Ala	Lys	Asn	Leu	Ser	Asp	Ala	Ile	Leu	Leu	Ser	Asp
Ile 305	Leu	Arg	Val	Asn	Thr	Glu	Ile	Thr	Lys	Ala	Pro	Leu	Ser	Ala	Ser
Met	Ile	Lys	Arg	Tyr	Asp	Glu	His	His	Gln	Asp	Leu	Thr	Leu	Leu	Lys
Ala	Leu	Val	Arg	Gln	Gln	Leu	Pro	Glu	Lys	Tyr	Lys	Glu	Ile	Phe	Phe
Asp	Gln	Ser	Lys	Asn	Gly	Tyr	Ala	Gly	Tyr	Ile	Asp	Gly	Gly	Ala	Ser
Gln	Glu	Glu	Phe	Tyr	Lys	Phe	Ile	Lys	Pro	Ile	Leu	Glu	Lys	Met	Asp
Gly 385	Thr	Glu	Glu	Leu	Leu	Val	Lys	Leu	Asn	Arg	Glu	Asp	Leu	Leu	Arg
Lys	Gln	Arg	Thr	Phe	Asp	Asn	Gly	Ser	Ile	Pro	His	Gln	Ile	His	Leu
Gly	Glu	Leu	His	Ala	Ile	Leu	Arg	Arg	Gln	Glu	Asp	Phe	Tyr	Pro	Phe
Leu	Lys	Asp	Asn	Arg	Glu	Lys	Ile	Glu	Lys	Ile	Leu	Thr	Phe	Arg	Ile
Pro	Tyr	Tyr	Val	Gly	Pro	Leu	Ala	Arg	Gly	Asn	Ser	Arg	Phe	Ala	Trp
Met 465	Thr	Arg	Lys	Ser	Glu	Glu	Thr	Ile	Thr	Pro	Trp	Asn	Phe	Glu	Glu
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Tyr	Val	Thr	Glu	Gly	Met	Arg	Lys	Pro	Ala	Phe	Leu	Ser	Gly	Glu	Gln
Lys 545	Lys	Ala	Ile	Val	Asp	Leu	Leu	Phe	Lys	Thr	Asn	Arg	Lys	Val	Thr
Val	Lys	Gln	Leu	Lys	Glu	Asp	Tyr	Phe	Lys	Lys	Ile	Glu	Cys	Phe	Asp
Ser	Val	Glu	Ile	Ser	Gly	Val	Glu	Asp	Arg	Phe	Asn	Ala	Ser	Leu	Gly
Thr	Tyr	His	Asp	Leu	Leu	Lys	Ile	Ile	Lys	Asp	Lys	Asp	Phe	Leu	Asp
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Leu 625	Phe	Glu	Asp	Arg	Glu	Met	Ile	Glu	Glu	Arg	Leu	Lys	Thr	Tyr	Ala
His	Leu	Phe	Asp	Asp	Lys	Val	Met	Lys	Gln	Leu	Lys	Arg	Arg	Arg	Tyr
Thr	Gly	Trp	Gly	Arg	Leu	Ser	Arg	Lys	Leu	Ile	Asn	Gly	Ile	Arg	Asp
Lys	Gln	Ser	Gly	Lys	Thr	Ile	Leu	Asp	Phe	Leu	Lys	Ser	Asp	Gly	Phe
Ala	Asn	Arg	Asn	Phe	Met	Gln	Leu	Ile	His	Asp	Asp	Ser	Leu	Thr	Phe
Lys 705	Glu	Asp	Ile	Gln	Lys	Ala	Gln	Val	Ser	Gly	Gln	Gly	Asp	Ser	Leu

His	Glu	His	Ile	Ala	Asn	Leu	Ala	Gly	Ser	Pro	Ala	Ile	Lys	Lys	Gly	725	730	735
Ile	Leu	Gln	Thr	Val	Lys	Val	Val	Asp	Glu	Leu	Val	Lys	Val	Met	Gly	740	745	750
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Glu	Glu	Gly	Ile	Lys	Glu	Leu	Gly	Ser	Gln	Ile	Leu	Lys	Glu	His	Pro	785	790	795
Val	Glu	Asn	Thr	Gln	Leu	Gln	Asn	Glu	Lys	Leu	Tyr	Leu	Tyr	Tyr	Leu	805	810	815
Gln	Asn	Gly	Arg	Asp	Met	Tyr	Val	Asp	Gln	Glu	Leu	Asp	Ile	Asn	Arg	820	825	830
Leu	Ser	Asp	Tyr	Asp	Val	Asp	His	Ile	Val	Pro	Gln	Ser	Phe	Leu	Lys	835	840	845
Asp	Asp	Ser	Ile	Asp	Asn	Lys	Val	Leu	Thr	Arg	Ser	Asp	Lys	Asn	Arg	850	855	860
Gly	Lys	Ser	Asp	Asn	Val	Pro	Ser	Glu	Glu	Val	Val	Lys	Lys	Met	Lys	865	870	875
Asn	Tyr	Trp	Arg	Gln	Leu	Leu	Asn	Ala	Lys	Leu	Ile	Thr	Gln	Arg	Lys	885	890	895
Phe	Asp	Asn	Leu	Thr	Lys	Ala	Glu	Arg	Gly	Gly	Leu	Ser	Glu	Leu	Asp	900	905	910
Lys	Ala	Gly	Phe	Ile	Lys	Arg	Gln	Leu	Val	Glu	Thr	Arg	Gln	Ile	Thr	915	920	925
Lys	His	Val	Ala	Gln	Ile	Leu	Asp	Ser	Arg	Met	Asn	Thr	Lys	Tyr	Asp	930	935	940
Glu	Asn	Asp	Lys	Leu	Ile	Arg	Glu	Val	Lys	Val	Ile	Thr	Leu	Lys	Ser	945	950	955
Lys	Leu	Val	Ser	Asp	Phe	Arg	Lys	Asp	Phe	Gln	Phe	Tyr	Lys	Val	Arg	965	970	975
Glu	Ile	Asn	Asn	Tyr	His	His	Ala	His	Asp	Ala	Tyr	Leu	Asn	Ala	Val	980	985	990
Val	Gly	Thr	Ala	Leu	Ile	Lys	Lys	Tyr	Pro	Lys	Leu	Glu	Ser	Glu	Phe	995	1000	1005
Val	Tyr	Gly	Asp	Tyr	Lys	Val	Tyr	Asp	Val	Arg	Lys	Met	Ile	Ala	Lys	1010	1015	1020
Ser	Glu	Gln	Glu	Ile	Gly	Lys	Ala	Thr	Ala	Lys	Tyr	Phe	Phe	Tyr	Ser	1025	1030	1035
Asn	Ile	Met	Asn	Phe	Phe	Lys	Thr	Glu	Ile	Thr	Leu	Ala	Asn	Gly	Glu	1045	1050	1055
Ile	Arg	Lys	Arg	Pro	Leu	Ile	Glu	Thr	Asn	Gly	Glu	Thr	Gly	Glu	Ile	1060	1065	1070
Val	Trp	Asp	Lys	Gly	Arg	Asp	Phe	Ala	Thr	Val	Arg	Lys	Val	Leu	Ser	1075	1080	1085
Met	Pro	Gln	Val	Asn	Ile	Val	Lys	Lys	Thr	Glu	Val	Gln	Thr	Gly	Gly	1090	1095	1100
Phe	Ser	Lys	Glu	Ser	Ile	Leu	Pro	Lys	Arg	Asn	Ser	Asp	Lys	Leu	Ile	1105	1110	1115
Ala	Arg	Lys	Lys	Asp	Trp	Asp	Pro	Lys	Lys	Tyr	Gly	Gly	Phe	Asp	Ser	1125	1130	1135
Pro	Thr	Val	Ala	Tyr	Ser	Val	Leu	Val	Val	Ala	Lys	Val	Glu	Lys	Gly	1140	1145	1150

Lys Ser Lys Lys Leu Lys Ser Val Lys Glu Leu Leu Gly Ile Thr Ile
 1155 1160 1165
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 Lys Gly Tyr Lys Glu Val Lys Lys Asp Leu Ile Ile Lys Leu Pro Lys
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 Tyr Ser Leu Phe Glu Leu Glu Asn Gly Arg Lys Arg Met Leu Ala Ser
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 Ala Gly Glu Leu Gln Lys Gly Asn Glu Leu Ala Leu Pro Ser Lys Tyr
 1220 1225 1230
 Val Asn Phe Leu Tyr Leu Ala Ser His Tyr Glu Lys Leu Lys Gly Ser
 1235 1240 1245
 Pro Glu Asp Asn Glu Gln Lys Gln Leu Phe Val Glu Gln His Lys His
 1250 1255 1260
 Tyr Leu Asp Glu Ile Ile Glu Gln Ile Ser Glu Phe Ser Lys Arg Val
 1265 1270 1275 1280
 Ile Leu Ala Asp Ala Asn Leu Asp Lys Val Leu Ser Ala Tyr Asn Lys
 1285 1290 1295
 His Arg Asp Lys Pro Ile Arg Glu Gln Ala Glu Asn Ile Ile His Leu
 1300 1305 1310
 Phe Thr Leu Thr Asn Leu Gly Ala Pro Ala Ala Phe Lys Tyr Phe Asp
 1315 1320 1325
 Thr Thr Ile Asp Arg Lys Arg Tyr Thr Ser Thr Lys Glu Val Leu Asp
 1330 1335 1340
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 Asp Leu Ser Gln Leu Gly Gly Asp
 1365

<210> 118

<211> 1205

<212> DNA

<213> Artificial Sequence

<220>

<223> EF1alpha promoter

<400> 118

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<210> 119

<211> 544

<212> DNA

<213> Artificial Sequence

<220>

<223> Ef1alpha promoter with HTLV1 enhancer

<400> 119

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actgggaaag tgatgtcgtg tactggctcc gcctttttcc cgagggtggg ggagaaccgt 180
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ctac                                           544

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<210> 120

<211> 66

<212> DNA

<213> Artificial Sequence

<220>

<223> P2A nucleotide sequence

<400> 120

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<210> 121

<211> 4107

<212> DNA

<213> streptococcus pyogenes

<220>

<223> Cas9 codon optimized nucleic acid sequence

<400> 121

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gccacaagggt tgaagcggac cgccaggagg cggatatacca ggagaaaagaa ccgcatatgc 240
tacctgcaag aaatcttcag taacgagatg gcaaagggtg acgatagctt tttccatcgc 300
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cccgccgcct tcaaatactt tgatacgact atcgaccgga aacggtatac cagtaccaa 4020
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<210> 122

<211> 1368

<212> PRT

<213> streptococcus pyogenes

<220>

<223> Cas9

<400> 122

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

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625															

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Leu	Ser	Asp	Tyr	Asp	Val	Asp	His	Ile	Val	Pro	Gln	Ser	Phe	Leu	Lys
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<211> 3249

<212> DNA

<213> Neisseria meningitidis

<220>

<223> Cas9 codon optimized nucleic acid sequence

<400> 123

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<210> 124

<211> 1082

<212> PRT

<213> Neisseria meningitidis

<220>

<223> Cas9

<400> 124

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<211> 1053

<212> PRT

<213> staphylococcus aureus

<220>

<223> Cas9

<400> 126

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Asp	Ile	Lys	Glu	Trp	Tyr	Glu	Met	Leu	Met	Gly	His	Cys	Thr	Tyr	Phe
225					230					235					240
Pro	Glu	Glu	Leu	Arg	Ser	Val	Lys	Tyr	Ala	Tyr	Asn	Ala	Asp	Leu	Tyr
				245					250					255	
Asn	Ala	Leu	Asn	Asp	Leu	Asn	Asn	Leu	Val	Ile	Thr	Arg	Asp	Glu	Asn
			260					265					270		
Glu	Lys	Leu	Glu	Tyr	Tyr	Glu	Lys	Phe	Gln	Ile	Ile	Glu	Asn	Val	Phe
	275						280					285			
Lys	Gln	Lys	Lys	Lys	Pro	Thr	Leu	Lys	Gln	Ile	Ala	Lys	Glu	Ile	Leu
	290					295					300				
Val	Asn	Glu	Glu	Asp	Ile	Lys	Gly	Tyr	Arg	Val	Thr	Ser	Thr	Gly	Lys
305					310					315					320
Pro	Glu	Phe	Thr	Asn	Leu	Lys	Val	Tyr	His	Asp	Ile	Lys	Asp	Ile	Thr
				325					330					335	
Ala	Arg	Lys	Glu	Ile	Ile	Glu	Asn	Ala	Glu	Leu	Leu	Asp	Gln	Ile	Ala
			340					345					350		
Lys	Ile	Leu	Thr	Ile	Tyr	Gln	Ser	Ser	Glu	Asp	Ile	Gln	Glu	Glu	Leu
	355						360					365			
Thr	Asn	Leu	Asn	Ser	Glu	Leu	Thr	Gln	Glu	Glu	Ile	Glu	Gln	Ile	Ser
	370					375					380				
Asn	Leu	Lys	Gly	Tyr	Thr	Gly	Thr	His	Asn	Leu	Ser	Leu	Lys	Ala	Ile
385					390				395						400
Asn	Leu	Ile	Leu	Asp	Glu	Leu	Trp	His	Thr	Asn	Asp	Asn	Gln	Ile	Ala
				405					410					415	
Ile	Phe	Asn	Arg	Leu	Lys	Leu	Val	Pro	Lys	Lys	Val	Asp	Leu	Ser	Gln
			420					425					430		
Gln	Lys	Glu	Ile	Pro	Thr	Thr	Leu	Val	Asp	Asp	Phe	Ile	Leu	Ser	Pro
	435						440					445			
Val	Val	Lys	Arg	Ser	Phe	Ile	Gln	Ser	Ile	Lys	Val	Ile	Asn	Ala	Ile
	450					455					460				
Ile	Lys	Lys	Tyr	Gly	Leu	Pro	Asn	Asp	Ile	Ile	Ile	Glu	Leu	Ala	Arg
465					470					475					480
Glu	Lys	Asn	Ser	Lys	Asp	Ala	Gln	Lys	Met	Ile	Asn	Glu	Met	Gln	Lys
				485					490					495	
Arg	Asn	Arg	Gln	Thr	Asn	Glu	Arg	Ile	Glu	Glu	Ile	Ile	Arg	Thr	Thr

			500				505				510				
Gly	Lys	Glu	Asn	Ala	Lys	Tyr	Leu	Ile	Glu	Lys	Ile	Lys	Leu	His	Asp
			515				520				525				
Met	Gln	Glu	Gly	Lys	Cys	Leu	Tyr	Ser	Leu	Glu	Ala	Ile	Pro	Leu	Glu
			530				535				540				
Asp	Leu	Leu	Asn	Asn	Pro	Phe	Asn	Tyr	Glu	Val	Asp	His	Ile	Ile	Pro
545			550				555				560				
Arg	Ser	Val	Ser	Phe	Asp	Asn	Ser	Phe	Asn	Asn	Lys	Val	Leu	Val	Lys
			565				570				575				
Gln	Glu	Glu	Asn	Ser	Lys	Lys	Gly	Asn	Arg	Thr	Pro	Phe	Gln	Tyr	Leu
			580				585				590				
Ser	Ser	Ser	Asp	Ser	Lys	Ile	Ser	Tyr	Glu	Thr	Phe	Lys	Lys	His	Ile
			595				600				605				
Leu	Asn	Leu	Ala	Lys	Gly	Lys	Gly	Arg	Ile	Ser	Lys	Thr	Lys	Lys	Glu
610			615				620								
Tyr	Leu	Leu	Glu	Glu	Arg	Asp	Ile	Asn	Arg	Phe	Ser	Val	Gln	Lys	Asp
625			630				635				640				
Phe	Ile	Asn	Arg	Asn	Leu	Val	Asp	Thr	Arg	Tyr	Ala	Thr	Arg	Gly	Leu
			645				650				655				
Met	Asn	Leu	Leu	Arg	Ser	Tyr	Phe	Arg	Val	Asn	Asn	Leu	Asp	Val	Lys
			660				665				670				
Val	Lys	Ser	Ile	Asn	Gly	Gly	Phe	Thr	Ser	Phe	Leu	Arg	Arg	Lys	Trp
675			680				685								
Lys	Phe	Lys	Lys	Glu	Arg	Asn	Lys	Gly	Tyr	Lys	His	His	Ala	Glu	Asp
690			695				700								
Ala	Leu	Ile	Ile	Ala	Asn	Ala	Asp	Phe	Ile	Phe	Lys	Glu	Trp	Lys	Lys
705			710				715				720				
Leu	Asp	Lys	Ala	Lys	Lys	Val	Met	Glu	Asn	Gln	Met	Phe	Glu	Glu	Lys
			725				730				735				
Gln	Ala	Glu	Ser	Met	Pro	Glu	Ile	Glu	Thr	Glu	Gln	Glu	Tyr	Lys	Glu
740			745				750								
Ile	Phe	Ile	Thr	Pro	His	Gln	Ile	Lys	His	Ile	Lys	Asp	Phe	Lys	Asp
755			760				765								
Tyr	Lys	Tyr	Ser	His	Arg	Val	Asp	Lys	Lys	Pro	Asn	Arg	Glu	Leu	Ile
770			775				780								
Asn	Asp	Thr	Leu	Tyr	Ser	Thr	Arg	Lys	Asp	Asp	Lys	Gly	Asn	Thr	Leu
785			790				795				800				
Ile	Val	Asn	Asn	Leu	Asn	Gly	Leu	Tyr	Asp	Lys	Asp	Asn	Asp	Lys	Leu
			805				810				815				
Lys	Lys	Leu	Ile	Asn	Lys	Ser	Pro	Glu	Lys	Leu	Leu	Met	Tyr	His	His
820			825				830								
Asp	Pro	Gln	Thr	Tyr	Gln	Lys	Leu	Lys	Leu	Ile	Met	Glu	Gln	Tyr	Gly
835			840				845								
Asp	Glu	Lys	Asn	Pro	Leu	Tyr	Lys	Tyr	Tyr	Glu	Glu	Thr	Gly	Asn	Tyr
850			855				860								
Leu	Thr	Lys	Tyr	Ser	Lys	Lys	Asp	Asn	Gly	Pro	Val	Ile	Lys	Lys	Ile
865			870				875				880				
Lys	Tyr	Tyr	Gly	Asn	Lys	Leu	Asn	Ala	His	Leu	Asp	Ile	Thr	Asp	Asp
			885				890				895				
Tyr	Pro	Asn	Ser	Arg	Asn	Lys	Val	Val	Lys	Leu	Ser	Leu	Lys	Pro	Tyr
900			905				910								
Arg	Phe	Asp	Val	Tyr	Leu	Asp	Asn	Gly	Val	Tyr	Lys	Phe	Val	Thr	Val
915			920				925								
Lys	Asn	Leu	Asp	Val	Ile	Lys	Lys	Glu	Asn	Tyr	Tyr	Glu	Val	Asn	Ser

930		935		940
Lys Cys Tyr Glu Glu Ala Lys Lys Leu Lys Lys Ile Ser Asn Gln Ala				
945		950		955
Glu Phe Ile Ala Ser Phe Tyr Asn Asn Asp Leu Ile Lys Ile Asn Gly				
	965		970	975
Glu Leu Tyr Arg Val Ile Gly Val Asn Asn Asp Leu Leu Asn Arg Ile				
	980		985	990
Glu Val Asn Met Ile Asp Ile Thr Tyr Arg Glu Tyr Leu Glu Asn Met				
	995		1000	1005
Asn Asp Lys Arg Pro Pro Arg Ile Ile Lys Thr Ile Ala Ser Lys Thr				
	1010		1015	1020
Gln Ser Ile Lys Lys Tyr Ser Thr Asp Ile Leu Gly Asn Leu Tyr Glu				
1025		1030		1035
Val Lys Ser Lys Lys His Pro Gln Ile Ile Lys Lys Gly				1040
	1045		1050	

<210> 127

<211> 326

<212> PRT

<213> Homo sapiens

<220>

<223> Human IgG2 Fc

<300>

<308> Uniprot P01859

<309> 2008-12-16

<400> 127

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

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

<210> 128

<211> 327

<212> PRT

<213> Homo sapiens

<220>

<223> Human IgG4 Fc

<300>

<308> Uniprot P01861

<309> 1986-07-21

<400> 128

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

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

<210> 129

<211> 228

<212> PRT

<213> Artificial Sequence

<220>

<223> Spacer

<400> 129

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

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

<210> 130
 <211> 133
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> SV40 poly A signal

<400> 130
 tgctttatatt gtgaaatttg tgatgctatt gctttatattg taaccattat aagctgcaat 60
 aaacaagtta acaacaacaa ttgcattcat tttatgtttc aggttcaggg ggaggtgtgg 120
 gaggtttttt aaa 133

<210> 131
 <211> 347
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> MND promoter

<400> 131
 gaacagagaa acaggagaat atgggccaac caggatatct gtggtaagca gttcctgccc 60
 cggctcaggg ccaagaacag ttggaacagc agaatatggg ccaaacagga tatctgtggg 120
 aagcagttcc tgccccggct cagggccaag aacagatggg cccagatgc ggtcccgccc 180
 tcagcagttt ctagagaacc atcagatggt tccagggtgc cccaaggacc tgaaatgacc 240
 ctgtgcctta tttgaactaa ccaatcagtt cgcttctcgc ttctgttcgc gcgcttctgc 300
 tccccgagct ctatataagc agagctcgtt tagtgaaccg tcagatc 347