

SEQUENCE LISTING

<110> Autolus Ltd
 5 <120> Chimeric Cytokine Receptor
 <130> P000575SG2
 10 <150> GB1514875.2
 <151> 2015-08-20
 <160> 55
 <170> PatentIn version 3.5
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 30 Val Thr Glu Tyr His Gly Asn Phe Ser Ala Trp Ser Gly Val Ser Lys
 20 25 30
 35 Gly Leu Ala Glu Ser Leu Gln Pro Asp Tyr Ser Glu Arg Leu Cys Leu
 35 40 45
 40 Val Ser Glu Ile Pro Pro Lys Gly Gly Ala Leu Gly Glu Gly Pro Gly
 50 55 60
 Ala Ser Pro Cys Asn Gln His Ser Pro Tyr Trp Ala Pro Pro Cys Tyr
 65 70 75 80
 45 Thr Leu Lys Pro Glu Thr
 85
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				20					25					30			
5	Gly	Asp	Val	Gln	Lys	Trp	Leu	Ser	Ser	Pro	Phe	Pro	Ser	Ser	Ser	Phe	
			35					40					45				
10	Ser	Pro	Gly	Gly	Leu	Ala	Pro	Glu	Ile	Ser	Pro	Leu	Glu	Val	Leu	Glu	
		50					55					60					
15	Arg	Asp	Lys	Val	Thr	Gln	Leu	Leu	Leu	Gln	Gln	Asp	Lys	Val	Pro	Glu	
	65					70					75					80	
20	Pro	Ala	Ser	Leu	Ser	Ser	Asn	His	Ser	Leu	Thr	Ser	Cys	Phe	Thr	Asn	
					85					90					95		
25	Gln	Gly	Tyr	Phe	Phe	Phe	His	Leu	Pro	Asp	Ala	Leu	Glu	Ile	Glu	Ala	
				100					105					110			
30	Cys	Gln	Val	Tyr	Phe	Thr	Tyr	Asp	Pro	Tyr	Ser	Glu	Glu	Asp	Pro	Asp	
			115					120					125				
35	Glu	Gly	Val	Ala	Gly	Ala	Pro	Thr	Gly	Ser	Ser	Pro	Gln	Pro	Leu	Gln	
		130					135					140					
40	Pro	Leu	Ser	Gly	Glu	Asp	Asp	Ala	Tyr	Cys	Thr	Phe	Pro	Ser	Arg	Asp	
	145					150					155					160	
45	Asp	Leu	Leu	Leu	Phe	Ser	Pro	Ser	Leu	Leu	Gly	Gly	Pro	Ser	Pro	Pro	
					165					170					175		
50	Ser	Thr	Ala	Pro	Gly	Gly	Ser	Gly	Ala	Gly	Glu	Glu	Arg	Met	Pro	Pro	
				180					185					190			
55	Ser	Leu	Gln	Glu	Arg	Val	Pro	Arg	Asp	Trp	Asp	Pro	Gln	Pro	Leu	Gly	
			195					200					205				
60	Pro	Pro	Thr	Pro	Gly	Val	Pro	Asp	Leu	Val	Asp	Phe	Gln	Pro	Pro	Pro	
		210					215					220					
65	Glu	Leu	Val	Leu	Arg	Glu	Ala	Gly	Glu	Glu	Val	Pro	Asp	Ala	Gly	Pro	
	225					230					235					240	
70	Arg	Glu	Gly	Val	Ser	Phe	Pro	Trp	Ser	Arg	Pro	Pro	Gly	Gln	Gly	Glu	
					245					250					255		
75	Phe	Arg	Ala	Leu	Asn	Ala	Arg	Leu	Pro	Leu	Asn	Thr	Asp	Ala	Tyr	Leu	

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

	180	185	190
5	Gln Asn Gln		
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	<223> hinge-CH2CH3 of human IgG1		
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	Ala Glu Pro Lys Ser Pro Asp Lys Thr His Thr Cys Pro Pro Cys Pro		
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	Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro		
	20 25 30		
25	Lys Asp Thr Leu Met Ile Ala Arg Thr Pro Glu Val Thr Cys Val Val		
	35 40 45		
30	Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val		
	50 55 60		
35	Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln		
	65 70 75 80		
	Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln		
40	85 90 95		
	Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala		
	100 105 110		
45	Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro		
	115 120 125		
50	Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr		
	130 135 140		
55	Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser		
	145 150 155 160		
	Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr		
60	165 170 175		
	Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr		

	180	185	190
5	Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe		
	195	200	205
10	Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys		
	210	215	220
15	Ser Leu Ser Leu Ser Pro Gly Lys Lys Asp		
	225	230	
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25	<220>		
	<223> human CD8 stalk		
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30	Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala		
	1 5 10 15		
35	Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly		
	20 25 30		
40	Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile		
	35 40 45		
45	<210> 6		
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	<223> human IgG1 hinge		
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55	Ala Glu Pro Lys Ser Pro Asp Lys Thr His Thr Cys Pro Pro Cys Pro		
	1 5 10 15		
60	Lys Asp Pro Lys		
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70	<220>		
	<223> transmembrane derived from human common gamma chain		

<400> 7

5 Val Val Ile Ser Val Gly Ser Met Gly Leu Ile Ile Ser Leu Leu Cys
1 5 10 15

10 Val Tyr Phe Trp Leu
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15 <213> Artificial Sequence

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<223> transmembrane derived from human IL-2Rbeta

20 <400> 8

Ile Pro Trp Leu Gly His Leu Leu Val Gly Leu Ser Gly Ala Phe Gly
1 5 10 15

25 Phe Ile Ile Leu Val Tyr Leu Leu Ile
20 25

30 <210> 9
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35 <220>
<223> transmembrane derived from human IL-7Ralpha

<400> 9

40 Pro Ile Leu Leu Thr Ile Ser Ile Leu Ser Phe Phe Ser Val Ala Leu
1 5 10 15

45 Leu Val Ile Leu Ala Cys Val Leu Trp
20 25

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Ala Ile Ser Thr Ser Thr Val Leu Leu Cys Gly Leu Ser Ala Val Ser
1 5 10 15

60 Leu Leu Ala Cys Tyr Leu

20

5 <210> 11
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 10 <220>
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 15 Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
 1 5 10 15

 Ser Val Lys Ile Ser Cys Lys Val Ser Gly Tyr Ala Ile Ser Ser Ser
 20 20 25 30

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

 25 Gly Arg Ile Tyr Pro Gly Asp Gly Asp Thr Lys Tyr Asn Gly Lys Phe
 50 55 60

 30 Lys Asp Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
 65 70 75 80

 35 Met Gln Leu Ser Ser Leu Thr Ser Val Asp Ser Ala Val Tyr Phe Cys
 85 90 95

 40 Ala Arg Asp Gly Tyr Arg Tyr Tyr Phe Asp Tyr Trp Gly Gln Gly Thr
 100 105 110

 Ser Val Thr Val Ser Ser
 115

 45 <210> 12
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 50 <220>
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 55 Asp Ile Val Met Thr Gln Thr Ala Pro Ser Val Phe Val Thr Pro Gly
 1 5 10 15

 60 Glu Ser Val Ser Ile Ser Cys Arg Ser Ser Lys Ser Leu Leu His Ser
 20 25 30

Asn Gly Asn Thr Tyr Leu Tyr Trp Phe Leu Gln Arg Pro Gly Gln Ser
 35 40 45
 5 Pro Gln Leu Leu Ile Tyr Arg Met Ser Asn Leu Ala Ser Gly Val Pro
 50 55 60
 10 Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Arg Ile
 65 70 75 80
 15 Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln His
 85 90 95
 20 Leu Glu Tyr Pro Val Thr Phe Gly Ala Gly Thr Lys Val Glu Ile Lys
 100 105 110
 25 <210> 13
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 Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Lys Pro Gly Ala
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 35 Ser Val Lys Met Ser Cys Lys Thr Ser Gly Tyr Ser Phe Ser Ser Tyr
 20 25 30
 40 Trp Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45
 45 Gly Tyr Ile Asn Pro Ser Thr Gly Tyr Thr Glu Asn Asn Gln Lys Phe
 50 55 60
 50 Lys Asp Lys Val Thr Leu Thr Ala Asp Lys Ser Ser Asn Thr Ala Tyr
 65 70 75 80
 55 Met Gln Leu Asn Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
 85 90 95
 60 Ala Arg Ser Gly Arg Leu Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr
 100 105 110
 Val Thr Val Ser Ser
 115

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 10 <400> 14

 Asp Ile Val Leu Thr Gln Ser Pro Pro Ser Leu Ala Val Ser Leu Gly
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 15 Gln Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser Ile Asp Leu Tyr
 20 20 25 30
 20 Gly Phe Thr Phe Met His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
 35 40 45
 25 Lys Ile Leu Ile Tyr Arg Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
 50 55 60
 30 Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Asn
 65 70 75 80
 Pro Val Glu Ala Asp Asp Val Ala Thr Tyr Tyr Cys Gln Gln Thr His
 85 90 95
 35 Glu Asp Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 100 105 110
 40 <210> 15
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 <223> ScFv based on 5D5A5
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 1 5 10 15
 55 Ser Val Lys Met Ser Cys Lys Thr Ser Gly Tyr Ser Phe Ser Ser Tyr
 20 25 30
 Trp Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45
 60 Gly Tyr Ile Asn Pro Ser Thr Gly Tyr Thr Glu Asn Asn Gln Lys Phe

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

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

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

Met Val Gly Leu Ile Leu Pro Gly Ile Val Ile Leu Ser Cys Tyr Cys
 210 215 220

5

Ile Ile Ile Ser Lys Leu Ser His Ser Lys Gly His Gln Lys Arg Lys
 225 230 235 240

10

Ala Leu Lys Thr Thr Val Ile Leu Ile Leu Ala Phe Phe Ala Cys Trp
 245 250 255

15

Leu Pro Tyr Tyr Ile Gly Ile Ser Ile Asp Ser Phe Ile Leu Leu Glu
 260 265 270

20

Ile Ile Lys Gln Gly Cys Glu Phe Glu Asn Thr Val His Lys Trp Ile
 275 280 285

25

Ser Ile Thr Glu Ala Leu Ala Phe Phe His Cys Cys Leu Asn Pro Ile
 290 295 300

30

Leu Tyr Ala Phe Leu Gly Ala Lys Phe Lys Thr Ser Ala Gln His Ala
 305 310 315 320

35

Leu Thr Ser Val Ser Arg Gly Ser Ser Leu Lys Ile Leu Ser Lys Gly
 325 330 335

40

Lys Arg Gly Gly His Ser Ser Val Ser Thr Glu Ser Glu Ser Ser Ser
 340 345 350

Phe His Ser Ser
 355

45

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

<220>
 <223> sequence of cell surface receptor CCR2

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<400> 18

Met Leu Ser Thr Ser Arg Ser Arg Phe Ile Arg Asn Thr Asn Glu Ser
 1 5 10 15

55

Gly Glu Glu Val Thr Thr Phe Phe Asp Tyr Asp Tyr Gly Ala Pro Cys
 20 25 30

60

His Lys Phe Asp Val Lys Gln Ile Gly Ala Gln Leu Leu Pro Pro Leu
 35 40 45

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

	290	295	300
5	Tyr 305	Ala Phe Val Gly Glu 310	Lys Phe Arg Ser Leu 315
10	Gly Cys Arg Ile Ala 325	Pro Leu Gln Lys Pro 330	Val Cys Gly Gly Pro 335
15	Val Arg Pro Gly 340	Lys Asn Val Lys Val 345	Thr Thr Gln Gly Leu 350
20	Gly Arg Gly Lys Gly Lys Ser 355	Ile Gly Arg Ala Pro 360	Glu Ala Ser Leu 365
25	Gln Asp Lys Glu Gly Ala 370		
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45	Gly Ile Lys Ala Phe Gly 35	Glu Leu Phe Leu 40	Pro Pro Leu Tyr Ser Leu 45
50	Val Phe Val Phe Gly 50	Leu Leu Gly Asn Ser 55	Val Val Val Leu Val Leu 60
55	Phe Lys Tyr Lys Arg 65	Leu Arg Ser Met Thr 70	Asp Val Tyr Leu Leu Asn 75
60	Leu Ala Ile Ser Asp 85	Leu Leu Phe Val Phe 90	Ser Leu Pro Phe Trp Gly 95
	Tyr Tyr Ala Ala Asp 100	Gln Trp Val Phe Gly 105	Leu Gly Leu Cys Lys Met 110
	Ile Ser Trp Met Tyr Leu Val Gly Phe Tyr Ser Gly Ile Phe Phe Val		

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 10 <400> 20

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

Gln Ser Glu Asp Leu Ala Asp Tyr Phe Cys Gln Gln Tyr Asn Ser Tyr
 210 215 220

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 Pro Leu Thr Phe Gly Ala Gly Thr Met Leu Asp Leu Lys Arg
 225 230 235

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 1 5 10 15

25 Asp His Ala Asp Gly
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30 <210> 22
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35 <220>
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40 Met Ser Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
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45 His Ala Ala Arg Pro
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50 <210> 23
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55 <220>
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60 Met Ala Val Pro Thr Gln Val Leu Gly Leu Leu Leu Leu Trp Leu Thr
 1 5 10 15

60 Asp Ala Arg Cys
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10  <400>  24

    Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly
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15  Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr
    20          25          30

20  Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys
    35          40          45

25  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

30  Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala
    85          90          95

35  Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
    100         105         110

40  <210>  25
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45  <220>
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    <400>  25

50  Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met Asn Met Thr Pro
    1          5          10          15

    Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro Tyr Ala Pro Pro
    20          25          30

    Arg Asp Phe Ala Ala Tyr Arg Ser Arg Val Lys Phe Ser Arg Ser Ala
    35          40          45

60  Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu

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

	100	105	110
5	Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys 115 120 125		
10	Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala 130 135 140		
15	Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys 145 150 155 160		
20	Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr 165 170 175		
25	Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg 180 185		
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45	Leu Thr Asp Val Thr Leu 35		
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55	Gln Arg Arg Lys Tyr Arg Ser Asn Lys Gly Glu Ser Pro Val Glu Pro 1 5 10 15		
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Ile Pro Ile Gln Glu Asp Tyr Arg Lys Pro Glu Pro Ala Cys Ser Pro
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 1 5 10 15

20
 Glu Ile Asn Leu Val Asp Ala His Leu Lys Ser Glu Gln Thr Glu Ala
 20 25 30

25
 Ser Thr Arg Gln Asn Ser Gln Val Leu Leu Ser Glu Thr Gly Ile Tyr
 35 40 45

30
 Asp Asn Asp Pro Asp Leu Cys Phe Arg Met Gln Glu Gly Ser Glu Val
 50 55 60

35
 Tyr Ser Asn Pro Cys Leu Glu Glu Asn Lys Pro Gly Ile Val Tyr Ala
 65 70 75 80

40
 Val Lys Glu Ala Pro Thr Glu Tyr Ala Ser Ile Cys Val Arg Ser
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45
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50
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 His Arg Arg Ala Cys Arg Lys Arg Ile Arg Gln Lys Leu His Leu Cys
 1 5 10 15

60
 Tyr Pro Val Gln Thr Ser Gln Pro Lys Leu Glu Leu Val Asp Ser Arg
 20 25 30

Pro Arg Arg Ser Ser Thr Gln Leu Arg Ser Gly Ala Ser Val Thr Glu

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

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 1 5 10 15

20 Ser Val Gln Arg Lys Arg Gln Glu Ala Glu Gly Glu Ala Thr Val Ile
 20 25 30

25 Glu Ala Leu Gln Ala Pro Pro Asp Val Thr Thr Val Ala Val Glu Glu
 35 40 45

Thr Ile Pro Ser Phe Thr Gly Arg Ser Pro Asn His
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35 <220>
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 <400> 33

40 Tyr His Ala Asp Tyr Tyr Lys Gln Arg Leu Ile His Asp Val Glu Met
 1 5 10 15

45 Asn Pro Gly Pro
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50 <210> 34
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60 His Tyr Ala Gly Tyr Phe Ala Asp Leu Leu Ile His Asp Ile Glu Thr
 1 5 10 15

Asn Pro Gly Pro

20

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 Asn Pro Gly Pro
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 35 Pro Gly Pro

 40 <210> 37
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 45 <220>
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 <400> 37

 50 Ala Ala Arg Gln Met Leu Leu Leu Leu Ser Gly Asp Val Glu Thr Asn
 1 5 10 15

 Pro Gly Pro
 55

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 20 <223> cleavage site, 2A-like sequence
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 25 Thr Arg Ala Glu Ile Glu Asp Glu Leu Ile Arg Ala Gly Ile Glu Ser
 1 5 10 15
 Asn Pro Gly Pro
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 Thr Arg Ala Glu Ile Glu Asp Glu Leu Ile Arg Ala Asp Ile Glu Ser
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 45 Asn Pro Gly Pro
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 1 5 10 15

Asn Pro Gly Pro
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 Ser Ser Ile Ile Arg Thr Lys Met Leu Val Ser Gly Asp Val Glu Glu
 1 5 10 15

20 Asn Pro Gly Pro
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25
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 1 5 10 15

40 Asn Pro Gly Pro
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60 Asn Pro Gly Pro
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<223> fusion construct with IL-2R beta chain

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Met Ser Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
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10

His Ala Ala Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Lys Lys
20 25 30

15

Pro Gly Thr Ser Val Arg Ile Ser Cys Lys Thr Ser Gly Tyr Thr Phe
35 40 45

20

Thr Glu Tyr Thr Ile His Trp Val Lys Gln Ser His Gly Lys Ser Leu
50 55 60

25

Glu Trp Ile Gly Asn Ile Asn Pro Asn Asn Gly Gly Thr Thr Tyr Asn
65 70 75 80

30

Gln Lys Phe Glu Asp Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser
85 90 95

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

35

Tyr Tyr Cys Ala Ala Gly Trp Asn Phe Asp Tyr Trp Gly Gln Gly Thr
115 120 125

40

Thr Leu Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
130 135 140

45

Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser His Lys Phe Met
145 150 155 160

50

Ser Thr Ser Val Gly Asp Arg Val Ser Ile Ile Cys Lys Ala Ser Gln
165 170 175

Asp Val Gly Thr Ala Val Asp Trp Tyr Gln Gln Lys Pro Gly Gln Ser
180 185 190

55

Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg His Thr Gly Val Pro
195 200 205

60

Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
210 215 220

	Thr	Asn	Val	Gln	Ser	Glu	Asp	Leu	Ala	Asp	Tyr	Phe	Cys	Gln	Gln	Tyr	
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5	Asn	Ser	Tyr	Pro	Leu	Thr	Phe	Gly	Ala	Gly	Thr	Met	Leu	Asp	Leu	Lys	
					245					250					255		
10	Arg	Ser	Asp	Pro	Ala	Glu	Pro	Lys	Ser	Pro	Asp	Lys	Thr	His	Thr	Cys	
				260					265					270			
15	Pro	Pro	Cys	Pro	Ala	Pro	Pro	Val	Ala	Gly	Pro	Ser	Val	Phe	Leu	Phe	
			275					280					285				
20	Pro	Pro	Lys	Pro	Lys	Asp	Thr	Leu	Met	Ile	Ala	Arg	Thr	Pro	Glu	Val	
			290				295					300					
25	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe	
	305					310					315					320	
30	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	
					325					330					335		
35	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Thr	
				340					345					350			
40	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	
			355					360					365				
45	Ser	Asn	Lys	Ala	Leu	Pro	Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	
		370					375					380					
50	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Arg	
	385					390					395					400	
55	Asp	Glu	Leu	Thr	Lys	Asn	Gln	Val	Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly	
					405					410					415		
60	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	
				420					425					430			
65	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	
			435					440					445				
70	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr	Val	Asp	Lys	Ser	Arg	Trp	Gln	Gln	
	450						455					460					
75	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val	Met	His	Glu	Ala	Leu	His	Asn	His	

	465		470		475		480
5	Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys Phe Trp Val Leu	485		490		495	
10	Val Val Val Gly Gly Val Leu Ala Cys Tyr Ser Leu Leu Val Thr Val	500		505		510	
15	Ala Phe Ile Ile Phe Trp Val Arg Arg Val Lys Phe Ser Arg Ser Ala	515		520		525	
20	Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu	530		535		540	
25	Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly	545		550		555	560
30	Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu	565		570		575	
35	Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser	580		585		590	
40	Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly	595		600		605	
45	Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu	610		615		620	
50	His Met Gln Ala Leu Pro Pro Arg Arg Ala Glu Gly Arg Gly Ser Leu	625		630		635	640
55	Leu Thr Cys Gly Asp Val Glu Glu Asn Pro Gly Pro Met Glu Thr Asp	645		650		655	
60	Thr Leu Ile Leu Trp Val Leu Leu Leu Leu Val Pro Gly Ser Thr Gly	660		665		670	
65	Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Lys Pro Gly Ala	675		680		685	
70	Ser Val Lys Met Ser Cys Lys Thr Ser Gly Tyr Ser Phe Ser Ser Tyr	690		695		700	
75	Trp Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile	705		710		715	720

	Gly	Tyr	Ile	Asn	Pro	Ser	Thr	Gly	Tyr	Thr	Glu	Asn	Asn	Gln	Lys	Phe	
					725					730					735		
5	Lys	Asp	Lys	Val	Thr	Leu	Thr	Ala	Asp	Lys	Ser	Ser	Asn	Thr	Ala	Tyr	
				740					745					750			
10	Met	Gln	Leu	Asn	Ser	Leu	Thr	Ser	Glu	Asp	Ser	Ala	Val	Tyr	Tyr	Cys	
			755					760					765				
15	Ala	Arg	Ser	Gly	Arg	Leu	Tyr	Phe	Asp	Val	Trp	Gly	Ala	Gly	Thr	Thr	
		770					775					780					
20	Val	Thr	Val	Ser	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	
	785					790					795					800	
	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Asp	Ile	Val	Leu	Thr	Gln	Ser	
					805					810					815		
25	Pro	Pro	Ser	Leu	Ala	Val	Ser	Leu	Gly	Gln	Arg	Ala	Thr	Ile	Ser	Cys	
				820					825					830			
30	Arg	Ala	Ser	Glu	Ser	Ile	Asp	Leu	Tyr	Gly	Phe	Thr	Phe	Met	His	Trp	
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35	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Pro	Pro	Lys	Ile	Leu	Ile	Tyr	Arg	Ala	
	850						855					860					
40	Ser	Asn	Leu	Glu	Ser	Gly	Ile	Pro	Ala	Arg	Phe	Ser	Gly	Ser	Gly	Ser	
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	Arg	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Asn	Pro	Val	Glu	Ala	Asp	Asp	Val	
					885					890					895		
45	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Thr	His	Glu	Asp	Pro	Tyr	Thr	Phe	Gly	
				900					905					910			
50	Gly	Gly	Thr	Lys	Leu	Glu	Ile	Lys	Ser	Asp	Pro	Ala	Thr	Thr	Thr	Pro	
			915					920					925				
55	Ala	Pro	Arg	Pro	Pro	Thr	Pro	Ala	Pro	Thr	Ile	Ala	Ser	Gln	Pro	Leu	
		930					935					940					
60	Ser	Leu	Arg	Pro	Glu	Ala	Cys	Arg	Pro	Ala	Ala	Gly	Gly	Ala	Val	His	
	945					950					955					960	
	Thr	Arg	Gly	Leu	Asp	Phe	Ala	Cys	Asp	Ile	Val	Val	Ile	Ser	Val	Gly	

965

970

975

5	Ser Met Gly Leu Ile Ile Ser Leu Leu Cys Val Tyr Phe Trp Leu Glu	980	985	990
10	Arg Thr Met Pro Arg Ile Pro Thr Leu Lys Asn Leu Glu Asp Leu Val	995	1000	1005
15	Thr Glu Tyr His Gly Asn Phe Ser Ala Trp Ser Gly Val Ser Lys	1010	1015	1020
20	Gly Leu Ala Glu Ser Leu Gln Pro Asp Tyr Ser Glu Arg Leu Cys	1025	1030	1035
25	Leu Val Ser Glu Ile Pro Pro Lys Gly Gly Ala Leu Gly Glu Gly	1040	1045	1050
30	Pro Gly Ala Ser Pro Cys Asn Gln His Ser Pro Tyr Trp Ala Pro	1055	1060	1065
35	Pro Cys Tyr Thr Leu Lys Pro Glu Thr Gln Cys Thr Asn Tyr Ala	1070	1075	1080
40	Leu Leu Lys Leu Ala Gly Asp Val Glu Ser Asn Pro Gly Pro Met	1085	1090	1095
45	Glu Thr Asp Thr Leu Ile Leu Trp Val Leu Leu Leu Leu Val Pro	1100	1105	1110
50	Gly Ser Thr Gly Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu	1115	1120	1125
55	Val Lys Pro Gly Ala Ser Val Lys Ile Ser Cys Lys Val Ser Gly	1130	1135	1140
60	Tyr Ala Ile Ser Ser Ser Trp Met Asn Trp Val Lys Gln Arg Pro	1145	1150	1155
	Gly Gln Gly Leu Glu Trp Ile Gly Arg Ile Tyr Pro Gly Asp Gly	1160	1165	1170
	Asp Thr Lys Tyr Asn Gly Lys Phe Lys Asp Lys Ala Thr Leu Thr	1175	1180	1185
	Val Asp Lys Ser Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu	1190	1195	1200

	Thr	Ser	Val	Asp	Ser	Ala	Val	Tyr	Phe	Cys	Ala	Arg	Asp	Gly	Tyr
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5	Arg	Tyr	Tyr	Phe	Asp	Tyr	Trp	Gly	Gln	Gly	Thr	Ser	Val	Thr	Val
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10	Ser	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly
	1235						1240					1245			
15	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Asp	Ile	Val	Met	Thr	Gln	Thr	Ala
	1250						1255					1260			
20	Pro	Ser	Val	Phe	Val	Thr	Pro	Gly	Glu	Ser	Val	Ser	Ile	Ser	Cys
	1265						1270					1275			
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	1280						1285					1290			
25	Tyr	Trp	Phe	Leu	Gln	Arg	Pro	Gly	Gln	Ser	Pro	Gln	Leu	Leu	Ile
	1295						1300					1305			
30	Tyr	Arg	Met	Ser	Asn	Leu	Ala	Ser	Gly	Val	Pro	Asp	Arg	Phe	Ser
	1310						1315					1320			
35	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Arg	Ile	Ser	Arg	Val
	1325						1330					1335			
40	Glu	Ala	Glu	Asp	Val	Gly	Val	Tyr	Tyr	Cys	Met	Gln	His	Leu	Glu
	1340						1345					1350			
	Tyr	Pro	Val	Thr	Phe	Gly	Ala	Gly	Thr	Lys	Val	Glu	Ile	Lys	Ser
	1355						1360					1365			
45	Asp	Pro	Ala	Lys	Ile	Glu	Val	Met	Tyr	Pro	Pro	Pro	Tyr	Leu	Asp
	1370						1375					1380			
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	1385						1390					1395			
55	Leu	Cys	Pro	Ser	Pro	Leu	Phe	Pro	Gly	Pro	Ser	Lys	Pro	Ile	Pro
	1400						1405					1410			
60	Trp	Leu	Gly	His	Leu	Leu	Val	Gly	Leu	Ser	Gly	Ala	Phe	Gly	Phe
	1415						1420					1425			
	Ile	Ile	Leu	Val	Tyr	Leu	Leu	Ile	Asn	Cys	Arg	Asn	Thr	Gly	Pro

	1430						1435						1440					
5	Trp	Leu	Lys	Lys	Val	Leu	Lys	Cys	Asn	Thr	Pro	Asp	Pro	Ser	Lys			
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10	Phe	Phe	Ser	Gln	Leu	Ser	Ser	Glu	His	Gly	Gly	Asp	Val	Gln	Lys			
		1460					1465					1470						
15	Trp	Leu	Ser	Ser	Pro	Phe	Pro	Ser	Ser	Ser	Phe	Ser	Pro	Gly	Gly			
		1475					1480					1485						
20	Leu	Ala	Pro	Glu	Ile	Ser	Pro	Leu	Glu	Val	Leu	Glu	Arg	Asp	Lys			
		1490					1495					1500						
25	Val	Thr	Gln	Leu	Leu	Leu	Gln	Gln	Asp	Lys	Val	Pro	Glu	Pro	Ala			
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30	Ser	Leu	Ser	Ser	Asn	His	Ser	Leu	Thr	Ser	Cys	Phe	Thr	Asn	Gln			
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35	Gly	Tyr	Phe	Phe	Phe	His	Leu	Pro	Asp	Ala	Leu	Glu	Ile	Glu	Ala			
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40	Cys	Gln	Val	Tyr	Phe	Thr	Tyr	Asp	Pro	Tyr	Ser	Glu	Glu	Asp	Pro			
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50	Leu	Gln	Pro	Leu	Ser	Gly	Glu	Asp	Asp	Ala	Tyr	Cys	Thr	Phe	Pro			
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65	Glu	Arg	Met	Pro	Pro	Ser	Leu	Gln	Glu	Arg	Val	Pro	Arg	Asp	Trp			
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70	Asp	Pro	Gln	Pro	Leu	Gly	Pro	Pro	Thr	Pro	Gly	Val	Pro	Asp	Leu			
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75	Val	Asp	Phe	Gln	Pro	Pro	Pro	Glu	Leu	Val	Leu	Arg	Glu	Ala	Gly			
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Glu Glu Val Pro Asp Ala Gly Pro Arg Glu Gly Val Ser Phe Pro
 1670 1675 1680
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 Trp Ser Arg Pro Pro Gly Gln Gly Glu Phe Arg Ala Leu Asn Ala
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 15 Gln Gly Gln Asp Pro Thr His Leu Val
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 35 Pro Gly Thr Ser Val Arg Ile Ser Cys Lys Thr Ser Gly Tyr Thr Phe
 35 40 45
 40 Thr Glu Tyr Thr Ile His Trp Val Lys Gln Ser His Gly Lys Ser Leu
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 45 Glu Trp Ile Gly Asn Ile Asn Pro Asn Asn Gly Gly Thr Thr Tyr Asn
 65 70 75 80
 Gln Lys Phe Glu Asp Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser
 85 90 95
 50 Thr Ala Tyr Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val
 100 105 110
 55 Tyr Tyr Cys Ala Ala Gly Trp Asn Phe Asp Tyr Trp Gly Gln Gly Thr
 115 120 125
 60 Thr Leu Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 130 135 140

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10	Asp	Val	Gly	Thr	Ala	Val	Asp	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ser
				180					185					190		
15	Pro	Lys	Leu	Leu	Ile	Tyr	Trp	Ala	Ser	Thr	Arg	His	Thr	Gly	Val	Pro
			195					200					205			
20	Asp	Arg	Phe	Thr	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile
		210					215					220				
25	Thr	Asn	Val	Gln	Ser	Glu	Asp	Leu	Ala	Asp	Tyr	Phe	Cys	Gln	Gln	Tyr
	225					230					235					240
30	Asn	Ser	Tyr	Pro	Leu	Thr	Phe	Gly	Ala	Gly	Thr	Met	Leu	Asp	Leu	Lys
					245					250					255	
35	Arg	Ser	Asp	Pro	Ala	Glu	Pro	Lys	Ser	Pro	Asp	Lys	Thr	His	Thr	Cys
				260					265					270		
40	Pro	Pro	Cys	Pro	Ala	Pro	Pro	Val	Ala	Gly	Pro	Ser	Val	Phe	Leu	Phe
			275					280					285			
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		290					295					300				
50	Thr	Cys	Val	Val	Val	Asp	Val	Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe
	305					310					315					320
55	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro
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60	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Thr
				340					345					350		
65	Val	Leu	His	Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val
			355					360					365			
70	Ser	Asn	Lys	Ala	Leu	Pro	Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala
		370					375					380				
75	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln	Val	Tyr	Thr	Leu	Pro	Pro	Ser	Arg

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10	Phe	Tyr	Pro	Ser 420	Asp	Ile	Ala	Val	Glu 425	Trp	Glu	Ser	Asn	Gly 430	Gln	Pro
15	Glu	Asn	Asn 435	Tyr	Lys	Thr	Thr	Pro 440	Pro	Val	Leu	Asp	Ser 445	Asp	Gly	Ser
20	Phe	Phe 450	Leu	Tyr	Ser	Lys	Leu 455	Thr	Val	Asp	Lys	Ser 460	Arg	Trp	Gln	Gln
25	Gly 465	Asn	Val	Phe	Ser	Cys 470	Ser	Val	Met	His	Glu 475	Ala	Leu	His	Asn	His 480
30	Tyr	Thr	Gln	Lys	Ser 485	Leu	Ser	Leu	Ser	Pro 490	Gly	Lys	Phe	Trp	Val 495	Leu
35	Val	Val	Val	Gly 500	Gly	Val	Leu	Ala	Cys 505	Tyr	Ser	Leu	Leu	Val 510	Thr	Val
40	Ala	Phe	Ile 515	Ile	Phe	Trp	Val	Arg 520	Arg	Val	Lys	Phe	Ser 525	Arg	Ser	Ala
45	Asp	Ala 530	Pro	Ala	Tyr	Gln	Gln 535	Gly	Gln	Asn	Gln	Leu 540	Tyr	Asn	Glu	Leu
50	Asn 545	Leu	Gly	Arg	Arg	Glu 550	Glu	Tyr	Asp	Val	Leu 555	Asp	Lys	Arg	Arg	Gly 560
55	Arg	Asp	Pro	Glu	Met 565	Gly	Gly	Lys	Pro	Arg 570	Arg	Lys	Asn	Pro	Gln 575	Glu
60	Gly	Leu	Tyr	Asn 580	Glu	Leu	Gln	Lys	Asp 585	Lys	Met	Ala	Glu	Ala 590	Tyr	Ser
65	Glu	Ile	Gly 595	Met	Lys	Gly	Glu	Arg 600	Arg	Arg	Gly	Lys	Gly 605	His	Asp	Gly
70	Leu	Tyr 610	Gln	Gly	Leu	Ser	Thr 615	Ala	Thr	Lys	Asp	Thr 620	Tyr	Asp	Ala	Leu
75	His 625	Met	Gln	Ala	Leu	Pro 630	Pro	Arg	Arg	Ala	Glu 635	Gly	Arg	Gly	Ser	Leu 640

	Leu	Thr	Cys	Gly	Asp	Val	Glu	Glu	Asn	Pro	Gly	Pro	Met	Glu	Thr	Asp	
					645					650					655		
5	Thr	Leu	Ile	Leu	Trp	Val	Leu	Leu	Leu	Leu	Val	Pro	Gly	Ser	Thr	Gly	
				660					665					670			
10	Gln	Val	Gln	Leu	Gln	Gln	Ser	Gly	Ala	Glu	Leu	Ala	Lys	Pro	Gly	Ala	
			675					680					685				
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	Gly	Tyr	Ile	Asn	Pro	Ser	Thr	Gly	Tyr	Thr	Glu	Asn	Asn	Gln	Lys	Phe	
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25	Lys	Asp	Lys	Val	Thr	Leu	Thr	Ala	Asp	Lys	Ser	Ser	Asn	Thr	Ala	Tyr	
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			755					760					765				
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		770					775					780					
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	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Gly	Ser	Asp	Ile	Val	Leu	Thr	Gln	Ser	
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		850					855					860					
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	865					870					875					880	
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	885	890	895
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15	Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu 930 935 940		
20	Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His 945 950 955 960		
25	Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Val Val Ile Ser Val Gly 965 970 975		
30	Ser Met Gly Leu Ile Ile Ser Leu Leu Cys Val Tyr Phe Trp Leu Glu 980 985 990		
35	Arg Thr Met Pro Arg Ile Pro Thr Leu Lys Asn Leu Glu Asp Leu Val 995 1000 1005		
40	Thr Glu Tyr His Gly Asn Phe Ser Ala Trp Ser Gly Val Ser Lys 1010 1015 1020		
45	Gly Leu Ala Glu Ser Leu Gln Pro Asp Tyr Ser Glu Arg Leu Cys 1025 1030 1035		
50	Leu Val Ser Glu Ile Pro Pro Lys Gly Gly Ala Leu Gly Glu Gly 1040 1045 1050		
55	Pro Gly Ala Ser Pro Cys Asn Gln His Ser Pro Tyr Trp Ala Pro 1055 1060 1065		
60	Pro Cys Tyr Thr Leu Lys Pro Glu Thr Gln Cys Thr Asn Tyr Ala 1070 1075 1080		
65	Leu Leu Lys Leu Ala Gly Asp Val Glu Ser Asn Pro Gly Pro Met 1085 1090 1095		
70	Glu Thr Asp Thr Leu Ile Leu Trp Val Leu Leu Leu Leu Val Pro 1100 1105 1110		
75	Gly Ser Thr Gly Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu 1115 1120 1125		

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	1160						1165					1170			
15	Asp	Thr	Lys	Tyr	Asn	Gly	Lys	Phe	Lys	Asp	Lys	Ala	Thr	Leu	Thr
	1175						1180					1185			
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	1190						1195					1200			
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25	Arg	Tyr	Tyr	Phe	Asp	Tyr	Trp	Gly	Gln	Gly	Thr	Ser	Val	Thr	Val
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	1250						1255					1260			
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	1265						1270					1275			
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	1280						1285					1290			
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	1295						1300					1305			
50	Tyr	Arg	Met	Ser	Asn	Leu	Ala	Ser	Gly	Val	Pro	Asp	Arg	Phe	Ser
	1310						1315					1320			
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	1325						1330					1335			
60	Glu	Ala	Glu	Asp	Val	Gly	Val	Tyr	Tyr	Cys	Met	Gln	His	Leu	Glu
	1340						1345					1350			
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10	Asn	Glu 1385	Lys	Ser	Asn	Gly	Thr 1390	Ile	Ile	His	Val	Lys 1395	Gly	Lys	His	
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25	Val	Trp 1445	Pro	Ser	Leu	Pro	Asp 1450	His	Lys	Lys	Thr	Leu 1455	Glu	His	Leu	
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10  Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
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15  Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
    85                90                95

20  Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
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    Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
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25  Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys
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30  Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
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35  Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
    165                170                175

    Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
        180                185                190

40  Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
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45  Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
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 Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly
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 Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln
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 Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu
 65 70 75 80
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Arg Xaa Xaa Arg
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