

SEQUENCE LISTING

<110> ALDERBIO HOLDINGS LLC
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 McNeill, Patricia D
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<120> MULTI-COPY STRATEGY FOR HIGH-TITER AND HIGH-PURITY PRODUCTION OF
 MULTI-SUBUNIT PROTEINS SUCH AS ANTIBODIES IN TRANSFORMED MICROBES
 SUCH AS PICHIA PASTORIS

<130> 67858.730202

<140> tba
 <141> 2012-08-20

<150> 61/525,307
 <151> 2011-08-19

<150> 13/466,795
 <151> 2012-05-08

<160> 54

<170> PatentIn version 3.5

<210> 1
 <211> 441
 <212> PRT
 <213> Artificial

<220>
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Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Leu Asp Leu Ser Ser Tyr
 20 25 30

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

Gly Val Ile Gly Ile Asn Asp Asn Thr Tyr Tyr Ala Ser Trp Ala Lys
 50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Thr Thr Val Tyr Leu
 65 70 75 80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Phe Cys Ala
85 90 95

Arg Gly Asp Ile Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala
100 105 110

Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser
115 120 125

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

Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly
145 150 155 160

Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu
165 170 175

Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr
180 185 190

Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Ala Arg
195 200 205

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

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
225 230 235 240

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
245 250 255

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
260 265 270

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
275 280 285

Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
290 295 300

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys

50 55 60
 Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Thr Thr Val Tyr Leu
 65 70 75 80
 Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Phe Cys Ala
 85 90 95
 Arg Gly Asp Ile Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 100 105 110

<210> 3
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<400> 3

Ser Tyr Tyr Met Gln
 1 5

<210> 4
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<400> 4

Val Ile Gly Ile Asn Asp Asn Thr Tyr Tyr Ala Ser Trp Ala Lys Gly
 1 5 10 15

<210> 5
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 120

ccagggaagg ggctggagtg ggtcggagtc attggtatca atgataacac atactacgcg
180

agctgggcga aaggccgatt caccatctcc agagacaatt ccaagaccac ggtgtatctt
240

caaatgaaca gcctgagagc tgaggacact gctgtgtatt tctgtgctag aggggacatc
300

tggggccaag ggaccctcgt caccgtctcg agc
333

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<213> Artificial

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120

ccagggaagg ggctggagtg ggtcggagtc attggtatca atgataacac atactacgcg
180

agctgggcga aaggccgatt caccatctcc agagacaatt ccaagaccac ggtgtatctt
240

caaatgaaca gcctgagagc tgaggacact gctgtgtatt tctgtgctag aggggacatc
300

tggggccaag ggaccctcgt caccgtctcg agcgcctcca ccaagggccc atcggctcttc
360

cccctggcac cctcctccaa gagcacctct gggggcacag cggccctggg ctgcctggtc
420

aaggactact tccccgaacc ggtgacggtg tcgtggaact caggcgcctt gaccagcggc
480

gtgcacacct tcccggctgt cctacagtcc tcaggactct actccctcag cagcgtggtg
540

accgtgccct ccagcagctt gggcacccag acctacatct gcaacgtgaa tcacaagccc
600

agcaacacca aggtggacgc gagagttgag cccaaatctt gtgacaaaac tcacacatgc
660

ccaccgtgcc cagcacctga actcctgggg ggaccgtcag tcttcctctt cccccaaaa
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cccaaggaca ccctcatgat ctcccggacc cctgaggta catgcgtggt ggtggacgtg
780

agccacgaag accctgaggt caagttcaac tggtagctgg acggcgtgga ggtgcataat
840

gccaagacaa agccgcggga ggagcagtac gccagcacgt accgtgtggt cagcgtcctc
900

accgtcctgc accaggactg gctgaatggc aaggagtaca agtgcaaggt ctccaacaaa
960

gccctcccag ccccatcga gaaaaccatc tccaaagcca aagggcagcc ccgagaacca
1020

caggtgtaca ccctgcccc atcccgggag gagatgacca agaaccaggt cagcctgacc
1080

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1140

ccggagaaca actacaagac cagcctccc gtgctggact ccgacggctc cttcttcctc
1200

tacagcaagc tcaccgtgga caagagcagg tggcagcagg ggaacgtctt ctcatgctcc
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aaatga
1326

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

Tyr	Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Val	Pro	Lys	Gln	Leu
		35					40					45			

Ile	Tyr	Ser	Thr	Ser	Thr	Leu	Ala	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser
	50					55					60				

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

Pro Glu Asp Val Ala Thr Tyr Tyr Cys Leu Gly Ser Tyr Asp Cys Ser
85 90 95

Ser Gly Asp Cys Phe Val Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

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

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

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

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

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

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

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

<210> 8
<211> 113
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<220>
<223> Humanized antibody sequence

<400> 8

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

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Gln Leu
35 40 45

Ile Tyr Ser Thr Ser Thr Leu Ala Ser Gly Val Pro Ser Arg Phe Ser
50 55 60

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

Pro Glu Asp Val Ala Thr Tyr Tyr Cys Leu Gly Ser Tyr Asp Cys Ser
85 90 95

Ser Gly Asp Cys Phe Val Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

Arg

<210> 9
<211> 13
<212> PRT
<213> Artificial

<220>
<223> Humanized antibody sequence

<400> 9

Gln Ala Ser Gln Ser Val Tyr Asp Asn Asn Tyr Leu Ala
1 5 10

<210> 10
<211> 7
<212> PRT
<213> Artificial

<220>
<223> Humanized antibody sequence

<400> 10

Ser Thr Ser Thr Leu Ala Ser
1 5

<210> 11
<211> 13
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<220>

<223> Humanized antibody sequence

<400> 11

Leu Gly Ser Tyr Asp Cys Ser Ser Gly Asp Cys Phe Val
1 5 10

<210> 12

<211> 339

<212> DNA

<213> Artificial

<220>

<223> Humanized antibody sequence

<400> 12

caagtgtga cccagtctcc atcctccctg tctgcatctg taggagacag agtcaccatc
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aattgccagg ccagtcagag tgtttatgat aacaactacc tagcctggta tcagcagaaa
120

ccagggaaaag ttcctaagca actgatctat tctacatcca ctctggcatc tgggggtccca
180

tctcgtttca gtggcagtgg atctgggaca gatttcactc tcaccatcag cagcctgcag
240

cctgaagatg ttgcaactta ttactgtcta ggcagttatg attgtagtag tggtgattgt
300

tttgttttcg gcggaggaac caaggtggaa atcaaacgt
339

<210> 13

<211> 660

<212> DNA

<213> Artificial

<220>

<223> Humanized antibody sequence

<400> 13

caagtgtga cccagtctcc atcctccctg tctgcatctg taggagacag agtcaccatc
60

aattgccagg ccagtcagag tgtttatgat aacaactacc tagcctggta tcagcagaaa
120

ccagggaaaag ttcctaagca actgatctat tctacatcca ctctggcatc tgggggtccca
180

tctcgtttca gtggcagtgg atctgggaca gatttcactc tcaccatcag cagcctgcag
240

cctgaagatg ttgcaactta ttactgtcta ggcagttatg attgtagtag tggtgattgt
300

tttgttttcg gcggaggaac caaggtggaa atcaaacgta cgggtggctgc accatctgtc
360

ttcatcttcc cgccatctga tgagcagttg aaatctggaa ctgcctctgt tgtgtgcctg
420

ctgaataact tctatcccag agaggccaaa gtacagtgga aggtggataa cgccctccaa
480

tcgggtaact cccaggagag tgtcacagag caggacagca aggacagcac ctacagcctc
540

agcagcaccg tgacgctgag caaagcagac tacgagaaac acaaagtcta cgctgcgaa
600

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<400> 14

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Ile Asp Leu Ser Gly Tyr
20 25 30

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

Gly Val Ile Gly Ile Asn Gly Ala Thr Tyr Tyr Ala Ser Trp Ala Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Thr Thr Val Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Phe Cys Ala
85 90 95

Arg Gly Asp Ile Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala

		100						105							110
Ser	Thr	Lys	Gly	Pro	Ser	Val	Phe	Pro	Leu	Ala	Pro	Ser	Ser	Lys	Ser
		115					120					125			
Thr	Ser	Gly	Gly	Thr	Ala	Ala	Leu	Gly	Cys	Leu	Val	Lys	Asp	Tyr	Phe
	130					135					140				
Pro	Glu	Pro	Val	Thr	Val	Ser	Trp	Asn	Ser	Gly	Ala	Leu	Thr	Ser	Gly
145					150					155					160
Val	His	Thr	Phe	Pro	Ala	Val	Leu	Gln	Ser	Ser	Gly	Leu	Tyr	Ser	Leu
				165					170					175	
Ser	Ser	Val	Val	Thr	Val	Pro	Ser	Ser	Ser	Leu	Gly	Thr	Gln	Thr	Tyr
			180					185					190		
Ile	Cys	Asn	Val	Asn	His	Lys	Pro	Ser	Asn	Thr	Lys	Val	Asp	Ala	Arg
		195					200					205			
Val	Glu	Pro	Lys	Ser	Cys	Asp	Lys	Thr	His	Thr	Cys	Pro	Pro	Cys	Pro
	210					215					220				
Ala	Pro	Glu	Leu	Leu	Gly	Gly	Pro	Ser	Val	Phe	Leu	Phe	Pro	Pro	Lys
225					230					235					240
Pro	Lys	Asp	Thr	Leu	Met	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	Cys	Val
				245					250					255	
Val	Val	Asp	Val	Ser	His	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr
			260					265					270		
Val	Asp	Gly	Val	Glu	Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu
		275					280					285			
Gln	Tyr	Ala	Ser	Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His
	290					295					300				
Gln	Asp	Trp	Leu	Asn	Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys
305					310					315					320
Ala	Leu	Pro	Ala	Pro	Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln
				325					330					335	

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met
340 345 350

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
355 360 365

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
370 375 380

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

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
405 410 415

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
420 425 430

Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440

<210> 15
<211> 111
<212> PRT
<213> Artificial

<220>
<223> Humanized antibody sequence

<400> 15

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Ile Asp Leu Ser Gly Tyr
20 25 30

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

Gly Val Ile Gly Ile Asn Gly Ala Thr Tyr Tyr Ala Ser Trp Ala Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Thr Thr Val Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Phe Cys Ala
85 90 95

Arg Gly Asp Ile Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
100 105 110

<210> 16
<211> 5
<212> PRT
<213> Artificial

<220>
<223> Humanized antibody sequence

<400> 16

Gly Tyr Tyr Met Asn
1 5

<210> 17
<211> 15
<212> PRT
<213> Artificial

<220>
<223> Humanized antibody sequence

<400> 17

Ile Gly Ile Asn Gly Ala Thr Tyr Tyr Ala Ser Trp Ala Lys Gly
1 5 10 15

<210> 18
<211> 333
<212> DNA
<213> Artificial

<220>
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120

ccaggggaagg ggctggagtg ggtcggagtc attggtatta atggtgccac atactacgcg
180

agctgggcga aaggccgatt caccatctcc agagacaatt ccaagaccac ggtgtatctt
240

caaatgaaca gcctgagagc tgaggacact gctgtgtatt tctgtgctag aggggacatc
300

tggggccaag ggaccctcgt caccgtctcg agc
333

<210> 19
<211> 1326
<212> DNA
<213> Artificial

<220>
<223> Humanized antibody sequence

<400> 19
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60

tcctgtgcag tctctggaat cgacctcagt ggctactaca tgaactgggt ccgtcaggct
120

ccagggaagg ggctggagtg ggtcggagtc attggtatta atggtgccac atactacgcg
180

agctgggcga aaggccgatt caccatctcc agagacaatt ccaagaccac ggtgtatctt
240

caaatgaaca gcctgagagc tgaggacact gctgtgtatt tctgtgctag aggggacatc
300

tggggccaag ggaccctcgt caccgtctcg agcgcctcca ccaagggccc atcggctctt
360

cccctggcac cctcctccaa gagcacctct gggggcacag cggccctggg ctgcctggtc
420

aaggactact tccccgaacc ggtgacggtg tcgtggaact caggcgcctt gaccagcggc
480

gtgcacacct tcccggctgt cctacagtcc tcaggactct actccctcag cagcgtggtg
540

accgtgccct ccagcagctt gggcacccag acctacatct gcaacgtgaa tcacaagccc
600

agcaacacca aggtggacgc gagagttgag cccaaatctt gtgacaaaac tcacacatgc
660

ccaccgtgcc cagcacctga actcctgggg ggaccgtcag tcttcctctt cccccaaaa
720

ccaaggaca ccctcatgat ctcccggacc cctgagggtca catgcgtggt ggtggacgtg
780

agccacgaag accctgaggt caagttcaac tgggtacgtg acggcgtgga ggtgcataat
840

gccaagacaa agccgcggga ggagcagtac gccagcacgt accgtgtggt cagcgtcctc
900

accgtcctgc accaggactg gctgaatggc aaggagtaca agtgcaaggt ctccaacaaa
960

gccctcccag ccccatcga gaaaaccatc tccaaagcca aagggcagcc ccgagaacca
1020

caggtgtaca ccctgcccc atcccgggag gagatgacca agaaccaggt cagcctgacc
1080

tgcctgggtca aaggcttcta tcccagcgac atcgccgtgg agtgggagag caatgggcag
1140

ccggagaaca actacaagac cagcctccc gtgctggact ccgacggctc cttcttcctc
1200

tacagcaagc tcaccgtgga caagagcagg tggcagcagg ggaacgtctt ctcatgctcc
1260

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1320

aaatga
1326

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<212> PRT
<213> Artificial

<220>
<223> Humanized antibody sequence

<400> 20

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

Arg	Val	Thr	Ile	Asn	Cys	Gln	Ala	Ser	Gln	Ser	Val	Tyr	His	Asn	Thr
			20					25					30		

Tyr	Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Val	Pro	Lys	Gln	Leu
		35					40					45			

Ile	Tyr	Asp	Ala	Ser	Thr	Leu	Ala	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser
	50					55					60				

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

Pro Glu Asp Val Ala Thr Tyr Tyr Cys Leu Gly Ser Tyr Asp Cys Thr
85 90 95

Asn Gly Asp Cys Phe Val Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

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

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

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

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

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

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

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

<210> 21
<211> 113
<212> PRT
<213> Artificial

<220>
<223> Humanized antibody sequence

<400> 21

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

Arg Val Thr Ile Asn Cys Gln Ala Ser Gln Ser Val Tyr His Asn Thr
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Gln Leu
35 40 45

Ile Tyr Asp Ala Ser Thr Leu Ala Ser Gly Val Pro Ser Arg Phe Ser
50 55 60

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

Pro Glu Asp Val Ala Thr Tyr Tyr Cys Leu Gly Ser Tyr Asp Cys Thr
85 90 95

Asn Gly Asp Cys Phe Val Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

Arg

<210> 22
<211> 13
<212> PRT
<213> Artificial

<220>
<223> Humanized antibody sequence

<400> 22

Gln Ala Ser Gln Ser Val Tyr His Asn Thr Tyr Leu Ala
1 5 10

<210> 23
<211> 7
<212> PRT
<213> Artificial

<220>
<223> Humanized antibody sequence

<400> 23

Asp Ala Ser Thr Leu Ala Ser
1 5

<210> 24
<211> 13
<212> PRT
<213> Artificial

<220>
<223> Humanized antibody sequence

<400> 24

Leu Gly Ser Tyr Asp Cys Thr Asn Gly Asp Cys Phe Val
1 5 10

<210> 25
<211> 339
<212> DNA
<213> Artificial

<220>
<223> Humanized antibody sequence

<400> 25
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aattgccagg ccagtcagag tgtttatcat aacacctacc tggcctggta tcagcagaaa
120

ccagggaag ttcctaagca actgatctat gatgcatcca ctctggcatc tgggggtcca
180

tctcgtttca gtggcagtgg atctgggaca gatttcactc tcaccatcag cagcctgcag
240

cctgaagatg ttgcaactta ttactgtctg ggcagttatg attgtactaa tggtgattgt
300

tttgttttcg gcggaggaac caaggtggaa atcaaacgt
339

<210> 26
<211> 660
<212> DNA
<213> Artificial

<220>
<223> Humanized antibody sequence

<400> 26
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aattgccagg ccagtcagag tgtttatcat aacacctacc tggcctggta tcagcagaaa
120

ccagggaag ttcctaagca actgatctat gatgcatcca ctctggcatc tgggggtcca
180

tctcgtttca gtggcagtgg atctgggaca gatttcactc tcaccatcag cagcctgcag
240

cctgaagatg ttgcaactta ttactgtctg ggcagttatg attgtactaa tggtgattgt
300

tttgttttcg gcggaggaac caaggtggaa atcaaacgta cgggtggctgc accatctgtc
360

ttcatcttcc cgccatctga tgagcagttg aaatctggaa ctgcctctgt tgtgtgcctg
420

ctgaataact tctatcccag agaggccaaa gtacagtgga aggtggataa cgccctccaa
480

tcgggtaact cccaggagag tgtcacagag caggacagca aggacagcac ctacagcctc
540

agcagcacc ctgacgctgag caaagcagac tacgagaaac acaaagtcta cgctgcgaa
600

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660

<210> 27
<211> 1350
<212> DNA
<213> Artificial

<220>
<223> Humanized antibody sequence

<400> 27
gaggtgcagc tggaggagtc tgggggaggc ttggtccagc ctgggggggc cctgagactc
60

tcctgtgcag cctctggatt ctccctcagt aactactacg tgacctgggt ccgtcaggct
120

ccagggaagg ggctggagtg ggtcggcatc atctatggta gtgatgaaac cgctacgct
180

acctccgcta taggcgatt caccatctcc agagacaatt ccaagaacac cctgtatctt
240

caaatgaaca gcctgagagc tgaggacact gctgtgtatt actgtgctag agatgatagt
300

agtgactggg atgcaaagtt caacttgtgg ggccaaggga ccctcgtcac cgtctcgagc
360

gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg
420

ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg
480

tggaaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca
540

ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg caccagacc
600

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacaagag agttgagccc
660

aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggggga
720

ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggaccctt
780

gaggtcacat gcgtgggtgt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg
840

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacgcc
900

agcacgtacc gtgtgggtcag cgtcctcacc gtcctgcacc aggactgggt gaatggcaag
960

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc
1020

aaagccaaag ggcagccccc agaaccacag gtgtacaccc tgcccccatc ccgggaggag
1080

atgaccaaga accaggtcag cctgacctgc ctgggtcaaag gcttctatcc cagcgacatc
1140

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccggtg
1200

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg
1260

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg
1320

cagaagagcc tctccctgtc tccgggtaaa
1350

<210> 28
<211> 450
<212> PRT
<213> Artificial

<220>
<223> Humanized antibody sequence

<400> 28

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Leu Ser Asn Tyr
20 25 30

Tyr Val Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Ile Ile Tyr Gly Ser Asp Glu Thr Ala Tyr Ala Thr Ser Ala Ile
50 55 60

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

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

Arg Asp Asp Ser Ser Asp Trp Asp Ala Lys Phe Asn Leu Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

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

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

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

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
180 185 190

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

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225 230 235 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
260 265 270

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

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

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
 305 310 315 320

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

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

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

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
 370 375 380

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

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

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
 420 425 430

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

Gly Lys
 450

<210> 29
 <211> 651
 <212> DNA
 <213> Artificial

<220>
 <223> Humanized antibody sequence

<400> 29

gctatccaga tgaccagtc tccttcctcc ctgtctgcat ctgtaggaga cagagtcacc
60
atcacttgcc aggccagtca gagcattaac aatgagttat cctgggtatca gcagaaacca
120
gggaaagccc ctaagctcct gatctatagg gcatccactc tggcatctgg ggtcccatca
180
aggttcagcg gcagtggatc tgggacagac ttactctca ccatcagcag cctgcagcct
240
gatgattttg caacttatta ctgccaacag gggtatagtc tgaggaacat tgataatgct
300
ttcggcggag ggaccaaggt ggaaatcaaa cgtacgggtg ctgcaccatc tgtcttcac
360
ttcccgccat ctgatgagca gttgaaatct ggaactgcct ctgttgtgtg cctgctgaat
420
aacttctatc ccagagaggc caaagtacag tggaagggtg ataacgccct ccaatcgggt
480
aactcccagg agagtgtcac agagcaggac agcaaggaca gcacctacag cctcagcagc
540
accctgacgc tgagcaaagc agactacgag aaacacaaag tctacgcctg cgaagtcacc
600
catcagggcc tgagctcgcc cgtcacaaag agcttcaaca ggggagagtg t
651

<210> 30
<211> 217
<212> PRT
<213> Artificial

<220>
<223> Humanized antibody sequence

<400> 30

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

Asp	Arg	Val	Thr	Ile	Thr	Cys	Gln	Ala	Ser	Gln	Ser	Ile	Asn	Asn	Glu
			20					25					30		

Leu	Ser	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Leu	Leu	Ile
		35					40					45			

Tyr	Arg	Ala	Ser	Thr	Leu	Ala	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly
	50					55					60				

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Tyr Ser Leu Arg Asn
85 90 95

Ile Asp Asn Ala Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr
100 105 110

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

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

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

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

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

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

Thr Lys Ser Phe Asn Arg Gly Glu Cys
210 215

<210> 31
<211> 18
<212> PRT
<213> Artificial

<220>
<223> Secretion signal peptide

<400> 31

Met Arg Ser Leu Leu Ile Leu Val Leu Cys Phe Leu Pro Leu Ala Ala
1 5 10 15

Leu Gly

<210> 32
<211> 16
<212> PRT
<213> Artificial

<220>
<223> Secretion signal peptide

<400> 32

Met Arg Leu Leu Leu Leu Leu Leu Leu Leu Pro Leu Ala Ala Leu Gly
1 5 10 15

<210> 33
<211> 19
<212> PRT
<213> Artificial

<220>
<223> Secretion signal peptide

<400> 33

Met Leu Leu Gln Ala Phe Leu Phe Leu Leu Ala Gly Phe Ala Ala Lys
1 5 10 15

Ile Ser Ala

<210> 34
<211> 35
<212> PRT
<213> Artificial

<220>
<223> Secretion signal peptide

<400> 34

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

Ala Leu Ala Ala Pro Val Asn Thr Thr Thr Glu Glu Gly Val Ser Leu
20 25 30

Glu Lys Arg
35

<210> 35
<211> 22

<212> PRT
<213> Artificial

<220>
<223> Secretion signal peptide

<400> 35

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

Ala Leu Ala Ala Pro Val
20

<210> 36
<211> 27
<212> PRT
<213> Artificial

<220>
<223> Secretion signal peptide

<400> 36

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

Ala Leu Ala Ala Pro Val Ser Leu Glu Lys Arg
20 25

<210> 37
<211> 41
<212> PRT
<213> Artificial

<220>
<223> Secretion signal peptide

<400> 37

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

Ala Leu Ala Ala Pro Val Asn Thr Thr Thr Glu Glu Gly Val Ser Leu
20 25 30

Glu Lys Arg Glu Ala Glu Ala Glu Ala
35 40

<210> 38
<211> 85

<212> PRT
<213> Artificial

<220>
<223> Secretion signal peptide

<400> 38

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

Ala Leu Ala Ala Pro Val Asn Thr Thr Thr Glu Asp Glu Thr Ala Gln
20 25 30

Ile Pro Ala Glu Ala Val Ile Gly Tyr Ser Asp Leu Glu Gly Asp Phe
35 40 45

Asp Val Ala Val Leu Pro Phe Ser Asn Ser Thr Asn Asn Gly Leu Leu
50 55 60

Phe Ile Asn Thr Thr Ile Ala Ser Ile Ala Ala Lys Glu Glu Gly Val
65 70 75 80

Ser Leu Glu Lys Arg
85

<210> 39
<211> 44
<212> PRT
<213> Artificial

<220>
<223> Secretion signal peptide

<400> 39

Met Thr Lys Pro Thr Gln Val Leu Val Arg Ser Val Ser Ile Leu Phe
1 5 10 15

Phe Ile Thr Leu Leu His Leu Val Val Ala Leu Asn Asp Val Ala Gly
20 25 30

Pro Ala Glu Thr Ala Pro Val Ser Leu Leu Pro Arg
35 40

<210> 40
<211> 22
<212> PRT
<213> Artificial

<220>

<223> Secretion signal peptide

<400> 40

Met Phe Ser Pro Ile Leu Ser Leu Glu Ile Ile Leu Ala Leu Ala Thr
1 5 10 15

Leu Gln Ser Val Phe Ala
20

<210> 41

<211> 22

<212> PRT

<213> Artificial

<220>

<223> Secretion signal peptide

<400> 41

Met Gln Thr Leu Leu Val Ser Ser Leu Val Val Ser Leu Ala Ala Ala
1 5 10 15

Leu Pro His Tyr Ile Arg
20

<210> 42

<211> 22

<212> PRT

<213> Artificial

<220>

<223> Secretion signal peptide

<400> 42

Met Ile Phe Leu Lys Leu Ile Lys Ser Ile Val Ile Gly Leu Gly Leu
1 5 10 15

Val Ser Ala Ile Gln Ala
20

<210> 43

<211> 24

<212> PRT

<213> Artificial

<220>

<223> Secretion signal peptide

<400> 43

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

Tyr Ser Arg Gly Val Phe Arg Arg
20

<210> 44

<211> 18

<212> PRT

<213> Artificial

<220>

<223> Secretion signal peptide

<400> 44

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

Tyr Ser

<210> 45

<211> 24

<212> PRT

<213> Artificial

<220>

<223> Secretion signal peptide

<400> 45

Met Ala Leu Trp Met Arg Leu Leu Pro Leu Leu Ala Leu Leu Ala Leu
1 5 10 15

Trp Gly Pro Asp Pro Ala Ala Ala
20

<210> 46

<211> 24

<212> PRT

<213> Artificial

<220>

<223> Secretion signal peptide

<400> 46

Met Lys Tyr Thr Ser Tyr Ile Leu Ala Phe Gln Leu Cys Ile Val Leu
1 5 10 15

Gly Ser Leu Gly Cys Asp Leu Pro
20

<210> 47
<211> 26
<212> PRT
<213> Artificial

<220>
<223> Secretion signal peptide

<400> 47

Met Ala Ala Asp Ser Gln Thr Pro Trp Leu Leu Thr Phe Ser Leu Leu
1 5 10 15

Cys Leu Leu Trp Pro Gln Glu Pro Gly Ala
20 25

<210> 48
<211> 27
<212> PRT
<213> Artificial

<220>
<223> Secretion signal peptide

<400> 48

Met Lys Lys Asn Arg Met Met Met Met Ile Trp Ser Val Gly Val Val
1 5 10 15

Trp Met Leu Leu Leu Val Gly Gly Ser Tyr Gly
20 25

<210> 49
<211> 18
<212> PRT
<213> Artificial

<220>
<223> Secretion signal peptide

<400> 49

Met Gln Lys Leu Ile Ile Phe Ala Leu Val Val Leu Cys Val Gly Ser
1 5 10 15

Glu Ala

<210> 50
<211> 18
<212> PRT
<213> Artificial

<220>
<223> Secretion signal peptide

<400> 50

Met Lys Ala Leu Ile Val Leu Gly Leu Val Leu Leu Ser Val Thr Val
1 5 10 15

Gln Gly

<210> 51
<211> 20
<212> PRT
<213> Artificial

<220>
<223> Secretion signal peptide

<400> 51

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

Pro Ser Pro Ser
20

<210> 52
<211> 19
<212> PRT
<213> Artificial

<220>
<223> Secretion signal peptide

<400> 52

Met Gly Ala Ala Ala Lys Leu Ala Phe Ala Val Phe Leu Ile Ser Cys
1 5 10 15

Ser Ser Gly

<210> 53
<211> 31

<212> PRT
<213> Artificial

<220>
<223> Secretion signal peptide

<400> 53

Met Leu Ser Leu Lys Pro Ser Trp Leu Thr Leu Ala Ala Leu Met Tyr
1 5 10 15

Ala Met Leu Leu Val Val Val Pro Phe Ala Lys Pro Val Arg Ala
20 25 30

<210> 54
<211> 22
<212> PRT
<213> Artificial

<220>
<223> Secretion signal peptide

<400> 54

Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1 5 10 15

Leu Pro Gly Ala Lys Cys
20