

SEQUENCE LISTING

<110> VIB VZW
UNIVERSITEIT GENT
THE UNITED STATES OF AMERICA, as represented by the
Secretary, Department of Health and Human Services, National
Institutes of Health, Office of Technology Transfer
TRUSTEES OF DARTMOUTH COLLEGE

<120> Immunoglobulin single variable domain against RSV F protein

<130> XS/RSVNb/521

<150> US 62/181,522

<151> 2015-06-18

<150> EP 15178653.0

<151> 2015-07-28

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<151> 2015-10-28

<160> 19

<170> PatentIn version 3.5

<210> 1

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> CDR1 sequence

<400> 1

Gly Phe Thr Leu Asp Tyr Tyr Tyr Ile Gly
1 5 10

<210> 2

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> CDR1 sequence

<400> 2

Gly Phe Thr Leu Asp Tyr Tyr Tyr Ile Gly
1 5 10

<210> 3
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR2 sequence

<400> 3

Cys Ile Ser Gly Ser Ser Gly Ser Thr Tyr Tyr Pro Asp Ser Val Lys
1 5 10 15

Gly

<210> 4
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> CDR2 sequence

<400> 4

Cys Ile Ser Ser Ser His Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

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

<220>
<223> CDR3 sequence

<400> 5

Ile Arg Ser Ser Ser Trp Gly Gly Cys Val His Tyr Gly Met Asp Tyr
 1 5 10 15

<210> 6
 <211> 16
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> CDR3 sequence

<400> 6

Val Ala Val Ala His Phe Arg Gly Cys Gly Val Asp Gly Met Asp Tyr
 1 5 10 15

<210> 7
 <211> 396
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> single domain antibody DS-Cav1-4

<220>
 <221> CDS
 <222> (1)..(396)

<400> 7
 cag gtg cag ctg cag gag tct ggg gga ggc ttg gtg cag cct ggg ggg 48
 Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

tct ctg aga ctc tcc tgt gca gcc tct gga ttc act ttg gat tat tat 96
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Asp Tyr Tyr
 20 25 30

tac ata ggc tgg ttc cgc cag gcc cca ggg aag gag cgc gag gca gtc 144
 Tyr Ile Gly Trp Phe Arg Gln Ala Pro Gly Lys Glu Arg Glu Ala Val
 35 40 45

tca tgt att agt ggt agt agt ggt agc aca tac tat cca gac tcc gtg 192
 Ser Cys Ile Ser Gly Ser Ser Gly Ser Thr Tyr Tyr Pro Asp Ser Val
 50 55 60

aag ggc cga ttc acc atc tcc aga gac aat gcc aag aac acg gtg tat 240
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Val Tyr

65	70	75	80	
ctg caa atg aac agc	ctg aaa cct gag gac	acg gcc gtt tat tac tgt		288
Leu Gln Met Asn Ser	Leu Lys Pro Glu Asp Thr	Ala Val Tyr Tyr Cys		
	85	90	95	
gcg aca att cgt agt agt agc	tgg ggg ggt tgc gtg cac	tac ggc atg		336
Ala Thr Ile Arg Ser Ser Ser	Trp Gly Gly Cys Val His	Tyr Gly Met		
	100	105	110	
gac tac tgg ggc aaa ggg acc	cag gtc acc gtc tcc agc	cac cac cat		384
Asp Tyr Trp Gly Lys Gly Thr	Gln Val Thr Val Ser Ser	His His His		
	115	120	125	
cac cat cac tag				396
His His His				
	130			

<210> 8
 <211> 131
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 8

Gln Val Gln Leu Gln 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 Thr Leu Asp Tyr Tyr
20 25 30

Tyr Ile Gly Trp Phe Arg Gln Ala Pro Gly Lys Glu Arg Glu Ala Val
35 40 45

Ser Cys Ile Ser Gly Ser Ser Gly Ser Thr Tyr Tyr Pro Asp Ser Val
50 55 60

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

Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Ala Val Tyr Tyr Cys

85

90

95

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

Asp Tyr Trp Gly Lys Gly Thr Gln Val Thr Val Ser Ser His His His
 115 120 125

His His His
 130

<210> 9

<211> 396

<212> DNA

<213> Artificial Sequence

<220>

<223> Single domain antibody DS-Cav1-L66

<220>

<221> CDS

<222> (1)..(396)

<400> 9

cag gtg cag ctg cag gag tct ggg gga ggc ttg gtg cag cct ggg ggg 48
 Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

tct ctg aga ctc tcc tgt gca gcc tct gga ttc act ttg gat tat tat 96
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Leu Asp Tyr Tyr
 20 25 30

tac ata ggc tgg ttc cgc cag gcc cca ggg aag gag cgc gag ggg gtc 144
 Tyr Ile Gly Trp Phe Arg Gln Ala Pro Gly Lys Glu Arg Glu Gly Val
 35 40 45

tca tgt att agt agt agt cat ggt agc aca tac tat gca gac tcc gtg 192
 Ser Cys Ile Ser Ser Ser His Gly Ser Thr Tyr Tyr Ala Asp Ser Val
 50 55 60

aag ggc cga ttc acc atc tcc aga gac aat gcc aag aac acg gtg tat 240
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Val Tyr
 65 70 75 80

ctg cag atg aac agc ctg aaa cct gag gac acg gcc gtt tat tac tgt 288

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

gcg aca gta gct gta gca cat ttc cgg ggt tgc gga gtc gac ggc atg 336
Ala Thr Val Ala Val Ala His Phe Arg Gly Cys Gly Val Asp Gly Met
100 105 110

gac tac tgg ggc aaa ggg acc cag gtc acc gtc tcc agc cac cac cat 384
Asp Tyr Trp Gly Lys Gly Thr Gln Val Thr Val Ser Ser His His His
115 120 125

cac cat cac tag 396
His His His
130

<210> 10
<211> 131
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 10

Gln Val Gln Leu Gln 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 Thr Leu Asp Tyr Tyr
20 25 30

Tyr Ile Gly Trp Phe Arg Gln Ala Pro Gly Lys Glu Arg Glu Gly Val
35 40 45

Ser Cys Ile Ser Ser Ser His Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

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

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

Ala Thr Val Ala Val Ala His Phe Arg Gly Cys Gly Val Asp Gly Met
100 105 110

Asp Tyr Trp Gly Lys Gly Thr Gln Val Thr Val Ser Ser His His His
115 120 125

His His His
130

<210> 11
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 11
caggaaacag ctatgacc 18

<210> 12
<211> 47
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 12
ggcgggtatc tctcgagaaa aggcaggtgc agctgcagga gtctggg 47

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

<220>
<223> Primer

<400> 13
ctaactagtc tagtgatggt gatggtggtg gctggagacg gtgacctgg 49

<210> 14
<211> 20

<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 14
tcacgaaggc tccacataca 20

<210> 15
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Primer

<400> 15
gcagggtcat cgtctttttc 20

<210> 16
<211> 461
<212> PRT
<213> Artificial Sequence

<220>
<223> prefusion-stabilized RSV F protein (figure 11a+b)

<400> 16

Gln Asn Ile Thr Glu Glu Phe Tyr Gln Ser Thr Cys Ser Ala Val Ser
1 5 10 15

Lys Gly Tyr Leu Ser Ala Leu Arg Thr Gly Trp Tyr Thr Ser Val Ile
20 25 30

Thr Ile Glu Leu Ser Asn Ile Lys Glu Asn Lys Cys Asn Gly Thr Asp
35 40 45

Ala Lys Val Lys Leu Ile Lys Gln Glu Leu Asp Lys Tyr Lys Asn Ala
50 55 60

Val Thr Glu Leu Gln Leu Leu Met Gln Ser Thr Pro Ala Thr Asn Asn
65 70 75 80

Arg Ala Arg Arg Phe Leu Gly Phe Leu Leu Gly Val Gly Ser Ala Ile
85 90 95

Ala Ser Gly Val Ala Val Cys Lys Val Leu His Leu Glu Gly Glu Val
100 105 110

Asn Lys Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys Ala Val Val Ser
115 120 125

Leu Ser Asn Gly Val Ser Val Leu Thr Phe Lys Val Leu Asp Leu Lys
130 135 140

Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Leu Asn Lys Gln Ser Cys
145 150 155 160

Ser Ile Ser Asn Ile Glu Thr Val Ile Glu Phe Gln Gln Lys Asn Asn
165 170 175

Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn Ala Gly Val Thr
180 185 190

Thr Pro Val Ser Thr Tyr Met Leu Thr Asn Ser Glu Leu Leu Ser Leu
195 200 205

Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys Leu Met Ser Asn
210 215 220

Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile Met Cys Ile Ile
225 230 235 240

Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro Leu Tyr Gly Val
245 250 255

Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro Leu Cys Thr Thr
260 265 270

Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg Thr Asp Arg Gly
275 280 285

Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe Pro Gln Ala Glu
290 295 300

Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp Thr Met Asn Ser
305 310 315 320

Leu Thr Leu Pro Ser Glu Val Asn Leu Cys Asn Val Asp Ile Phe Asn
325 330 335

Pro Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr Asp Val Ser Ser
340 345 350

Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys Tyr Gly Lys Thr
355 360 365

Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile Lys Thr Phe Ser
370 375 380

Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp Thr Val Ser Val
385 390 395 400

Gly Asn Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly Lys Ser Leu Tyr
405 410 415

Val Lys Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro Leu Val Phe Pro
420 425 430

Ser Asp Glu Phe Asp Ala Ser Ile Ser Gln Val Asn Glu Lys Ile Asn
435 440 445

Gln Ser Leu Ala Phe Ile Arg Lys Ser Asp Glu Leu Leu
450 455 460

<210> 17

<211> 568

<212> PRT

<213> Artificial Sequence

<220>

<223> prefusion-stabilized RSV F protein (figure 11c)

<400> 17

Met Glu Leu Leu Ile Leu Lys Ala Asn Ala Ile Thr Thr Ile Leu Thr
1 5 10 15

Ala Val Thr Phe Cys Phe Ala Ser Gly Gln Asn Ile Thr Glu Glu Phe
20 25 30

Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
35 40 45

Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
50 55 60

Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65 70 75 80

Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
85 90 95

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

Arg Phe Met Asn Tyr Thr Leu Asn Asn Ala Lys Lys Thr Asn Val Thr
115 120 125

Leu Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val
130 135 140

Gly Ser Ala Ile Ala Ser Gly Val Ala Val Cys Lys Val Leu His Leu
145 150 155 160

Glu Gly Glu Val Asn Lys Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys
165 170 175

Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Phe Lys Val
180 185 190

Leu Asp Leu Lys Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Leu Asn
195 200 205

Lys Gln Ser Cys Ser Ile Ser Asn Ile Glu Thr Val Ile Glu Phe Gln
210 215 220

Gln Lys Asn Asn Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn
225 230 235 240

Ala Gly Val Thr Thr Pro Val Ser Thr Tyr Met Leu Thr Asn Ser Glu
245 250 255

Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
260 265 270

Leu Met Ser Asn Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
275 280 285

Met Cys Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
290 295 300

Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
305 310 315 320

Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg
325 330 335

Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe
340 345 350

Pro Gln Ala Glu Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp
355 360 365

Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Val Asn Leu Cys Asn Val
370 375 380

Asp Ile Phe Asn Pro Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr
385 390 395 400

Asp Val Ser Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys
405 410 415

Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile
420 425 430

Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp
435 440 445

Thr Val Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly
450 455 460

Lys Ser Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro
465 470 475 480

Leu Val Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ser Gln Val Asn
485 490 495

Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Lys Ser Asp Glu Leu
500 505 510

Leu Ser Ala Ile Gly Gly Tyr Ile Pro Glu Ala Pro Arg Asp Gly Gln
515 520 525

Ala Tyr Val Arg Lys Asp Gly Glu Trp Val Leu Leu Ser Thr Phe Leu
530 535 540

Gly Gly Leu Val Pro Arg Gly Ser His His His His His His Ser Ala
545 550 555 560

Trp Ser His Pro Gln Phe Glu Lys
565

<210> 18
<211> 574
<212> PRT
<213> Artificial Sequence

<220>
<223> RSV A F consensus sequence

<400> 18

Met Glu Leu Pro Ile Leu Lys Thr Asn Ala Ile Thr Thr Ile Leu Ala
1 5 10 15

Ala Val Thr Leu Cys Phe Ala Ser Ser Gln Asn Ile Thr Glu Glu Phe
20 25 30

Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu
35 40 45

Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
50 55 60

Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys
65 70 75 80

Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
85 90 95

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

Arg Phe Met Asn Tyr Thr Leu Asn Asn Thr Lys Asn Asn Asn Val Thr
115 120 125

Leu Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val
130 135 140

Gly Ser Ala Ile Ala Ser Gly Ile Ala Val Ser Lys Val Leu His Leu
145 150 155 160

Glu Gly Glu Val Asn Lys Ile Lys Asn Ala Leu Leu Ser Thr Asn Lys
165 170 175

Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Ser Lys Val
180 185 190

Leu Asp Leu Lys Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Val Asn
195 200 205

Lys Gln Ser Cys Ser Ile Ser Asn Ile Glu Thr Val Ile Glu Phe Gln
210 215 220

Gln Lys Asn Asn Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn
225 230 235 240

Ala Gly Val Thr Thr Pro Val Ser Thr Tyr Met Leu Thr Asn Ser Glu
245 250 255

Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
260 265 270

Leu Met Ser Asn Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
275 280 285

Met Ser Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
290 295 300

Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
305 310 315 320

Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg
325 330 335

Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe
340 345 350

Pro Gln Ala Glu Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp
355 360 365

Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Val Asn Leu Cys Asn Ile
370 375 380

Asp Ile Phe Asn Pro Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr
385 390 395 400

Asp Val Ser Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys
405 410 415

Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile
420 425 430

Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp
435 440 445

Thr Val Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly
450 455 460

Lys Ser Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro
465 470 475 480

Leu Val Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ser Gln Val Asn
485 490 495

Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Lys Ser Asp Glu Leu
500 505 510

Leu His Asn Val Asn Val Gly Lys Ser Thr Thr Asn Ile Met Ile Thr
515 520 525

Thr Ile Ile Ile Val Ile Ile Val Ile Leu Leu Leu Leu Ile Ala Val
530 535 540

Gly Leu Phe Leu Tyr Cys Lys Ala Arg Ser Thr Pro Val Thr Leu Ser
545 550 555 560

Lys Asp Gln Leu Ser Gly Ile Asn Asn Ile Ala Phe Ser Asn
565 570

<210> 19
<211> 574
<212> PRT
<213> Artificial Sequence

<220>
<223> RSV B F consensus sequence

<400> 19

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

Ile Asn Ala Leu Tyr Leu Thr Ser Ser Gln Asn Ile Thr Glu Glu Phe
20 25 30

Tyr Gln Ser Thr Cys Ser Ala Val Ser Arg Gly Tyr Leu Ser Ala Leu
35 40 45

Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile
50 55 60

Lys Glu Thr Lys Cys Asn Gly Thr Asp Thr Lys Val Lys Leu Ile Lys
65 70 75 80

Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu
85 90 95

Met Gln Asn Thr Pro Ala Ala Asn Asn Arg Ala Arg Arg Glu Ala Pro
100 105 110

Gln Tyr Met Asn Tyr Thr Ile Asn Thr Thr Lys Asn Leu Asn Val Ser
115 120 125

Ile Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val
130 135 140

Gly Ser Ala Ile Ala Ser Gly Ile Ala Val Ser Lys Val Leu His Leu
145 150 155 160

Glu Gly Glu Val Asn Lys Ile Lys Asn Ala Leu Leu Ser Thr Asn Lys
165 170 175

Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Ser Lys Val
180 185 190

Leu Asp Leu Lys Asn Tyr Ile Asn Asn Gln Leu Leu Pro Ile Val Asn
195 200 205

Gln Gln Ser Cys Arg Ile Ser Asn Ile Glu Thr Val Ile Glu Phe Gln
210 215 220

Gln Lys Asn Ser Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn
225 230 235 240

Ala Gly Val Thr Thr Pro Leu Ser Thr Tyr Met Leu Thr Asn Ser Glu
245 250 255

Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys
260 265 270

Leu Met Ser Ser Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile
275 280 285

Met Ser Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro
290 295 300

Ile Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro
305 310 315 320

Leu Cys Thr Thr Asn Ile Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg
325 330 335

Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe
340 345 350

Pro Gln Ala Asp Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp
355 360 365

Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Val Ser Leu Cys Asn Thr
370 375 380

Asp Ile Phe Asn Ser Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr
385 390 395 400

Asp Ile Ser Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys
405 410 415

Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile
420 425 430

Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp
435 440 445

Thr Val Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Leu Glu Gly
450 455 460

Lys Asn Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Tyr Tyr Asp Pro
465 470 475 480

Leu Val Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ser Gln Val Asn
485 490 495

Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Arg Ser Asp Glu Leu
500 505 510

Leu His Asn Val Asn Thr Gly Lys Ser Thr Thr Asn Ile Met Ile Thr
515 520 525

Ala Ile Ile Ile Val Ile Ile Val Val Leu Leu Ser Leu Ile Ala Ile
530 535 540

Gly Leu Leu Leu Tyr Cys Lys Ala Lys Asn Thr Pro Val Thr Leu Ser
545 550 555 560

Lys Asp Gln Leu Ser Gly Ile Asn Asn Ile Ala Phe Ser Lys
565 570