

SEQUENCE LISTING

<110> ONCOTHERAPY SCIENCE, INC.

<120> ANTI-MELK MONOCLONAL ANTIBODY AND USE THEREOF

<130> ONC-A1606P

<150> JP 2016-169085

<151> 2016-08-31

<160> 22

<170> PatentIn version 3.5

<210> 1

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<212> PRT

<213> Artificial Sequence

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<223> VH CDR1

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Asp Tyr Tyr Met His

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10

15

Gly

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Leu Val Lys Leu Ser Cys Lys Ala Ser Gly Phe Asn Ile Lys Asp Tyr
20 25 30

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

Gly Trp Ile Asp Pro Glu Asn Gly Asn Thr Ile Tyr Asp Pro Lys Phe
50 55 60

Gln Gly Lys Ala Ser Val Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr
65 70 75 80

Leu Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
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Thr Ser His His Tyr Ser Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
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Val Thr Val Ser Ser
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			20					25					30		

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

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

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

Thr	Tyr	Val	Pro	Leu	Thr	Phe	Gly	Ala	Gly	Thr	Lys	Leu	Glu	Leu	Lys
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Arg	Ala	Asp
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<223> MELK fragment for immunogen

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20 25 30

Asn Asn Arg Gln Thr Met Glu Asp Leu Ile Ser Leu Trp Gln Tyr Asp
35 40 45

His Leu Thr Ala Thr Tyr Leu Leu Leu Leu Ala Lys Lys Ala Arg Gly
50 55 60

Lys Pro Val Arg Leu Arg Leu Ser Ser Phe Ser Cys Gly Gln Ala Ser
65 70 75 80

Ala Thr Pro Phe Thr Asp Ile Lys Ser Asn Asn Trp Ser Leu Glu Asp
85 90 95

Val Thr Ala Ser Asp Lys Asn Tyr Val Ala Gly Leu Ile Asp Tyr Asp
100 105 110

Trp Cys Glu Asp Asp Leu Ser Thr Gly Ala Ala Thr Pro Arg Thr Ser
115 120 125

Gln Phe Thr Lys Tyr Trp Thr Glu Ser Asn Gly Val Glu Ser Lys Ser
130 135 140

Leu Thr Pro Ala Leu Cys Arg Thr Pro Ala Asn Lys Leu Lys Asn Lys
145 150 155 160

Glu Asn Val Tyr Thr Pro Lys Ser Ala Val Lys Asn Glu Glu Tyr Phe
165 170 175

Met Phe Pro Glu Pro Lys Thr Pro Val Asn Lys Asn Gln His Lys Arg
180 185 190

Glu Ile Leu Thr Thr Pro Asn Arg Tyr Thr Thr Pro Ser Lys Ala Arg
 195 200 205

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

Gly Thr Asp Lys Leu Met Thr Gly Val Ile Ser Pro Glu Arg Arg Cys
 225 230 235 240

Arg Ser Val Glu Leu Asp Leu Asn Gln Ala His Met Glu Glu Thr Pro
 245 250 255

Lys Arg Lys Gly Ala Lys Val Phe Gly Ser Leu Glu Arg Gly Leu Asp
 260 265 270

Lys Val Ile Thr Val Leu Thr Arg Ser Lys Arg Lys Gly Ser Ala Arg
 275 280 285

Asp Gly Pro Arg Arg Leu Lys Leu His Tyr Asn Val Thr Thr Thr Arg
 290 295 300

Leu Val Asn Pro Asp Gln Leu Leu Asn Glu Ile Met Ser Ile Leu Pro
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Thr Gln

<210> 10

<211> 351

<212> DNA

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 cctgaacagg gcctggagtg gattggatgg attgatcctg agaatggtaa tactatatat 180
 gacccgaagt tccagggcaa ggccagtgtg acagcagaca catcctccaa cacagcctac 240
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 tacctgcaga agccaggcca gtctccaaaa ctctgatct acaaagtttc caaccgattt 180
 tctgggggtcc cagacaggtt cagtggcagt ggatcaggga cagatttcac actcataatc 240
 agcagagtgg aggctgagga tctgggagtt tatttctgct ctcaaagtac atatgttcg 300
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<210> 12
 <211> 18
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> An artificially synthesized forward primer sequence for MELK

<400> 12
 atgatcacct cacggcta 18

<210> 13
 <211> 17

<212> DNA
 <213> Artificial Sequence

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<223> An artificially synthesized reverse primer sequence for MELK

<400> 13

aggtgttctg cataagg

17

<210> 14

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> An artificially synthesized forward primer sequence for
 beta-actin

<400> 14

aggatgcaga aggagatcac

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<210> 15

<211> 20

<212> DNA

<213> Artificial Sequence

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<223> An artificially synthesized reverse primer sequence for
 beta-actin

<400> 15

agaaagggtg taacgcaact

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<210> 16

<211> 18

<212> DNA

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<223> An artificially synthesized 3' primer sequence for VH

<400> 16

ctgggaaggt gtgcacac

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<210> 17

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<223> An artificially synthesized 3' primer sequence for VL

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gtgtttcaag aagcacacga c

21

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<223> An artificially synthesized 5' primer sequence for VH and VL

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<222> (24)..(25)

<223> n is inosine

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tggacaggga tccagagttc c

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<223> An artificially synthesized 3' primer sequence for VL

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cagatgttaa ctgctcactg gatgg

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<210> 21
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<309> 2015-09-25

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gtcagccgt gccctccgcc cctcaggttc tttttctaata tccaaataaa cttgcaagag 180

gact atg aaa gat tat gat gaa ctt ctc aaa tat tat gaa tta cat gaa 229

Met Lys Asp Tyr Asp Glu Leu Leu Lys Tyr Tyr Glu Leu His Glu
 1 5 10 15

act att ggg aca ggt ggc ttt gca aag gtc aaa ctt gcc tgc cat atc 277

Thr Ile Gly Thr Gly Gly Phe Ala Lys Val Lys Leu Ala Cys His Ile
 20 25 30

ctt act gga gag atg gta gct ata aaa atc atg gat aaa aac aca cta 325

Leu Thr Gly Glu Met Val Ala Ile Lys Ile Met Asp Lys Asn Thr Leu
 35 40 45

ggg agt gat ttg ccc cgg atc aaa acg gag att gag gcc ttg aag aac 373

Gly	Ser	Asp	Leu	Pro	Arg	Ile	Lys	Thr	Glu	Ile	Glu	Ala	Leu	Lys	Asn	
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Leu	Arg	His	Gln	His	Ile	Cys	Gln	Leu	Tyr	His	Val	Leu	Glu	Thr	Ala	
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aac	aaa	ata	ttc	atg	gtt	ctt	gag	tac	tgc	cct	gga	gga	gag	ctg	ttt	469
Asn	Lys	Ile	Phe	Met	Val	Leu	Glu	Tyr	Cys	Pro	Gly	Gly	Glu	Leu	Phe	
80					85					90					95	
gac	tat	ata	att	tcc	cag	gat	cgc	ctg	tca	gaa	gag	gag	acc	cgg	gtt	517
Asp	Tyr	Ile	Ile	Ser	Gln	Asp	Arg	Leu	Ser	Glu	Glu	Glu	Thr	Arg	Val	
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gtc	ttc	cgt	cag	ata	gta	tct	gct	gtt	gct	tat	gtg	cac	agc	cag	ggc	565
Val	Phe	Arg	Gln	Ile	Val	Ser	Ala	Val	Ala	Tyr	Val	His	Ser	Gln	Gly	
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tat	gct	cac	agg	gac	ctc	aag	cca	gaa	aat	ttg	ctg	ttt	gat	gaa	tat	613
Tyr	Ala	His	Arg	Asp	Leu	Lys	Pro	Glu	Asn	Leu	Leu	Phe	Asp	Glu	Tyr	
	130						135					140				
cat	aaa	tta	aag	ctg	att	gac	ttt	ggt	ctc	tgt	gca	aaa	ccc	aag	ggt	661
His	Lys	Leu	Lys	Leu	Ile	Asp	Phe	Gly	Leu	Cys	Ala	Lys	Pro	Lys	Gly	
	145					150					155					
aac	aag	gat	tac	cat	cta	cag	aca	tgc	tgt	ggg	agt	ctg	gct	tat	gca	709
Asn	Lys	Asp	Tyr	His	Leu	Gln	Thr	Cys	Cys	Gly	Ser	Leu	Ala	Tyr	Ala	
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Ala	Pro	Glu	Leu	Ile	Gln	Gly	Lys	Ser	Tyr	Leu	Gly	Ser	Glu	Ala	Asp	
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gtt	tgg	agc	atg	ggc	ata	ctg	tta	tat	gtt	ctt	atg	tgt	gga	ttt	cta	805
Val	Trp	Ser	Met	Gly	Ile	Leu	Leu	Tyr	Val	Leu	Met	Cys	Gly	Phe	Leu	
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Pro	Phe	Asp	Asp	Asp	Asn	Val	Met	Ala	Leu	Tyr	Lys	Lys	Ile	Met	Arg	
	210						215					220				
gga	aaa	tat	gat	gtt	ccc	aag	tgg	ctc	tct	ccc	agt	agc	att	ctg	ctt	901
Gly	Lys	Tyr	Asp	Val	Pro	Lys	Trp	Leu	Ser	Pro	Ser	Ser	Ile	Leu	Leu	
	225					230					235					
ctt	caa	caa	atg	ctg	cag	gtg	gac	cca	aag	aaa	cgg	att	tct	atg	aaa	949
Leu	Gln	Gln	Met	Leu	Gln	Val	Asp	Pro	Lys	Lys	Arg	Ile	Ser	Met	Lys	

240	245	250	255	
aat cta ttg aac cat ccc tgg atc atg caa gat tac aac tat cct gtt				997
Asn Leu Leu Asn His Pro Trp Ile Met Gln Asp Tyr Asn Tyr Pro Val				
	260	265	270	
gag tgg caa agc aag aat cct ttt att cac ctc gat gat gat tgc gta				1045
Glu Trp Gln Ser Lys Asn Pro Phe Ile His Leu Asp Asp Asp Cys Val				
	275	280	285	
aca gaa ctt tct gta cat cac aga aac aac agg caa aca atg gag gat				1093
Thr Glu Leu Ser Val His His Arg Asn Asn Arg Gln Thr Met Glu Asp				
	290	295	300	
tta att tca ctg tgg cag tat gat cac ctc acg gct acc tat ctt ctg				1141
Leu Ile Ser Leu Trp Gln Tyr Asp His Leu Thr Ala Thr Tyr Leu Leu				
	305	310	315	
ctt cta gcc aag aag gct cgg gga aaa cca gtt cgt tta agg ctt tot				1189
Leu Leu Ala Lys Lys Ala Arg Gly Lys Pro Val Arg Leu Arg Leu Ser				
	320	325	330	335
tct ttc tcc tgt gga caa gcc agt gct acc cca ttc aca gac atc aag				1237
Ser Phe Ser Cys Gly Gln Ala Ser Ala Thr Pro Phe Thr Asp Ile Lys				
	340	345	350	
tca aat aat tgg agt ctg gaa gat gtg acc gca agt gat aaa aat tat				1285
Ser Asn Asn Trp Ser Leu Glu Asp Val Thr Ala Ser Asp Lys Asn Tyr				
	355	360	365	
gtg gcg gga tta ata gac tat gat tgg tgt gaa gat gat tta tca aca				1333
Val Ala Gly Leu Ile Asp Tyr Asp Trp Cys Glu Asp Asp Leu Ser Thr				
	370	375	380	
ggt gct gct act ccc cga aca tca cag ttt acc aag tac tgg aca gaa				1381
Gly Ala Ala Thr Pro Arg Thr Ser Gln Phe Thr Lys Tyr Trp Thr Glu				
	385	390	395	
tca aat ggg gtg gaa tct aaa tca tta act cca gcc tta tgc aga aca				1429
Ser Asn Gly Val Glu Ser Lys Ser Leu Thr Pro Ala Leu Cys Arg Thr				
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cct gca aat aaa tta aag aac aaa gaa aat gta tat act cct aag tct				1477
Pro Ala Asn Lys Leu Lys Asn Lys Glu Asn Val Tyr Thr Pro Lys Ser				
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gct gta aag aat gaa gag tac ttt atg ttt cct gag cca aag act cca				1525
Ala Val Lys Asn Glu Glu Tyr Phe Met Phe Pro Glu Pro Lys Thr Pro				
	435	440	445	

gtt aat aag aac cag cat aag aga gaa ata ctc act acg cca aat cgt Val Asn Lys Asn Gln His Lys Arg Glu Ile Leu Thr Thr Pro Asn Arg 450 455 460	1573
tac act aca ccc tca aaa gct aga aac cag tgc ctg aaa gaa act cca Tyr Thr Thr Pro Ser Lys Ala Arg Asn Gln Cys Leu Lys Glu Thr Pro 465 470 475	1621
att aaa ata cca gta aat tca aca gga aca gac aag tta atg aca ggt Ile Lys Ile Pro Val Asn Ser Thr Gly Thr Asp Lys Leu Met Thr Gly 480 485 490 495	1669
gtc att agc cct gag agg cgg tgc cgc tca gtg gaa ttg gat ctc aac Val Ile Ser Pro Glu Arg Arg Cys Arg Ser Val Glu Leu Asp Leu Asn 500 505 510	1717
caa gca cat atg gag gag act cca aaa aga aag gga gcc aaa gtg ttt Gln Ala His Met Glu Glu Thr Pro Lys Arg Lys Gly Ala Lys Val Phe 515 520 525	1765
ggg agc ctt gaa agg ggg ttg gat aag gtt atc act gtg ctc acc agg Gly Ser Leu Glu Arg Gly Leu Asp Lys Val Ile Thr Val Leu Thr Arg 530 535 540	1813
agc aaa agg aag ggt tct gcc aga gac ggg ccc aga aga cta aag ctt Ser Lys Arg Lys Gly Ser Ala Arg Asp Gly Pro Arg Arg Leu Lys Leu 545 550 555	1861
cac tat aac gtg act aca act aga tta gtg aat cca gat caa ctg ttg His Tyr Asn Val Thr Thr Thr Arg Leu Val Asn Pro Asp Gln Leu Leu 560 565 570 575	1909
aat gaa ata atg tct att ctt cca aag aag cat gtt gac ttt gta caa Asn Glu Ile Met Ser Ile Leu Pro Lys Lys His Val Asp Phe Val Gln 580 585 590	1957
aag ggt tat aca ctg aag tgt caa aca cag tca gat ttt ggg aaa gtg Lys Gly Tyr Thr Leu Lys Cys Gln Thr Gln Ser Asp Phe Gly Lys Val 595 600 605	2005
aca atg caa ttt gaa tta gaa gtg tgc cag ctt caa aaa ccc gat gtg Thr Met Gln Phe Glu Leu Glu Val Cys Gln Leu Gln Lys Pro Asp Val 610 615 620	2053
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aga tta gtg gaa gac atc cta tct agc tgc aag gta taa ttgatggatt      2150
Arg Leu Val Glu Asp Ile Leu Ser Ser Cys Lys Val
640                      645                      650

cttcacatcct gccggatgag tgtgggtgtg atacagccta cataaagact gttatgatcg  2210

ctttgatttt aaagttcatt ggaactacca acttgtttct aaagagctat ctttaagacca  2270

atatctcttt gtttttaaac aaaagatatt attttgtgta tgaatctaaa tcaagcccat  2330

ctgtcattat gttactgtct tttttaatca tgtggttttg tatattaata attgttgact  2390

ttottagatt cacttccata tgtgaatgta agctottaac tatgtctctt tgtaatgtgt  2450

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<210> 22
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<213> Homo sapiens

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                20                      25                      30

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Thr Gly Glu Met Val Ala Ile Lys Ile Met Asp Lys Asn Thr Leu Gly
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Ser Asp Leu Pro Arg Ile Lys Thr Glu Ile Glu Ala Leu Lys Asn Leu
50                      55                      60

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Arg His Gln His Ile Cys Gln Leu Tyr His Val Leu Glu Thr Ala Asn
65                      70                      75                      80

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Lys Ile Phe Met Val Leu Glu Tyr Cys Pro Gly Gly Glu Leu Phe Asp
        85                      90                      95

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Tyr Ile Ile Ser Gln Asp Arg Leu Ser Glu Glu Glu Thr Arg Val Val

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

Ile Ser Leu Trp Gln Tyr Asp His Leu Thr Ala Thr Tyr Leu Leu Leu
305 310 315 320

Leu Ala Lys Lys Ala Arg Gly Lys Pro Val Arg Leu Arg Leu Ser Ser
325 330 335

Phe Ser Cys Gly Gln Ala Ser Ala Thr Pro Phe Thr Asp Ile Lys Ser
340 345 350

Asn Asn Trp Ser Leu Glu Asp Val Thr Ala Ser Asp Lys Asn Tyr Val
355 360 365

Ala Gly Leu Ile Asp Tyr Asp Trp Cys Glu Asp Asp Leu Ser Thr Gly
370 375 380

Ala Ala Thr Pro Arg Thr Ser Gln Phe Thr Lys Tyr Trp Thr Glu Ser
385 390 395 400

Asn Gly Val Glu Ser Lys Ser Leu Thr Pro Ala Leu Cys Arg Thr Pro
405 410 415

Ala Asn Lys Leu Lys Asn Lys Glu Asn Val Tyr Thr Pro Lys Ser Ala
420 425 430

Val Lys Asn Glu Glu Tyr Phe Met Phe Pro Glu Pro Lys Thr Pro Val
435 440 445

Asn Lys Asn Gln His Lys Arg Glu Ile Leu Thr Thr Pro Asn Arg Tyr
450 455 460

Thr Thr Pro Ser Lys Ala Arg Asn Gln Cys Leu Lys Glu Thr Pro Ile
465 470 475 480

Lys Ile Pro Val Asn Ser Thr Gly Thr Asp Lys Leu Met Thr Gly Val
485 490 495

Ile Ser Pro Glu Arg Arg Cys Arg Ser Val Glu Leu Asp Leu Asn Gln
 500 505 510

Ala His Met Glu Glu Thr Pro Lys Arg Lys Gly Ala Lys Val Phe Gly
 515 520 525

Ser Leu Glu Arg Gly Leu Asp Lys Val Ile Thr Val Leu Thr Arg Ser
 530 535 540

Lys Arg Lys Gly Ser Ala Arg Asp Gly Pro Arg Arg Leu Lys Leu His
 545 550 555 560

Tyr Asn Val Thr Thr Thr Arg Leu Val Asn Pro Asp Gln Leu Leu Asn
 565 570 575

Glu Ile Met Ser Ile Leu Pro Lys Lys His Val Asp Phe Val Gln Lys
 580 585 590

Gly Tyr Thr Leu Lys Cys Gln Thr Gln Ser Asp Phe Gly Lys Val Thr
 595 600 605

Met Gln Phe Glu Leu Glu Val Cys Gln Leu Gln Lys Pro Asp Val Val
 610 615 620

Gly Ile Arg Arg Gln Arg Leu Lys Gly Asp Ala Trp Val Tyr Lys Arg
 625 630 635 640

Leu Val Glu Asp Ile Leu Ser Ser Cys Lys Val
 645 650