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ASTRAZENECA PHARMACEUTICALS LP

<120> METHODS FOR TREATING HEPCIDIN-MEDIATED DISORDERS

<130> 32601-34392/PCT

<140> PCT/US2016/044528

<141> 2016-07-28

<150> 62/268,788

<151> 2015-12-17

<150> 62/199,434

<151> 2015-07-31

<160> 25

<170> PatentIn version 3.5

<210> 1

<211> 84

<212> PRT

<213> Homo sapiens

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Arg Glu Ser Ser Ala Phe Arg Ser Glu Thr Ala Lys Ala Gln Lys Met
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Gln Gly Pro Lys Asp Leu Met Leu Lys Leu Arg Leu Glu Trp Thr Leu
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Asp Tyr Asp Val Ala Leu Leu Gln Leu Asp His Pro Val Val Arg Ser
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Gln Val Thr Pro Arg Met Leu Cys Ala Gly Tyr Arg Lys Gly Lys Lys
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Tyr Phe Leu Gly Tyr Lys Ala Glu Val Met Val Ser Gln Val Tyr Ser
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Leu Lys Glu Leu Ile Thr Ser Thr Arg Leu Gly Thr Tyr Tyr Asn Ser
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Leu Val Ile Leu Glu Ala Ser Val Lys Asp Ile Ala Ala Leu Asn Ser
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Thr Leu Gly Cys Tyr Arg Tyr Ser Tyr Val Gly Gln Gly Gln Val Leu
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Arg Leu Lys Gly Pro Asp His Leu Ala Ser Ser Cys Leu Trp His Leu
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Gln Gly Pro Lys Asp Leu Met Leu Lys Leu Arg Leu Glu Trp Thr Leu
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Glu Lys Arg Leu Ile Thr Ser Val Tyr Gly Cys Ser Arg Gln Glu Pro
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Val Val Glu Val Leu Ala Ser Gly Ala Ile Met Ala Val Val Trp Lys
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Lys Gly Leu His Ser Tyr Tyr Asp Pro Phe Val Leu Ser Val Gln Pro
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Pro Gln Thr His Cys Ser Trp His Leu Thr Val Pro Ser Leu Asp Tyr
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Asp Leu Pro Cys Thr Gln Gly Gln Trp Thr Ile Gln Asn Arg Arg Leu
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Cys Gly Leu Arg Ile Leu Gln Pro Tyr Ala Glu Arg Ile Pro Val Val
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Cys Gly Gly Ala Leu Ile Ala Asp Arg Trp Val Ile Thr Ala Ala His
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Cys Phe Gln Glu Asp Ser Met Ala Ser Thr Val Leu Trp Thr Val Phe
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Leu Gly Lys Val Trp Gln Asn Ser Arg Trp Pro Gly Glu Val Ser Phe
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Lys Val Ser Arg Leu Leu Leu His Pro Tyr His Glu Glu Asp Ser His
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Gln Val Thr Pro Arg Met Leu Cys Ala Gly Tyr Arg Lys Gly Lys Lys
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770 775 780

Ser Gly Arg Trp Phe Leu Ala Gly Leu Val Ser Trp Gly Leu Gly Cys
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Gln Leu Cys Thr Ala Thr Gln Asp Thr Val Cys Arg Cys Arg Ala Gly
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Pro Pro Gly His Phe Ser Pro Gly Asp Asn Gln Ala Cys Lys Pro Trp
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aagaggcact ggcagaaaac aacctgaacc ttccaaagat ggctgaaaaa gatggatgct 420
tccaatctgg attcaatgag gagacttgcc tggtgaaaat catcactggg cttttggagt 480

ttgaggtata cctagagtac ctccagaaca gatttgagag tagtgaggaa caagccagag	540
ctgtgcagat gagtacaaaa gtcctgatcc agttcctgca gaaaaaggca aagaatctag	600
atgcaataac caccctgac ccaaccacaa atgccagcct gctgacgaag ctgcaggcac	660
agaaccagtg gctgcaggac atgacaactc atctcattct gcgcagcttt aaggagttcc	720
tgcagtccag cctgagggct cttcggcaaa tgtagcatgg gcacctcaga ttgttgttgt	780
taatgggcat tccttcttct ggtcagaaac ctgtccactg ggcacagaac ttatgttgtt	840
ctctatggag aactaaaagt atgagcgtta ggacactatt ttaattattt ttaatttatt	900
aatattttaa tatgtgaagc tgagttaatt tatgtaagtc atatttatat ttttaagaag	960
taccatttga aacattttat gtattagttt tgaaataata atggaaaagt gctatgcagt	1020
ttgaatatcc ttgttttcag agccagatca tttcttggaa agtgtaggct tacctcaaat	1080
aaatggctaa cttatacata tttttaaaga aatatttata ttgtatttat ataatgtata	1140
aatggttttt ataccaataa atggcatttt aaaaaattca gcaaaaaaaaa aaaaaaaaaa	1200
a	1201

<210> 8
 <211> 468
 <212> PRT
 <213> Homo sapiens

<400> 8
 Met Leu Ala Val Gly Cys Ala Leu Leu Ala Ala Leu Leu Ala Ala Pro
 1 5 10 15

 Gly Ala Ala Leu Ala Pro Arg Arg Cys Pro Ala Gln Glu Val Ala Arg
 20 25 30

 Gly Val Leu Thr Ser Leu Pro Gly Asp Ser Val Thr Leu Thr Cys Pro
 35 40 45

 Gly Val Glu Pro Glu Asp Asn Ala Thr Val His Trp Val Leu Arg Lys
 50 55 60

 Pro Ala Ala Gly Ser His Pro Ser Arg Trp Ala Gly Met Gly Arg Arg
 65 70 75 80

 Leu Leu Leu Arg Ser Val Gln Leu His Asp Ser Gly Asn Tyr Ser Cys

85

90

95

Tyr Arg Ala Gly Arg Pro Ala Gly Thr Val His Leu Leu Val Asp Val
 100 105 110

Pro Pro Glu Glu Pro Gln Leu Ser Cys Phe Arg Lys Ser Pro Leu Ser
 115 120 125

Asn Val Val Cys Glu Trp Gly Pro Arg Ser Thr Pro Ser Leu Thr Thr
 130 135 140

Lys Ala Val Leu Leu Val Arg Lys Phe Gln Asn Ser Pro Ala Glu Asp
 145 150 155 160

Phe Gln Glu Pro Cys Gln Tyr Ser Gln Glu Ser Gln Lys Phe Ser Cys
 165 170 175

Gln Leu Ala Val Pro Glu Gly Asp Ser Ser Phe Tyr Ile Val Ser Met
 180 185 190

Cys Val Ala Ser Ser Val Gly Ser Lys Phe Ser Lys Thr Gln Thr Phe
 195 200 205

Gln Gly Cys Gly Ile Leu Gln Pro Asp Pro Pro Ala Asn Ile Thr Val
 210 215 220

Thr Ala Val Ala Arg Asn Pro Arg Trp Leu Ser Val Thr Trp Gln Asp
 225 230 235 240

Pro His Ser Trp Asn Ser Ser Phe Tyr Arg Leu Arg Phe Glu Leu Arg
 245 250 255

Tyr Arg Ala Glu Arg Ser Lys Thr Phe Thr Thr Trp Met Val Lys Asp
 260 265 270

Leu Gln His His Cys Val Ile His Asp Ala Trp Ser Gly Leu Arg His
 275 280 285

Val Val Gln Leu Arg Ala Gln Glu Glu Phe Gly Gln Gly Glu Trp Ser
 290 295 300

Glu Trp Ser Pro Glu Ala Met Gly Thr Pro Trp Thr Glu Ser Arg Ser
305 310 315 320

Pro Pro Ala Glu Asn Glu Val Ser Thr Pro Met Gln Ala Leu Thr Thr
325 330 335

Asn Lys Asp Asp Asp Asn Ile Leu Phe Arg Asp Ser Ala Asn Ala Thr
340 345 350

Ser Leu Pro Val Gln Asp Ser Ser Ser Val Pro Leu Pro Thr Phe Leu
355 360 365

Val Ala Gly Gly Ser Leu Ala Phe Gly Thr Leu Leu Cys Ile Ala Ile
370 375 380

Val Leu Arg Phe Lys Lys Thr Trp Lys Leu Arg Ala Leu Lys Glu Gly
385 390 395 400

Lys Thr Ser Met His Pro Pro Tyr Ser Leu Gly Gln Leu Val Pro Glu
405 410 415

Arg Pro Arg Pro Thr Pro Val Leu Val Pro Leu Ile Ser Pro Pro Val
420 425 430

Ser Pro Ser Ser Leu Gly Ser Asp Asn Thr Ser Ser His Asn Arg Pro
435 440 445

Asp Ala Arg Asp Pro Arg Ser Pro Tyr Asp Ile Ser Asn Thr Asp Tyr
450 455 460

Phe Phe Pro Arg
465

<210> 9
<211> 918
<212> PRT
<213> Homo sapiens

<400> 9
Met Leu Thr Leu Gln Thr Trp Leu Val Gln Ala Leu Phe Ile Phe Leu
1 5 10 15

Thr Thr Glu Ser Thr Gly Glu Leu Leu Asp Pro Cys Gly Tyr Ile Ser
20 25 30

Pro Glu Ser Pro Val Val Gln Leu His Ser Asn Phe Thr Ala Val Cys
35 40 45

Val Leu Lys Glu Lys Cys Met Asp Tyr Phe His Val Asn Ala Asn Tyr
50 55 60

Ile Val Trp Lys Thr Asn His Phe Thr Ile Pro Lys Glu Gln Tyr Thr
65 70 75 80

Ile Ile Asn Arg Thr Ala Ser Ser Val Thr Phe Thr Asp Ile Ala Ser
85 90 95

Leu Asn Ile Gln Leu Thr Cys Asn Ile Leu Thr Phe Gly Gln Leu Glu
100 105 110

Gln Asn Val Tyr Gly Ile Thr Ile Ile Ser Gly Leu Pro Pro Glu Lys
115 120 125

Pro Lys Asn Leu Ser Cys Ile Val Asn Glu Gly Lys Lys Met Arg Cys
130 135 140

Glu Trp Asp Gly Gly Arg Glu Thr His Leu Glu Thr Asn Phe Thr Leu
145 150 155 160

Lys Ser Glu Trp Ala Thr His Lys Phe Ala Asp Cys Lys Ala Lys Arg
165 170 175

Asp Thr Pro Thr Ser Cys Thr Val Asp Tyr Ser Thr Val Tyr Phe Val
180 185 190

Asn Ile Glu Val Trp Val Glu Ala Glu Asn Ala Leu Gly Lys Val Thr
195 200 205

Ser Asp His Ile Asn Phe Asp Pro Val Tyr Lys Val Lys Pro Asn Pro
210 215 220

Pro His Asn Leu Ser Val Ile Asn Ser Glu Glu Leu Ser Ser Ile Leu

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

Ser Val Lys Lys Tyr Ile Leu Glu Trp Cys Val Leu Ser Asp Lys Ala
450 455 460

Pro Cys Ile Thr Asp Trp Gln Gln Glu Asp Gly Thr Val His Arg Thr
465 470 475 480

Tyr Leu Arg Gly Asn Leu Ala Glu Ser Lys Cys Tyr Leu Ile Thr Val
485 490 495

Thr Pro Val Tyr Ala Asp Gly Pro Gly Ser Pro Glu Ser Ile Lys Ala
500 505 510

Tyr Leu Lys Gln Ala Pro Pro Ser Lys Gly Pro Thr Val Arg Thr Lys
515 520 525

Lys Val Gly Lys Asn Glu Ala Val Leu Glu Trp Asp Gln Leu Pro Val
530 535 540

Asp Val Gln Asn Gly Phe Ile Arg Asn Tyr Thr Ile Phe Tyr Arg Thr
545 550 555 560

Ile Ile Gly Asn Glu Thr Ala Val Asn Val Asp Ser Ser His Thr Glu
565 570 575

Tyr Thr Leu Ser Ser Leu Thr Ser Asp Thr Leu Tyr Met Val Arg Met
580 585 590

Ala Ala Tyr Thr Asp Glu Gly Gly Lys Asp Gly Pro Glu Phe Thr Phe
595 600 605

Thr Thr Pro Lys Phe Ala Gln Gly Glu Ile Glu Ala Ile Val Val Pro
610 615 620

Val Cys Leu Ala Phe Leu Leu Thr Thr Leu Leu Gly Val Leu Phe Cys
625 630 635 640

Phe Asn Lys Arg Asp Leu Ile Lys Lys His Ile Trp Pro Asn Val Pro
645 650 655

Asp Pro Ser Lys Ser His Ile Ala Gln Trp Ser Pro His Thr Pro Pro

660					665					670					
Arg	His	Asn	Phe	Asn	Ser	Lys	Asp	Gln	Met	Tyr	Ser	Asp	Gly	Asn	Phe
		675					680					685			
Thr	Asp	Val	Ser	Val	Val	Glu	Ile	Glu	Ala	Asn	Asp	Lys	Lys	Pro	Phe
	690					695					700				
Pro	Glu	Asp	Leu	Lys	Ser	Leu	Asp	Leu	Phe	Lys	Lys	Glu	Lys	Ile	Asn
705					710					715					720
Thr	Glu	Gly	His	Ser	Ser	Gly	Ile	Gly	Gly	Ser	Ser	Cys	Met	Ser	Ser
				725					730					735	
Ser	Arg	Pro	Ser	Ile	Ser	Ser	Ser	Asp	Glu	Asn	Glu	Ser	Ser	Gln	Asn
			740					745						750	
Thr	Ser	Ser	Thr	Val	Gln	Tyr	Ser	Thr	Val	Val	His	Ser	Gly	Tyr	Arg
	755						760					765			
His	Gln	Val	Pro	Ser	Val	Gln	Val	Phe	Ser	Arg	Ser	Glu	Ser	Thr	Gln
	770					775					780				
Pro	Leu	Leu	Asp	Ser	Glu	Glu	Arg	Pro	Glu	Asp	Leu	Gln	Leu	Val	Asp
785					790					795					800
His	Val	Asp	Gly	Gly	Asp	Gly	Ile	Leu	Pro	Arg	Gln	Gln	Tyr	Phe	Lys
				805					810					815	
Gln	Asn	Cys	Ser	Gln	His	Glu	Ser	Ser	Pro	Asp	Ile	Ser	His	Phe	Glu
			820					825					830		
Arg	Ser	Lys	Gln	Val	Ser	Ser	Val	Asn	Glu	Glu	Asp	Phe	Val	Arg	Leu
		835					840					845			
Lys	Gln	Gln	Ile	Ser	Asp	His	Ile	Ser	Gln	Ser	Cys	Gly	Ser	Gly	Gln
	850					855					860				
Met	Lys	Met	Phe	Gln	Glu	Val	Ser	Ala	Ala	Asp	Ala	Phe	Gly	Pro	Gly
865					870					875					880

Thr Glu Gly Gln Val Glu Arg Phe Glu Thr Val Gly Met Glu Ala Ala
885 890 895

Thr Asp Glu Gly Met Pro Lys Ser Tyr Leu Pro Gln Thr Val Arg Gln
900 905 910

Gly Gly Tyr Met Pro Gln
915

<210> 10
<211> 193
<212> PRT
<213> Homo sapiens

<400> 10
Met Gly Val His Glu Cys Pro Ala Trp Leu Trp Leu Leu Leu Ser Leu
1 5 10 15

Leu Ser Leu Pro Leu Gly Leu Pro Val Leu Gly Ala Pro Pro Arg Leu
20 25 30

Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu Leu Glu Ala Lys Glu
35 40 45

Ala Glu Asn Ile Thr Thr Gly Cys Ala Glu His Cys Ser Leu Asn Glu
50 55 60

Asn Ile Thr Val Pro Asp Thr Lys Val Asn Phe Tyr Ala Trp Lys Arg
65 70 75 80

Met Glu Val Gly Gln Gln Ala Val Glu Val Trp Gln Gly Leu Ala Leu
85 90 95

Leu Ser Glu Ala Val Leu Arg Gly Gln Ala Leu Leu Val Asn Ser Ser
100 105 110

Gln Pro Trp Glu Pro Leu Gln Leu His Val Asp Lys Ala Val Ser Gly
115 120 125

Leu Arg Ser Leu Thr Thr Leu Leu Arg Ala Leu Gly Ala Gln Lys Glu
130 135 140

Ala Ile Ser Pro Pro Asp Ala Ala Ser Ala Ala Pro Leu Arg Thr Ile
 145 150 155 160

Thr Ala Asp Thr Phe Arg Lys Leu Phe Arg Val Tyr Ser Asn Phe Leu
 165 170 175

Arg Gly Lys Leu Lys Leu Tyr Thr Gly Glu Ala Cys Arg Thr Gly Asp
 180 185 190

Arg

<210> 11
 <211> 224
 <212> PRT
 <213> Homo sapiens

<400> 11
 Met Glu Lys Leu Leu Cys Phe Leu Val Leu Thr Ser Leu Ser His Ala
 1 5 10 15

Phe Gly Gln Thr Asp Met Ser Arg Lys Ala Phe Val Phe Pro Lys Glu
 20 25 30

Ser Asp Thr Ser Tyr Val Ser Leu Lys Ala Pro Leu Thr Lys Pro Leu
 35 40 45

Lys Ala Phe Thr Val Cys Leu His Phe Tyr Thr Glu Leu Ser Ser Thr
 50 55 60

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

Ile Leu Ile Phe Trp Ser Lys Asp Ile Gly Tyr Ser Phe Thr Val Gly
 85 90 95

Gly Ser Glu Ile Leu Phe Glu Val Pro Glu Val Thr Val Ala Pro Val
 100 105 110

His Ile Cys Thr Ser Trp Glu Ser Ala Ser Gly Ile Val Glu Phe Trp
 115 120 125

Val	Asp	Gly	Lys	Pro	Arg	Val	Arg	Lys	Ser	Leu	Lys	Lys	Gly	Tyr	Thr
130						135					140				

Val	Gly	Ala	Glu	Ala	Ser	Ile	Ile	Leu	Gly	Gln	Glu	Gln	Asp	Ser	Phe
145					150					155					160

Gly	Gly	Asn	Phe	Glu	Gly	Ser	Gln	Ser	Leu	Val	Gly	Asp	Ile	Gly	Asn
			165						170					175	

Val	Asn	Met	Trp	Asp	Phe	Val	Leu	Ser	Pro	Asp	Glu	Ile	Asn	Thr	Ile
		180						185					190		

Tyr	Leu	Gly	Gly	Pro	Phe	Ser	Pro	Asn	Val	Leu	Asn	Trp	Arg	Ala	Leu
		195					200					205			

Lys	Tyr	Glu	Val	Gln	Gly	Glu	Val	Phe	Thr	Lys	Pro	Gln	Leu	Trp	Pro
210						215					220				

<210> 12
 <211> 5
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic peptide

<400> 12
 Ser Asn Tyr Met Ile
 1 5

<210> 13
 <211> 17
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic peptide

<400> 13
 Asp Leu Tyr Tyr Tyr Ala Gly Asp Thr Tyr Tyr Ala Asp Ser Val Lys
 1 5 10 15

Gly

<210> 14
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 14
Trp Ala Asp Asp His Pro Pro Trp Ile Asp Leu
1 5 10

<210> 15
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 15
Arg Ala Ser Gln Gly Ile Ser Ser Trp Leu Ala
1 5 10

<210> 16
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 16
Lys Ala Ser Thr Leu Glu Ser
1 5

<210> 17
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 17

Gln Gln Ser Trp Leu Gly Gly Ser
1 5

<210> 18

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 18

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 Thr Ile Ser Ser Asn
20 25 30

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

Ser Asp Leu Tyr Tyr Tyr Ala Gly Asp Thr Tyr Tyr Ala Asp Ser Val
50 55 60

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

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

Ala Arg Trp Ala Asp Asp His Pro Pro Trp Ile Asp Leu Trp Gly Arg
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 Tyr Ile
245 250 255

Thr Arg Glu 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 Asn 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> 19

<211> 213

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 19

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

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Trp
 20 25 30

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

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

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

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Trp Leu Gly Gly Ser

85

90

95

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala Pro
 100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
 115 120 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
 130 135 140

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

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

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

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

Asn Arg Gly Glu Cys
 210

<210> 20

<211> 16

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 probe

<400> 20

cggctctgca gccttg

16

<210> 21

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic oligonucleotide

<400> 21
cttccaggag cgagatcccg ctaa 24

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

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 22
gcatgaggtc cttggggccc tgcag 25

<210> 23
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 23
ctgcagggcc ccaaggacct catgc 25

<210> 24
<211> 29
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 24
cctggtagcg ataggcctcg ctgcacagg 29

<210> 25
<211> 29
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic primer

<400> 25

cctgtgcagc gaggcctatc gctaccagg

29