

_Sequence_Listing_92116_ST25
SEQUENCE LISTING

<110> Genentech, Inc. et al.

<120> OPTIMIZED VARIANTS OF ANTI-VEGF ANTIBODIES

<130> 50474-110W03

<150> US 62/271,913

<151> 2015-12-28

<150> US 62/222,698

<151> 2015-09-23

<160> 69

<170> PatentIn version 3.5

<210> 1

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 1

Asp Tyr Trp Ile His

1 5

<210> 2

<211> 17

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<213> Artificial Sequence

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<220>

<221> MISC_FEATURE

<222> (2)..(2)

<223> Xaa is Ile or His

<220>

<221> MISC_FEATURE

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<222> (5)..(5)
<223> Xaa is Ala or Arg

<220>
<221> MISC_FEATURE
<222> (8)..(8)
<223> Xaa is Tyr or Lys

<220>
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<222> (9)..(9)
<223> Xaa is Thr or Glu

<220>
<221> MISC_FEATURE
<222> (10)..(10)
<223> Xaa is Arg, Tyr, Gln, or Glu

<220>
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<222> (12)..(12)
<223> Xaa is Ala or Glu

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<222> (16)..(16)
<223> Xaa is Lys or Glu

<220>
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<222> (17)..(17)
<223> Xaa is Gly or Glu

<400> 2

Gly	Xaa	Thr	Pro	Xaa	Gly	Gly	Xaa	Xaa	Xaa	Tyr	Xaa	Asp	Ser	Val	Xaa
1				5				10						15	

Xaa

<210> 3
<211> 11
<212> PRT
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_Sequence_Listing_92116_ST25

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<400> 3

Phe Val Phe Phe Leu Pro Tyr Ala Met Asp Tyr
1 5 10

<210> 4

<211> 11

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<220>

<221> MISC_FEATURE

<222> (5)..(5)

<223> Xaa is Asp or Arg

<400> 4

Arg Ala Ser Gln Xaa Val Ser Thr Ala Val Ala
1 5 10

<210> 5

<211> 7

<212> PRT

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<222> (1)..(1)

<223> Xaa is Ser or Met

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Xaa Ala Ser Phe Leu Tyr Ser
1 5

Sequence_Listing_92116_ST25

<210> 6
<211> 9
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<222> (1)..(1)
<223> Xaa is Gln, Asn, or Thr

<220>
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<222> (6)..(6)
<223> Xaa is Ala, Asn, Gln, or Arg

<400> 6

Xaa Gln Gly Tyr Gly Xaa Pro Phe Thr
1 5

<210> 7
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<400> 7

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

Gly

<210> 8
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_Sequence_Listing_92116_ST25

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<400> 8

Arg Ala Ser Gln Asp Val Ser Thr Ala Val Ala
1 5 10

<210> 9

<211> 7

<212> PRT

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<400> 9

Ser Ala Ser Phe Leu Tyr Ser
1 5

<210> 10

<211> 9

<212> PRT

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<400> 10

Gln Gln Gly Tyr Gly Ala Pro Phe Thr
1 5

<210> 11

<211> 120

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<400> 11

Sequence_Listing_92116_ST25

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 Asp Tyr
20 25 30

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

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

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

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

Ala Arg Phe Val Phe Phe Leu Pro Tyr Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 12

<211> 107

<212> PRT

<213> Artificial Sequence

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<223> Synthetic Construct

<400> 12

Asp 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 Arg Ala Ser Gln Asp Val Ser Thr Ala
20 25 30

Sequence_Listing_92116_ST25

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

Tyr Ser Ala Ser Phe Leu Tyr 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

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Gly Tyr Gly Ala Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 13
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<220>
<223> Synthetic Construct

<400> 13

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
20 25 30

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Sequence_Listing_92116_ST25

<400> 14

Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala
1 5 10

<210> 15

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<400> 15

Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr Leu Gln
1 5 10 15

Met Arg Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
20 25 30

<210> 16

<211> 11

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<220>

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<400> 16

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
1 5 10

<210> 17

<211> 23

<212> PRT

<213> Artificial Sequence

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<223> Synthetic Construct

<400> 17

_Sequence_Listing_92116_ST25

Asp 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
 20

<210> 18
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 18

Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
1 5 10 15

<210> 19
<211> 32
<212> PRT
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<220>
<223> Synthetic Construct

<400> 19

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
1 5 10 15

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

<210> 20
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<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

Sequence_Listing_92116_ST25

<400> 20

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
1 5 10

<210> 21

<211> 17

<212> PRT

<213> Artificial Sequence

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<223> Synthetic Construct

<400> 21

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

Gly

<210> 22

<211> 17

<212> PRT

<213> Artificial Sequence

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<223> Synthetic Construct

<400> 22

Gly Ile Thr Pro Ala Gly Gly Tyr Glu Tyr Tyr Ala Asp Ser Val Glu
1 5 10 15

Gly

<210> 23

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<212> PRT

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_Sequence_Listing_92116_ST25

<223> Synthetic Construct

<400> 23

Gln Gln Gly Tyr Gly Asn Pro Phe Thr
1 5

<210> 24

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<213> Artificial Sequence

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<223> Synthetic Construct

<400> 24

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
1 5 10 15

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
20 25 30

<210> 25

<211> 23

<212> PRT

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<400> 25

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

Asp Glu Val Thr Ile Thr Cys
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<210> 26

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Sequence_Listing_92116_ST25

<220>

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<400> 26

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

Asp	Glu	Val	Thr	Ile	Thr	Cys
			20			

<210> 27

<211> 15

<212> PRT

<213> Artificial Sequence

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<223> Synthetic Construct

<400> 27

Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Glu	Ala	Pro	Lys	Leu	Leu	Ile	Tyr
1				5					10					15

<210> 28

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<212> PRT

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<400> 28

Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr
1				5				10						15	

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

<210> 29

<211> 30

_Sequence_Listing_92116_ST25

<212> PRT

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<223> Synthetic Construct

<400> 29

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

Ser Leu Glu Leu Ser Cys Ala Ala Ser Gly Phe Glu Ile Ser
20 25 30

<210> 30

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

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<400> 30

Trp Val Arg Gln Glu Pro Gly Glu Gly Leu Glu Trp Val Ala
1 5 10

<210> 31

<211> 32

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 31

Arg Phe Thr Ile Ser Ala Asp Thr Ser Glu Asn Thr Ala Tyr Leu Gln
1 5 10 15

Met Asn Glu Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg
20 25 30

_Sequence_Listing_92116_ST25

<210> 32
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<400> 32

Trp Gly Gln Gly Glu Leu Val Thr Val Ser Ser
1 5 10

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<400> 33

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

Ser Leu Glu Leu Ser Cys Ala Ala Ser Gly Phe Glu Ile Ser Asp Tyr
20 25 30

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

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

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

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

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Ala Arg Phe Val Phe Phe Leu Pro Tyr Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Glu Leu Val Thr Val Ser Ser
115 120

<210> 34
<211> 107
<212> PRT
<213> Artificial Sequence

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<400> 34

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

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

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

Tyr Ser Ala Ser Phe Leu Tyr 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

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Gly Tyr Gly Ala Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 35
<211> 107

_Sequence_Listing_92116_ST25

<212> PRT

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<400> 35

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

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

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

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

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

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Gly Tyr Gly Ala Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 36

<211> 107

<212> PRT

<213> Artificial Sequence

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<223> Synthetic Construct

<400> 36

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

Sequence_Listing_92116_ST25

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

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

Tyr Ser Ala Ser Phe Leu Tyr 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

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Gly Tyr Gly Ala Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 37
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 37

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

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

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

Sequence_Listing_92116_ST25

Tyr Ser Ala Ser Phe Leu Tyr 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

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Gly Tyr Gly Ala Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 38

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 38

Asp 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 Arg Ala Ser Gln Asp Val Ser Thr Ala
20 25 30

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

Tyr Ser Ala Ser Phe Leu Tyr 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

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Tyr Gly Asn Pro Phe
85 90 95

_Sequence_Listing_92116_ST25

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 39
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<400> 39

Trp Val Arg Gln Glu Pro Gly Lys Gly Leu Glu Trp Val Ala
1 5 10

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<400> 40

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 Asp Tyr
20 25 30

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

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

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

Sequence_Listing_92116_ST25

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

Ala Arg Phe Val Phe Phe Leu Pro Tyr Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 41
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<400> 41

Asp 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 Arg Ala Ser Gln Asp Val Ser Thr Ala
20 25 30

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

Tyr Ser Ala Ser Phe Leu Tyr 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

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Tyr Gly Ala Pro Phe
85 90 95

Sequence_Listing_92116_ST25

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 42
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<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 42

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 Asp Tyr
20 25 30

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

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

Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala 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 Phe Val Phe Phe Leu Pro Tyr Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 43
<211> 227

_Sequence_Listing_92116_ST25

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 43

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 Asp Tyr
20 25 30

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

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

Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala 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 Phe Val Phe Phe Leu Pro Tyr Ala Met Asp Tyr 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

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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 Lys Val Glu Pro Lys Ser Cys Asp
210 215 220

Lys Thr His
225

<210> 44
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<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 44

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
1 5 10 15

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

<210> 45
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<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 45

Sequence_Listing_92116_ST25

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

Asp Arg Val Thr Ile Asp Cys
20

<210> 46
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 46

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

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

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

Tyr Ser Ala Ser Phe Leu Tyr 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

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Gly Tyr Gly Ala Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 47
<211> 232

Sequence_Listing_92116_ST25

<212> PRT

<213> Homo sapiens

<400> 47

Met Asn Phe Leu Leu Ser Trp Val His Trp Ser Leu Ala Leu Leu Leu
1 5 10 15

Tyr Leu His His Ala Lys Trp Ser Gln Ala Ala Pro Met Ala Glu Gly
20 25 30

Gly Gly Gln Asn His His Glu Val Val Lys Phe Met Asp Val Tyr Gln
35 40 45

Arg Ser Tyr Cys His Pro Ile Glu Thr Leu Val Asp Ile Phe Gln Glu
50 55 60

Tyr Pro Asp Glu Ile Glu Tyr Ile Phe Lys Pro Ser Cys Val Pro Leu
65 70 75 80

Met Arg Cys Gly Gly Cys Cys Asn Asp Glu Gly Leu Glu Cys Val Pro
85 90 95

Thr Glu Glu Ser Asn Ile Thr Met Gln Ile Met Arg Ile Lys Pro His
100 105 110

Gln Gly Gln His Ile Gly Glu Met Ser Phe Leu Gln His Asn Lys Cys
115 120 125

Glu Cys Arg Pro Lys Lys Asp Arg Ala Arg Gln Glu Lys Lys Ser Val
130 135 140

Arg Gly Lys Gly Lys Gly Gln Lys Arg Lys Arg Lys Lys Ser Arg Tyr
145 150 155 160

Lys Ser Trp Ser Val Tyr Val Gly Ala Arg Cys Cys Leu Met Pro Trp
165 170 175

_Sequence_Listing_92116_ST25

Ser Leu Pro Gly Pro His Pro Cys Gly Pro Cys Ser Glu Arg Arg Lys
180 185 190

His Leu Phe Val Gln Asp Pro Gln Thr Cys Lys Cys Ser Cys Lys Asn
195 200 205

Thr Asp Ser Arg Cys Lys Ala Arg Gln Leu Glu Leu Asn Glu Arg Thr
210 215 220

Cys Arg Cys Asp Lys Pro Arg Arg
225 230

<210> 48
<211> 228
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<220>
<223> Synthetic Construct

<400> 48

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 Asp Tyr
20 25 30

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

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

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

Leu Gln Met Arg Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys

_Sequence_Listing_92116_ST25

85

90

95

Ala Arg Phe Val Phe Phe Leu Pro Tyr Ala Met Asp Tyr 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 Lys Val Glu Pro Lys Ser Cys Asp
210 215 220

Lys Thr His Thr
225

<210> 49
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<400> 49

_Sequence_Listing_92116_ST25

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 Asp Tyr
20 25 30

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

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

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

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

Ala Arg Phe Val Phe Phe Leu Pro Tyr Ala Met Asp Tyr 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

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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 Lys Val Glu Pro Lys Ser Cys Asp
210 215 220

Lys Thr His Leu
225

<210> 50
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 50

Asp 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 Arg Ala Ser Gln Asp Val Ser Thr Ala
20 25 30

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

Tyr Ser Ala Ser Phe Leu Tyr 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

Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Gly Tyr Gly Ala Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala

_Sequence_Listing_92116_ST25

100

105

110

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

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

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

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

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

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

Phe Asn Arg Gly Glu Cys
210

<210> 51

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 51

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

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

Sequence_Listing_92116_ST25

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

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

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

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

Ala Arg Phe Val Phe Phe Leu Pro Tyr Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Glu Leu Val Thr Val Ser Ser
115 120

<210> 52
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 52

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

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Glu Ile Ser
20 25 30

<210> 53
<211> 17
<212> PRT
<213> Artificial Sequence

Sequence_Listing_92116_ST25

<220>

<223> Synthetic Construct

<400> 53

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

Gly

<210> 54

<211> 32

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 54

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
1 5 10 15

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Val Ala Thr Tyr Tyr Cys
20 25 30

<210> 55

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 55

Phe Gly Gln Gly Thr Lys Val Glu Val Lys
1 5 10

<210> 56

<211> 34

<212> DNA

_Sequence_Listing_92116_ST25

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 56

catcagatgg cgggaagatg aagacagatg gtgc

34

<210> 57

<211> 23

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 57

gccatccaga tgacccagtc tcc

23

<210> 58

<211> 19

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 58

ggctgcacca tctgtcttc

19

<210> 59

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 59

Asp 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 Arg Ala Ser Gln Asp Val Ser Thr Ala

_Sequence_Listing_92116_ST25

20

25

30

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

Tyr Ser Ala Ser Phe Leu Tyr 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

Glu Asp Val Ala Thr Tyr Tyr Cys Gln Gln Gly Tyr Gly Asn Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 60

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 60

Asp 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 Arg Ala Ser Gln Asp Val Ser Thr Ala
20 25 30

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

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

Sequence_Listing_92116_ST25

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

Glu Asp Val Ala Thr Tyr Tyr Cys Gln Gln Gly Tyr Gly Ala Pro Phe
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 61
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic construct

<400> 61

Gly Gly Gly Gly Ser
1 5

<210> 62
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic construct

<400> 62

Gly Tyr Tyr Met His
1 5

<210> 63
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic construct

Sequence_Listing_92116_ST25

<400> 63

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

Gly

<210> 64

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic construct

<400> 64

Ser	Pro	Asn	Pro	Tyr	Tyr	Tyr	Asp	Ser	Ser	Gly	Tyr	Tyr	Tyr	Pro	Gly
1				5					10					15	

Ala	Phe	Asp	Ile
			20

<210> 65

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic construct

<400> 65

Gly	Gly	Asn	Asn	Ile	Gly	Ser	Lys	Ser	Val	His
1				5					10	

<210> 66

<211> 7

<212> PRT

<213> Artificial Sequence

Sequence_Listing_92116_ST25

<220>

<223> Synthetic construct

<400> 66

Asp Asp Ser Asp Arg Pro Ser
1 5

<210> 67

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic construct

<400> 67

Gln Val Trp Asp Ser Ser Ser Asp His Trp Val
1 5 10

<210> 68

<211> 129

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic construct

<400> 68

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

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30

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

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Sequence_Listing_92116_ST25

Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

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

Ala Arg Ser Pro Asn Pro Tyr Tyr Tyr Asp Ser Ser Gly Tyr Tyr Tyr
100 105 110

Pro Gly Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser
115 120 125

Ser

<210> 69
<211> 110
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic construct

<400> 69

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

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
20 25 30

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

Asp Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Arg Val Glu Ala Gly

_Sequence_Listing_92116_ST25

65

70

75

80

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Ser Asp His
85 90 95

Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln
100 105 110