

myeloid cells, such as human umbilical vascular endothelial cells (HUVEC), murine dermal, liver, pulmonary and renal proximal tubules (Monsinjon, T. et al. FASEB J. 2003, 17,1003–1014; Gerard, C. et al. Annu. Rev. Immunol. 1994, 12, 775–808; Haviland, D.L. et al. J. Immunol. 1995, 154, 1861–1869). Also, it was demonstrated that C5aR was expressed in glomerular endothelial cells but not in podocytes, indicating that C5a may cause proteinuria on the primary target of renal endothelial cells (Tsai, I.J. et al. Cell. Mol. Life Sci. 2015, 72, 3157–3171).

[0005] Neutralization of C5a binding to C5aR is therefore a therapeutic approach to treating diseases and conditions mediated through C5a. An antibody against human C5a, designated INab308 (InflaRx), was described in WO2011063980. Other C5a antibodies such as MEDI-7814 (MedImmune) was described in WO2012088247, and BNJ383 (Alexion) was described in US10450370.

[0006] The disclosures of all publications, patents, patent applications and published patent applications referred to herein are hereby incorporated herein by reference in their entirety.

BRIEF SUMMARY OF THE APPLICATION

[0007] In one aspect, the present application provides an isolated anti-C5a antibody that specifically binds to an epitope on human C5a, wherein the isolated anti-C5a antibody specifically binds to at least one amino acid residue selected from residue D at position 31, residue E at position 32 and residue R at position 40 of human C5a as shown in SEQ ID NO: 141. In some embodiments, the isolated anti-C5a antibody specifically binds to residues 31-40 of human C5a as shown in SEQ ID NO: 141. In some embodiments, the isolated anti-C5a antibody that specifically binds to an epitope within, consisting of or comprising the sequence as follows: (i)DGACVNNDTCEQRAARISLGPR (SEQ ID NO: 145), (ii)NDETCEQRAARISLGPR (SEQ ID NO: 146), or (iii)DETCEQRAAR (SEQ ID NO: 147). In some embodiments, the isolated anti-C5a antibody that specifically binds to a peptide consisting of or comprising the sequence as follows: (i)DGACVNNDTCEQRAARISLGPR (SEQ ID NO: 145), (ii)NDETCEQRAARISLGPR (SEQ ID NO: 146), or (iii)DETCEQRAAR (SEQ ID NO: 147). In some embodiments, the isolated anti-C5a antibody binds to the human C5a with a Kd from about 0.1 pM to about 1nM. In some embodiments, the isolated anti-C5a antibody binds to free human C5a polypeptide in the presence of a 2-fold or more molar excess of uncleaved, native human C5.

[0008] In some embodiments according to any one of the isolated anti-C5a antibodies described above, the isolated anti-C5a antibody comprises: a heavy chain variable domain (VH) comprising a heavy chain complementarity determining region HC-CDR1 comprising X1YYX2Q (SEQ ID NO: 67), wherein X1 is D, or N, and X2 is M, or I; an HC-CDR2 comprising

epitopes of Cab44-IgG1 or Cab45-IgG1 were linear, and position D31 also significantly affected the antibodies Cab44-IgG1 and Cab45-IgG1 binding to C5a.

[00442] Linear peptide mapping of anti-C5a antibodies:

Table 9

peptide	position	sequence
C5a-p1	24-46 amino acid positions of human C5a (SEQ ID NO 141)	DGACVNND ET C EQ RAARISLGPR (SEQ ID NO: 145)
C5a-p2	30-46 amino acid positions of human C5a (SEQ ID NO 141)	NDETCEQRAARISLGPR (SEQ ID NO: 146)
C5a-p4	31-40 amino acid positions of human C5a (SEQ ID NO 141)	DETCEQRAAR (SEQ ID NO: 147)

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[00443] The amino acid sequences of the C5a-p1, C5a-p2, and C5a-p4 were shown in Table 9, the sequence of peptide-Fc fusion: C5a-p1-Fc, C5a-p2-Fc, or C5a-p4-Fc, and the peptide C5a or Fc were synthesized and subcloned into the Eukaryotic expression vector pTT5. The Expression of C5a-p1-Fc, C5a-p2-Fc, or C5a-p4-Fc proteins was performed in 293 cells, and the purification was carried out according to the manufacturer's protocol.

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[00444] The binding of the anti-C5a antibody Cab42 or INab308 to each of the peptide-Fc fusion was tested in an ELISA format. Briefly, linear peptides C5a-p1-Fc, C5a-p2-Fc, or C5a-p4-Fc corresponding to various regions within human C5a was diluted in coating buffer and placed on Microtiter Plates, The biotinylated anti-C5a antibody Cab42 or INab308 was added to each well followed by incubation at 37°C for 1 h, the wells were then washed with PBST buffer, the bound Biotinylated C5a antibody was detected by reaction with SA-HRP (horseradish peroxidase-labeled streptomyces Avidin) for 1 h at 37°C, then washed with PBST, TMB was added to the wells for color development, the reaction was terminated by addition of 50 µL of 3M NaOH per well, and then the absorbance at 410nm was read.

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[00445] Results of these ELISA-based assays were shown in FIGS. 12A-12B, as shown in FIG. 12A, the antibody Cab42 that specifically binds to a peptide comprising the amino acid positions 24-46, positions 30-46, or positions 31-40 of SEQ ID NO: 141. But the antibody INab308 doesn't bind to any of the 3 peptide-Fc fusions: C5a-p1-Fc, C5a-p2-Fc, or C5a-p4-Fc as shown in FIG. 12B.

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[00446] According to the result of Western Blot, Alanine scanning, and linear peptide mapping of anti-C5a antibodies, exemplary epitopes of antibodies Cab42-IgG1, Cab44-IgG1 and Cab45-IgG1 were identified as linear epitopes. Position D31 was the key binding site, position E32 and

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position R40 also affected the antibody binding to human C5a. The isolated anti-C5a antibodies described herein specially binds to residue D at position 31, or binds to residue D at position 31 and residue E at position 32, or binds to residue D at position 31, residue E at position 32 and residue R at position 40 of human C5a (SEQ ID NO: 141). The isolated anti-C5a antibodies described herein specially binds to an epitope of human C5a within, consisting of or comprising the sequence as follows: (i)DGACVNNDTCEQRAARISLGPR (SEQ ID NO: 145); (ii)NDETCEQRAARISLGPR (SEQ ID NO: 146); or (iii)DETCEQRAAR (SEQ ID NO: 147). The isolated anti-C5a antibodies described herein specially binds to a peptide consisting of or comprising the sequence as follows: (i)DGACVNNDTCEQRAARISLGPR (SEQ ID NO: 145); (ii)NDETCEQRAARISLGPR (SEQ ID NO: 146); or (iii)DETCEQRAAR (SEQ ID NO: 147). The numbering of the amino acid residues in C5a is according to SEQ ID NO: 141.

Example 9: The therapeutic effects of anti-C5a antibody on coronavirus-related ARDS in vivo

[00447] A coronavirus-related ARDS animal model was established to evaluate the therapeutic effects of Cab35, Cab42, Cab44 and Cab45 antibodies in vivo.

[00448] ARDS animal model and Normal Control: C5a-humanized mice (available from Shanghai Model Organisms Center, Inc.) were utilized. The mice were raised under the condition of room temperature 20°C~26°C, relative humidity of 40-70% and 12h light/dark cycle. On day 4, 3 and 2 before the study, the mice were infected with adenovirus carrying and expressing Covid-19 N protein (see Ting Gao etc., Highly pathogenic coronavirus N protein aggravates lung injury by MASP-2-mediated complement over-activation, medRxiv 2020.03.29.20041962; <https://doi.org/10.1101/2020.03.29.20041962>), with the dose of 7.5×10^8 PFU/100μL/mouse/once a day and sodium chloride solution instead of the adenovirus was injected into the mice as Normal Control group. On day 0 (the day of the experiment), Cab35, Cab42, Cab44 or Cab45 antibody with different doses or sodium chloride solution was injected into mice in groups respectively as followed.

[00449] Groups and Administration: The mice were divided into groups and treated with different reagents respectively as followed: (1) Normal Control Group (n=6), injected with 100μL 0.9% sodium chloride solution. (2) Model Control Group (n=10), injected with 100μL 0.9% sodium chloride solution. (3) Low Dose Experimental Group (n=10), injected with antibody in the dose of 1mg/kg. (4) Middle Dose Experimental Group (n=10), injected with antibody in the dose of 3mg/kg. (5) High Dose Experimental Group (n=10), injected with antibody in the dose of 10mg/kg. 30 min after administration, LPS-K235 (Sigma-Aldrich) was

SEQUENCE LISTING

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<223> Xaa = Arg or Lys

<220>

<221> VARIANT

<222> 5

<223> Xaa = Ala or Val

<220>

<221> VARIANT

<222> 8

<223> Xaa = Pro or Leu

<400> 72

Xaa Gln His Xaa Xaa Leu Pro Xaa Thr

1 5

<210> 73

<211> 117

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 73

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Met Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Arg Val Ser Cys Ala Ala Ser Gly Phe Thr Phe Thr Lys Tyr
20 25 30
Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
35 40 45
Gly Leu Ile Arg Asn Lys Ala Asn Gly Gly Thr Ala Glu Tyr Val Ala
50 55 60
Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ile
65 70 75 80
Ala Tyr Leu Gln Met Ser Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Met Arg Asp Asn Gly Tyr His Trp Gly Gln Gly Val Leu
100 105 110
Val Thr Val Ser Ser
115

<210> 74

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 74

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Lys Val Ser Cys Ala Ala Ser Gly Phe Ile Phe Ser Asp Tyr
20 25 30
Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
35 40 45
Gly Leu Ile Arg Lys Lys Val Asn Gly Gly Thr Thr Glu Tyr Ala Ala
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ile
65 70 75 80
Ala Tyr Leu Gln Met Ser Ser Leu Lys Ile Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Thr Trp Gly Gln Gly
100 105 110
Val Leu Val Thr Ile Ser Ser
115

<210> 75

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 75

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Lys Val Ser Cys Ala Ala Ser Gly Phe Ile Phe Ser Asp Tyr
20 25 30
Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
35 40 45
Gly Leu Ile Arg Lys Lys Val Asn Gly Gly Thr Thr Glu Tyr Ala Ala
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ile
65 70 75 80
Val Tyr Leu Gln Met Ser Ser Leu Lys Ile Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Thr Trp Gly Gln Gly
100 105 110
Val Leu Val Thr Val Ser Ser
115

<210> 76

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 76

Glu Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Lys Val Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30
Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
35 40 45
Gly Leu Ile Arg Asn Lys Ala Ile Gly Gly Thr Thr Gln Tyr Ala Ala
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ile
65 70 75 80
Val Tyr Leu Gln Met Ser Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Ser Trp Gly Gln Gly
100 105 110
Val Val Val Thr Val Ser Ser
115

<210> 77

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 77

Asp Met Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Lys Val Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30
Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
35 40 45
Gly Leu Ile Arg Asn Lys Ala Val Gly Gly Thr Thr Gln Tyr Ala Ala
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ile
65 70 75 80
Val Tyr Leu Glu Met Ser Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Ser Trp Gly Gln Gly
100 105 110
Val Leu Val Thr Val Ser Ser
115

<210> 78

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 78

Glu Val His Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Lys Val Ser Cys Ala Ala Ser Gly Phe Ile Phe Ser Asp Tyr
20 25 30
Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
35 40 45
Gly Leu Ile Arg Lys Lys Val Asn Gly Gly Thr Thr Glu Tyr Ala Ala
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ile
65 70 75 80
Val Tyr Leu Gln Met Ser Ser Leu Lys Ile Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Thr Trp Gly Gln Gly
100 105 110
Val Leu Val Thr Ile Ser Ser
115

<210> 79

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 79

Asp Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15
 Ser Leu Lys Val Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
 20 25 30
 Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
 35 40 45
 Gly Leu Ile Arg Asn Lys Ala Ile Gly Glu Thr Thr Glu Tyr Ala Ala
 50 55 60
 Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ile
 65 70 75 80
 Val Tyr Leu Gln Met Ser Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
 85 90 95
 Tyr Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Ser Trp Gly Gln Gly
 100 105 110
 Val Leu Val Thr Ile Ser Ser
 115

<210> 80
 <211> 118
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 80
 Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Ile Gln Pro Gly Gly
 1 5 10 15
 Ser Leu Arg Val Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
 20 25 30
 Tyr Leu Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
 35 40 45
 Gly Leu Ile Arg Thr Lys Arg Tyr Gly Gly Thr Ser Glu Tyr Ala Ala
 50 55 60
 Ser Val Lys Gly Arg Tyr Thr Ile Ser Arg Asp Asp Ser Lys Ala Ile
 65 70 75 80
 Ala Tyr Leu Gln Met Ser Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
 85 90 95
 Tyr Cys Val Val Arg Ile Phe Thr Gly Leu His Trp Gly Lys Gly Thr
 100 105 110
 Pro Val Thr Val Ser Ser
 115

<210> 81
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 81
 Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

Ser Leu Lys Val Ser Cys Ala Ala Ser Gly Phe Ile Phe Ser Asp Tyr
 20 25 30
 Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
 35 40 45
 Gly Leu Ile Arg Lys Lys Val Asn Gly Gly Thr Thr Glu Tyr Ala Ala
 50 55 60
 Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ile
 65 70 75 80
 Ala Tyr Leu Gln Met Ser Ser Leu Lys Ile Glu Asp Thr Ala Val Tyr
 85 90 95
 Tyr Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Thr Trp Gly Gln Gly
 100 105 110
 Val Leu Val Thr Ile Ser Ser
 115

<210> 82
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 82
 Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15
 Ser Leu Lys Val Ser Cys Ala Ala Ser Gly Phe Ile Phe Ser Asp Tyr
 20 25 30
 Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
 35 40 45
 Gly Leu Ile Arg Lys Lys Val Asn Gly Gly Thr Thr Glu Tyr Ala Ala
 50 55 60
 Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ile
 65 70 75 80
 Val Tyr Leu Gln Met Ser Ser Leu Lys Ile Glu Asp Thr Ala Val Tyr
 85 90 95
 Tyr Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Thr Trp Gly Gln Gly
 100 105 110
 Val Leu Ile Thr Val Ser Ser
 115

<210> 83
 <211> 117
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 83
 Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15
 Ser Leu Arg Val Ser Cys Ala Ala Ser Gly Phe Arg Phe Ser Asp Phe
 20 25 30

Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Arg Pro Glu Trp Val
 35 40 45
 Gly Leu Ile Arg Asn Lys Pro Tyr Gly Gly Thr Ala Glu Tyr Ala Ala
 50 55 60
 Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Val
 65 70 75 80
 Thr Asp Leu Gln Met Ser Ser Leu Lys Thr Glu Asp Thr Ala Ile Tyr
 85 90 95
 Tyr Cys Val Met Arg Asn Asn Gly Tyr His Trp Gly Gln Gly Val Leu
 100 105 110
 Val Thr Ile Ser Ser
 115

<210> 84
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 84
 Val Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15
 Ser Leu Lys Val Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
 20 25 30
 Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
 35 40 45
 Gly Leu Ile Arg Asn Lys Ala Ile Gly Glu Thr Thr Gln Tyr Ala Ala
 50 55 60
 Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ile
 65 70 75 80
 Val Tyr Leu Gln Met Ser Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
 85 90 95
 Tyr Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Ser Trp Gly Gln Gly
 100 105 110
 Val Leu Val Thr Ile Ser Ser
 115

<210> 85
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 85
 Val Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15
 Ser Leu Lys Val Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
 20 25 30
 Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
 35 40 45

Gly Leu Ile Arg Asn Lys Ala Ile Gly Gly Thr Thr Gln Tyr Ala Ala
 50 55 60
 Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ile
 65 70 75 80
 Val Tyr Leu Gln Met Ser Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
 85 90 95
 Tyr Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Ser Trp Gly Gln Gly
 100 105 110
 Val Leu Val Thr Ile Ser Ser
 115

<210> 86
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 86
 Val Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15
 Ser Leu Lys Val Ser Cys Ala Thr Ser Gly Phe Thr Phe Ser Asp Tyr
 20 25 30
 Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Leu
 35 40 45
 Gly Leu Ile Arg Asn Lys Ala Ile Gly Gly Thr Thr Gln Tyr Ala Ala
 50 55 60
 Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Gly Ile
 65 70 75 80
 Ala Tyr Leu Gln Met Ser Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
 85 90 95
 Tyr Cys Val Cys Arg Ala Gly Pro Pro Gly Leu Ser Trp Gly Gln Gly
 100 105 110
 Val Leu Val Thr Val Ser Ser
 115

<210> 87
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 87
 Val Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15
 Ser Leu Lys Val Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
 20 25 30
 Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
 35 40 45
 Gly Leu Ile Arg Asn Lys Ala Ile Gly Glu Thr Thr Glu Tyr Ala Ala
 50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ile
65 70 75 80
Val Tyr Leu Gln Met Ser Ser Leu Lys Pro Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Ala Gly Arg Leu Gly Pro Pro Gly Leu Ser Trp Gly Gln Gly
100 105 110
Val Leu Val Thr Val Ser Ser
115

<210> 88
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 88
Glu Val His Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Lys Val Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30
Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
35 40 45
Gly Leu Ile Arg Asn Lys Ala Ile Gly Glu Thr Thr Glu Tyr Ala Ala
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ile
65 70 75 80
Val Tyr Leu Gln Met Ser Ser Leu Lys Pro Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Ala Gly Arg Leu Gly Pro Pro Gly Leu Ser Trp Gly Gln Gly
100 105 110
Val Leu Val Thr Val Ser Ser
115

<210> 89
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 89
Val Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Leu Pro Gly Gly
1 5 10 15
Ser Leu Lys Val Ser Cys Ala Ala Ser Gly Phe Ile Phe Ser Asp Tyr
20 25 30
Tyr Ile Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
35 40 45
Gly Leu Ile Arg Asn Lys Ala Val Gly Glu Thr Val Gln Tyr Ala Ala
50 55 60
Ser Leu Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ile
65 70 75 80

Ala Tyr Leu Gln Met Thr Ser Leu Lys Thr Glu Asp Thr Ala Met Tyr
85 90 95
Tyr Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Thr Trp Gly Gln Gly
100 105 110
Val Leu Val Thr Val Ser Ser
115

<210> 90
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 90
Val Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Lys Val Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30
Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
35 40 45
Gly Leu Ile Arg Asn Lys Ala Ile Gly Glu Thr Thr Gln Tyr Ala Ala
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ile
65 70 75 80
Val Tyr Leu Gln Met Ser Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Ser Trp Gly Gln Gly
100 105 110
Val Leu Val Thr Val Ser Ser
115

<210> 91
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 91
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Lys Val Ser Cys Val Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30
Tyr Ile Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
35 40 45
Gly Leu Ile Arg Asn Lys Ala Val Gly Gly Thr Thr Ser Tyr Ala Ala
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Val
65 70 75 80
Ala Tyr Leu Gln Met Thr Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Phe Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Ser Trp Gly Gln Gly
100 105 110
Val Leu Val Thr Val Ser Ser
115

<210> 92
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 92
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Lys Val Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Asp Tyr
20 25 30
Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
35 40 45
Gly Leu Ile Arg Asn Lys Ala Ile Gly Glu Thr Ala Glu Tyr Ala Ala
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ile
65 70 75 80
Val Tyr Leu Gln Met Ser Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Thr Ser Arg Ala Gly Pro Pro Gly Leu Ser Trp Gly Gln Gly
100 105 110
Val Leu Val Thr Val Ser Ser
115

<210> 93
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 93
Glu Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Lys Val Ser Cys Ala Ala Ser Gly Phe Ile Phe Ser Asn Tyr
20 25 30
Tyr Ile Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
35 40 45
Gly Leu Ile Arg Asn Lys Ala Ile Gly Glu Thr Thr Glu Phe Ala Ala
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ile
65 70 75 80
Val Tyr Leu Gln Met Thr Arg Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Ala Gly Arg Leu Gly Pro Pro Gly Leu Thr Trp Gly Gln Gly
100 105 110

Val Leu Val Thr Ile Ser Ser
115

<210> 94
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 94
Val Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Lys Val Ser Cys Thr Ala Ser Gly Phe Ile Phe Asn Asp Tyr
20 25 30
Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
35 40 45
Gly Leu Ile Arg Asn Lys Ala Asn Gly Gly Thr Thr Glu Tyr Ala Ala
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ile
65 70 75 80
Val Tyr Leu Gln Met Ser Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95
Phe Cys Thr Gly Arg Leu Gly Pro Pro Gly Leu Thr Trp Gly Gln Gly
100 105 110
Val Leu Val Thr Ile Ser Ser
115

<210> 95
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 95
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 Phe Ser Asp Tyr
20 25 30
Tyr Ile Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
35 40 45
Gly Leu Ile Arg Asn Lys Ala Ile Gly Gly Thr Val Glu Tyr Ala Ala
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Arg Ile
65 70 75 80
Ala Tyr Leu Gln Met Arg Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95
Phe Cys Thr Gly Arg Val Gly Pro Pro Gly Leu Thr Trp Gly Gln Gly
100 105 110
Val Leu Val Thr Ile Ser Ser
115

<210> 96
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 96
Val Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Lys Val Ser Cys Ala Ala Ser Gly Phe Ile Phe Ser Asp Tyr
20 25 30
Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
35 40 45
Gly Leu Ile Arg Lys Lys Val Asn Gly Gly Thr Thr Glu Tyr Ala Ala
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ile
65 70 75 80
Val Tyr Leu Gln Met Ser Ser Leu Lys Ile Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Ala Trp Gly Gln Gly
100 105 110
Val Leu Val Thr Ile Ser Ser
115

<210> 97
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 97
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Phe Val Gln Pro Gly Gly
1 5 10 15
Ser Leu Lys Val Ser Cys Val Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30
Tyr Ile Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
35 40 45
Gly Leu Ile Arg Asn Lys Ala Val Gly Gly Thr Thr Thr Tyr Ala Ala
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Val
65 70 75 80
Ala Tyr Leu Gln Met Thr Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95
Phe Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Ser Trp Gly Gln Gly
100 105 110
Val Leu Val Thr Ile Ser Ser
115

<210> 98
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 98
 Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Leu Pro Gly Gly
 1 5 10 15
 Ser Leu Lys Val Ser Cys Ala Ala Ser Gly Phe Ile Phe Ser Asp Tyr
 20 25 30
 Tyr Ile Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
 35 40 45
 Gly Leu Ile Arg Asn Lys Ala Val Gly Glu Thr Val Gln Tyr Ala Ala
 50 55 60
 Ser Leu Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ile
 65 70 75 80
 Ala Tyr Leu Gln Met Thr Ser Leu Lys Thr Glu Asp Thr Ala Met Tyr
 85 90 95
 Tyr Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Thr Trp Gly Gln Gly
 100 105 110
 Val Leu Val Thr Ile Ser Ser
 115

<210> 99
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 99
 Glu Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15
 Ser Leu Lys Val Ser Cys Ala Ala Ser Gly Phe Thr Phe Arg Asp Tyr
 20 25 30
 Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
 35 40 45
 Gly Leu Ile Arg Asn Lys Ala Ile Gly Gly Thr Thr Gln Tyr Ala Ala
 50 55 60
 Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ile
 65 70 75 80
 Val Tyr Leu Gln Met Ser Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
 85 90 95
 Tyr Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Ser Trp Gly Gln Gly
 100 105 110
 Val Leu Val Thr Val Ser Ser
 115

<210> 100
 <211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 100

Glu Met 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 Phe Ser Asp Tyr
20 25 30
Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
35 40 45
Gly Leu Ile Arg Asn Lys Ala Val Gly Gly Thr Thr Gln Tyr Ala Ala
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80
Val Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Ser Trp Gly Gln Gly
100 105 110
Val Leu Val Thr Val Ser Ser
115

<210> 101

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 101

Glu Met 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 Phe Ser Asp Tyr
20 25 30
Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
35 40 45
Gly Leu Ile Arg Asn Lys Ala Val Gly Gly Thr Thr Glu Tyr Ala Ala
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80
Val Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Ser Trp Gly Gln Gly
100 105 110
Val Leu Val Thr Val Ser Ser
115

<210> 102

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 102

Glu Met 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 Phe Ser Asp Tyr
20 25 30
Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
35 40 45
Gly Leu Ile Arg Asn Lys Ala Val Gly Glu Thr Thr Gln Tyr Ala Ala
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80
Val Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Ser Trp Gly Gln Gly
100 105 110
Val Leu Val Thr Val Ser Ser
115

<210> 103

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 103

Glu Met 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 Phe Ser Asp Tyr
20 25 30
Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
35 40 45
Gly Leu Ile Arg Asn Lys Ala Val Gly Glu Thr Thr Glu Tyr Ala Ala
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80
Val Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Ser Trp Gly Gln Gly
100 105 110
Val Leu Val Thr Val Ser Ser
115

<210> 104

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 104

Glu Met 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 Phe Ser Asp Tyr
20 25 30
Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
35 40 45
Gly Leu Ile Arg Asn Lys Ala Val Gly Phe Thr Thr Gln Tyr Ala Ala
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80
Val Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Ser Trp Gly Gln Gly
100 105 110
Val Leu Val Thr Val Ser Ser
115

<210> 105

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 105

Glu Met 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 Phe Ser Asp Tyr
20 25 30
Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
35 40 45
Gly Leu Ile Arg Asn Lys Ala Val Gly His Thr Thr Gln Tyr Ala Ala
50 55 60
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
65 70 75 80
Val Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95
Tyr Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Ser Trp Gly Gln Gly
100 105 110
Val Leu Val Thr Val Ser Ser
115

<210> 106

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 106
 Glu Met 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 Phe Ser Asp Tyr
 20 25 30
 Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
 35 40 45
 Gly Leu Ile Arg Asn Lys Ala Val Gly Ile Thr Thr Gln Tyr Ala Ala
 50 55 60
 Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
 65 70 75 80
 Val Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
 85 90 95
 Tyr Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Ser Trp Gly Gln Gly
 100 105 110
 Val Leu Val Thr Val Ser Ser
 115

<210> 107
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 107
 Glu Met 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 Phe Ser Asp Tyr
 20 25 30
 Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
 35 40 45
 Gly Leu Ile Arg Asn Lys Ala Val Gly Gln Thr Thr Gln Tyr Ala Ala
 50 55 60
 Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
 65 70 75 80
 Val Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
 85 90 95
 Tyr Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Ser Trp Gly Gln Gly
 100 105 110
 Val Leu Val Thr Val Ser Ser
 115

<210> 108
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 108
 Glu Met 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 Phe Ser Asp Tyr
 20 25 30
 Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
 35 40 45
 Gly Leu Ile Arg Asn Lys Ala Val Gly Arg Thr Thr Gln Tyr Ala Ala
 50 55 60
 Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
 65 70 75 80
 Val Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
 85 90 95
 Tyr Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Ser Trp Gly Gln Gly
 100 105 110
 Val Leu Val Thr Val Ser Ser
 115

<210> 109
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 109
 Glu Met 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 Phe Ser Asp Tyr
 20 25 30
 Tyr Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
 35 40 45
 Gly Leu Ile Arg Asn Lys Ala Val Gly Glu Thr Thr Gln Tyr Ala Ala
 50 55 60
 Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
 65 70 75 80
 Val Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
 85 90 95
 Tyr Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Ser Trp Gly Gln Gly
 100 105 110
 Val Leu Val Thr Val Ser Ser
 115

<210> 110
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 110
 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 Phe Ser Asn Tyr

20 25 30
 Tyr Ile Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
 35 40 45
 Gly Leu Ile Arg Asn Lys Ala Ile Gly Glu Thr Thr Glu Phe Ala Ala
 50 55 60
 Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
 65 70 75 80
 Val Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
 85 90 95
 Tyr Cys Ala Gly Arg Leu Gly Pro Pro Gly Leu Thr Trp Gly Gln Gly
 100 105 110
 Val Leu Val Thr Val Ser Ser
 115

<210> 111
 <211> 119
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 111
 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 Phe Ser Asp Tyr
 20 25 30
 Tyr Ile Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Pro Glu Trp Val
 35 40 45
 Gly Leu Ile Arg Asn Lys Ala Val Gly Gly Thr Thr Thr Tyr Ala Ala
 50 55 60
 Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Ser
 65 70 75 80
 Ala Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
 85 90 95
 Phe Cys Val Ser Arg Ala Gly Pro Pro Gly Leu Ser Trp Gly Gln Gly
 100 105 110
 Val Leu Val Thr Val Ser Ser
 115

<210> 112
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 112
 Asp Ile Val Leu Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Pro Gly
 1 5 10 15
 Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Arg Leu Leu His Ser
 20 25 30
 Asp Gly Tyr Thr Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser

35 40 45
 Pro Gln Leu Leu Ile Tyr Gly Gly Ser Asn Arg Ala Ser Gly Val Pro
 50 55 60
 Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80
 Ser Lys Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln His
 85 90 95
 Lys Ala Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 100 105 110

<210> 113
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 113
 Asp Ile Val Met Ile Gln Thr Pro Leu Ser Leu Pro Val Thr Pro Gly
 1 5 10 15
 Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Arg Leu Leu His Ser
 20 25 30
 Asp Gly Tyr Thr Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35 40 45
 Pro Gln Leu Leu Ile Tyr Gly Gly Ser Asn Arg Ala Ser Gly Val Pro
 50 55 60
 Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80
 Ser Lys Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln His
 85 90 95
 Lys Ala Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 100 105 110

<210> 114
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 114
 Asp Ile Val Leu Thr Gln Thr Pro Leu Ser Leu Ala Val Ser Pro Gly
 1 5 10 15
 Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Ala Ser
 20 25 30
 Asp Gly Tyr Thr Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35 40 45
 Pro Gln Ile Leu Ile Tyr Gly Gly Ser Asn Arg Ala Ser Gly Val Pro
 50 55 60
 Asp Arg Phe Ser Gly Arg Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80
 Thr Lys Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln His

85 90 95
 Arg Ala Leu Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
 100 105 110

<210> 115
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 115
 Asp Ile Val Met Ile Gln Thr Pro Leu Ser Leu Pro Val Thr Pro Gly
 1 5 10 15
 Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Arg Leu Leu His Thr
 20 25 30
 Asp Gly Tyr Thr Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35 40 45
 Pro Gln Leu Leu Ile Tyr Gly Gly Ser Asn Arg Ala Ser Gly Val Pro
 50 55 60
 Asp Arg Phe Ser Gly Ser Gly Ser Gly Ser Asp Phe Thr Leu Lys Ile
 65 70 75 80
 Ser Lys Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln His
 85 90 95
 Lys Ala Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 100 105 110

<210> 116
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 116
 Asp Ala Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Pro Gly
 1 5 10 15
 Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Ala Ser
 20 25 30
 Asp Gly Tyr Asn Tyr Ile Asp Trp Tyr Leu Gln Arg Pro Gly Gln Ser
 35 40 45
 Pro Lys Val Leu Ile Tyr Gly Gly Ser Asn Arg Ala Ser Gly Val Pro
 50 55 60
 Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Tyr Phe Thr Leu Lys Ile
 65 70 75 80
 Ser Lys Val Glu Ala Glu Asp Val Gly Phe Tyr Phe Cys Leu Gln His
 85 90 95
 Arg Ala Leu Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
 100 105 110

<210> 117

<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 117
Asp Ile Val Met Ile Gln Asn Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Ala Ser
20 25 30
Asp Gly Tyr Asn Tyr Met Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45
Pro Lys Val Leu Ile Tyr Gly Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80
Thr Lys Val Glu Ala Glu Asp Val Gly Ile Tyr Tyr Cys Met Gln His
85 90 95
Lys Val Leu Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 118
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 118
Asp Thr Val Met Thr Gln Ile Pro Leu Ser Leu Ser Val Thr Pro Gly
1 5 10 15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Arg Leu Leu His Thr
20 25 30
Asp Gly Tyr Thr Tyr Leu Asp Trp Tyr His Gln Lys Pro Gly Gln Ser
35 40 45
Pro Gln Leu Leu Ile Tyr Gly Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Ser Val Thr Asp Phe Thr Leu Lys Ile
65 70 75 80
Ser Lys Met Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln His
85 90 95
Lys Ala Leu Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 119
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 119

Asp Ile Val Met Thr Gln Thr Pro Leu Ser Arg Pro Val Thr Pro Gly
1 5 10 15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Thr
20 25 30
Asp Gly Tyr Thr Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45
Pro Gln Leu Leu Ile Tyr Gly Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80
Ser Lys Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln His
85 90 95
Lys Ala Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 120

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 120

Asp Ile Val Met Ile Gln Thr Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
20 25 30
Asp Gly Tyr Thr Tyr Val Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45
Pro Gln Ile Leu Ile Tyr Gly Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80
Thr Asn Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln His
85 90 95
Lys Ala Leu Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 121

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 121

Asp Thr Val Met Ser Gln Ile Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Thr
20 25 30

Asp Gly Tyr Ile Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35 40 45
 Pro Gln Leu Leu Ile Tyr Gly Gly Ser Asn Arg Ala Ser Gly Val Pro
 50 55 60
 Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80
 Ser Lys Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln His
 85 90 95
 Lys Ala Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 100 105 110

<210> 122
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 122
 Asp Ala Val Met Thr Gln Ile Pro Leu Ser Leu Pro Val Thr Pro Gly
 1 5 10 15
 Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Thr
 20 25 30
 Asp Gly Tyr Thr Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35 40 45
 Pro Gln Leu Leu Ile Tyr Gly Gly Ser Asn Arg Ala Ser Gly Val Pro
 50 55 60
 Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80
 Ser Lys Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln His
 85 90 95
 Lys Ala Leu Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 100 105 110

<210> 123
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 123
 Asp Ile Val Leu Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Pro Gly
 1 5 10 15
 Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Arg Leu Leu His Ser
 20 25 30
 Asp Gly Tyr Thr Tyr Met Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35 40 45
 Pro Gln Ile Leu Ile Tyr Gly Gly Ser Asn Arg Ala Ser Gly Val Pro
 50 55 60
 Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80

Ser Lys Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln His
85 90 95
Lys Ala Leu Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 124
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 124
Asp Ile Glu Leu Thr Gln Thr Pro Leu Ser Arg Pro Val Thr Pro Gly
1 5 10 15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Thr
20 25 30
Asp Gly Tyr Thr Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45
Pro Gln Leu Leu Ile Tyr Gly Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80
Ser Lys Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln His
85 90 95
Lys Ala Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 125
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 125
Asp Ile Val Met Thr Gln Asn Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Ala Thr
20 25 30
Asp Gly Tyr Thr Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45
Pro Gln Val Leu Ile Tyr Gly Gly Ser Lys Arg Ala Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80
Thr Lys Val Glu Ala Glu Asp Val Gly Ile Tyr Tyr Cys Met Gln His
85 90 95
Lys Ala Leu Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 126
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 126
 Asp Ala Val Met Thr Gln Ile Pro Leu Ser Leu Pro Val Thr Pro Gly
 1 5 10 15
 Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Thr
 20 25 30
 Asp Gly Tyr Thr Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35 40 45
 Pro Gln Leu Leu Ile Tyr Gly Gly Ser Asn Arg Ala Ser Gly Val Pro
 50 55 60
 Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80
 Ser Lys Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln His
 85 90 95
 Lys Ala Leu Pro Leu Thr Phe Gly Gly Gly Thr Arg Leu Glu Ile Lys
 100 105 110

<210> 127
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 127
 Asp Ile Val Met Ile Gln Asn Pro Leu Ser Leu Ser Val Thr Pro Gly
 1 5 10 15
 Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Arg Leu Leu Ala Ser
 20 25 30
 Asp Gly Tyr Thr Tyr Val Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35 40 45
 Pro Gln Ile Leu Ile Tyr Gly Gly Ser Asn Arg Ala Ser Gly Val Pro
 50 55 60
 Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80
 Ser Lys Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln His
 85 90 95
 Lys Ala Leu Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
 100 105 110

<210> 128
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 128

Asp Ile Val Met Thr Gln Asn Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Asp Ser
20 25 30
Asn Arg Tyr Ala Tyr Val Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45
Pro Gln Ile Leu Val Tyr Gly Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80
Ser Lys Val Glu Ala Glu Asp Val Gly Ile Tyr Tyr Cys Met Gln His
85 90 95
Lys Val Leu Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 129

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 129

Asp Ile Val Met Ile Gln Asn Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
20 25 30
Asp Gly Tyr Thr Tyr Leu Asp Trp Tyr Gln Gln Lys Pro Gly Gln Ala
35 40 45
Pro Gln Leu Leu Ile Tyr Gly Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Ser Ala Thr Asp Phe Thr Leu Lys Ile
65 70 75 80
Ser Lys Met Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln His
85 90 95
Lys Ala Leu Pro Pro Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 130

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 130

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

20 25 30
 Asp Gly Tyr Thr Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35 40 45
 Pro Gln Leu Leu Ile Tyr Gly Gly Ser Asn Arg Ala Ser Gly Val Pro
 50 55 60
 Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80
 Ser Lys Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln His
 85 90 95
 Lys Val Leu Pro Leu Thr Phe Ala Gly Gly Thr Lys Leu Glu Ile Lys
 100 105 110

<210> 131
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 131
 Asp Ile Val Met Ile Gln Asn Pro Leu Ser Leu Pro Val Thr Pro Gly
 1 5 10 15
 Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Asn Leu Leu Ala Thr
 20 25 30
 Asp Gly Tyr Thr Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35 40 45
 Pro Gln Val Leu Ile Tyr Gly Gly Ser Lys Arg Ala Ser Gly Val Pro
 50 55 60
 Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80
 Ser Lys Val Glu Ala Glu Asp Val Gly Ile Tyr Tyr Cys Leu Gln His
 85 90 95
 Arg Ala Leu Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
 100 105 110

<210> 132
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 132
 Asp Ile Val Met Ile Gln Asn Pro Leu Ser Leu Ser Val Ser Leu Gly
 1 5 10 15
 Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Ala Thr
 20 25 30
 Asp Gly Tyr Glu Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35 40 45
 Pro Gln Ile Leu Ile Tyr Gly Ala Ser Asn Arg Ala Ser Gly Val Pro
 50 55 60
 Asp Arg Phe Ser Gly Arg Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile

65 70 75 80
 Thr Lys Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln His
 85 90 95
 Lys Ala Leu Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
 100 105 110

<210> 133
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 133
 Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Pro Gly
 1 5 10 15
 Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
 20 25 30
 Asp Gly Tyr Thr Tyr Leu Asp Trp Tyr Leu Gln Arg Pro Gly Gln Ser
 35 40 45
 Pro His Leu Leu Ile Tyr Gly Gly Ser Asn Arg Ala Ser Gly Val Pro
 50 55 60
 Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80
 Ser Lys Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln His
 85 90 95
 Lys Val Leu Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
 100 105 110

<210> 134
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 134
 Asp Thr Val Met Ser Gln Ile Pro Leu Ser Leu Pro Val Thr Pro Gly
 1 5 10 15
 Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
 20 25 30
 Asp Gly Tyr Thr Tyr Met Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35 40 45
 Pro Gln Leu Leu Ile Tyr Gly Gly Ser Asn Arg Ala Ser Gly Val Pro
 50 55 60
 Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80
 Ser Lys Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln His
 85 90 95
 Lys Val Leu Pro Pro Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
 100 105 110

<210> 135
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 135
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Ala Ser
20 25 30
Asp Gly Tyr Asn Tyr Ile Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45
Pro Gln Leu Leu Ile Tyr Gly Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Leu Gln His
85 90 95
Arg Ala Leu Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 136
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 136
Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Ala Ser
20 25 30
Asp Gly Tyr Ile Tyr Ile Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45
Pro Gln Leu Leu Ile Tyr Gly Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Leu Gln His
85 90 95
Arg Ala Leu Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 137
<211> 112
<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 137

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Ala Ser
20 25 30
Asp Gly Tyr Asn Tyr Ile Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45
Pro Gln Leu Leu Ile Tyr Gly Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Leu Gln His
85 90 95
Lys Ala Leu Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 138

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 138

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15
Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Ala Ser
20 25 30
Asp Ala Tyr Asn Tyr Ile Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45
Pro Gln Leu Leu Ile Tyr Gly Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Leu Gln His
85 90 95
Arg Ala Leu Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 139

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 139

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

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Asn Leu Leu Ala Thr
 20 25 30
 Asp Gly Tyr Thr Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35 40 45
 Pro Gln Leu Leu Ile Tyr Gly Gly Ser Lys Arg Ala Ser Gly Val Pro
 50 55 60
 Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80
 Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln His
 85 90 95
 Arg Ala Leu Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
 100 105 110

<210> 140
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 140
 Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
 1 5 10 15
 Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Ala Thr
 20 25 30
 Asp Gly Tyr Glu Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35 40 45
 Pro Gln Leu Leu Ile Tyr Gly Ala Ser Asn Arg Ala Ser Gly Val Pro
 50 55 60
 Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80
 Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Leu Gln His
 85 90 95
 Lys Ala Leu Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
 100 105 110

<210> 141
 <211> 74
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 141
 Thr Leu Gln Lys Lys Ile Glu Glu Ile Ala Ala Lys Tyr Lys His Ser
 1 5 10 15
 Val Val Lys Lys Cys Cys Tyr Asp Gly Ala Cys Val Asn Asn Asp Glu
 20 25 30
 Thr Cys Glu Gln Arg Ala Ala Arg Ile Ser Leu Gly Pro Arg Cys Ile
 35 40 45
 Lys Ala Phe Thr Glu Cys Cys Val Val Ala Ser Gln Leu Arg Ala Asn
 50 55 60

Ile Ser His Lys Asp Met Gln Leu Gly Arg
65 70

<210> 142
<211> 330
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 142
Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys
1 5 10 15
Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
20 25 30
Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
35 40 45
Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
50 55 60
Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr
65 70 75 80
Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys
85 90 95
Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys
100 105 110
Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
115 120 125
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
130 135 140
Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
145 150 155 160
Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
165 170 175
Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
180 185 190
His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
195 200 205
Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
210 215 220
Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
225 230 235 240
Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
245 250 255
Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
260 265 270
Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
275 280 285
Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
290 295 300
Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
305 310 315 320
Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
325 330

<210> 143
 <211> 327
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 143
 Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg
 1 5 10 15
 Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr
 20 25 30
 Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser
 35 40 45
 Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser
 50 55 60
 Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr
 65 70 75 80
 Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys
 85 90 95
 Arg Val Glu Ser Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro Ala Pro
 100 105 110
 Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
 115 120 125
 Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
 130 135 140
 Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
 145 150 155 160
 Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
 165 170 175
 Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
 180 185 190
 Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
 195 200 205
 Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
 210 215 220
 Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys
 225 230 235 240
 Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
 245 250 255
 Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
 260 265 270
 Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
 275 280 285
 Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
 290 295 300
 Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
 305 310 315 320
 Leu Ser Leu Ser Leu Gly Lys
 325

<210> 144
 <211> 107

<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 144
Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
1 5 10 15
Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
20 25 30
Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
35 40 45
Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
50 55 60
Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
65 70 75 80
Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
85 90 95
Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> 145
<211> 23
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic Construct

<400> 145
Asp Gly Ala Cys Val Asn Asn Asp Glu Thr Cys Glu Gln Arg Ala Ala
1 5 10 15

Arg Ile Ser Leu Gly Pro Arg
20

<210> 146
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct

<400> 146
Asn Asp Glu Thr Cys Glu Gln Arg Ala Ala Arg Ile Ser Leu Gly Pro
1 5 10 15

Arg

<210> 147

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic Construct

<400> 147

Asp Glu Thr Cys Glu Gln Arg Ala Ala Arg

1 5 10

CLAIMS

1. An isolated anti-C5a antibody or antigen binding fragment thereof that specifically binds to at least one amino acid residue selected from residue D at position 31, residue E at position 32 and residue R at position 40 of human C5a as shown in SEQ ID NO: 141.

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2. The isolated anti-C5a antibody or antigen binding fragment of claim 1 that specifically binds to residues 31-40 of human C5a as shown in SEQ ID NO: 141.

10

3. The isolated anti-C5a antibody or antigen binding fragment of claim 1 that specifically binds to an epitope of human C5a within, consisting of or comprising the sequence as follows:

(i) DGACVNND~~ET~~CEQRAARISLGPR (SEQ ID NO: 145);

(ii) N~~DE~~TCEQRAARISLGPR (SEQ ID NO: 146); or

(iii) ~~DET~~CEQRAAR (SEQ ID NO: 147).

15

4. The isolated anti-C5a antibody or antigen binding fragment of claim 1 that specifically binds to a peptide consisting of or comprising the sequence as follows:

(i) DGACVNND~~ET~~CEQRAARISLGPR (SEQ ID NO: 145);

(ii) N~~DE~~TCEQRAARISLGPR (SEQ ID NO: 146); or

(iii) ~~DET~~CEQRAAR (SEQ ID NO: 147).

20

5. The isolated anti-C5a antibody or antigen binding fragment of any one of claims 1-4, wherein the anti-C5a antibody or antigen binding fragment binds to human C5a with a Kd from about 0.1 pM to about 1nM.

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6. The isolated anti-C5a antibody or antigen binding fragment of any one of claims 1-5, wherein the anti-C5a antibody or antigen binding fragment binds to free human C5a polypeptide in the presence of a 2-fold or more molar excess of uncleaved, native human C5.

7. An isolated anti-C5a antibody or antigen binding fragment thereof, wherein the anti-C5a antibody or antigen binding fragment comprises:

a heavy chain variable domain (V_H) comprising a heavy chain complementarity determining region HC-CDR1 comprising X₁YYX₂Q (SEQ ID NO: 67), wherein X₁ is D, or N, and X₂ is M, or I;

an HC-CDR2 comprising LIRX₁KX₂X₃GX₄TX₅X₆X₇AASX₈KG (SEQ ID NO: 68), wherein X₁ is K, or N, X₂ is A, or V, X₃ is V, N, or I, X₄ is G, E, F, H, I, Q, or R, X₅ is T, V, or A, X₆ is Q, E, T, or S, X₇ is Y or F, and X₈ is V or L; and

an HC-CDR3 comprising RX₁GPPGLX₂ (SEQ ID NO: 69), wherein X₁ is A, L, or V, and X₂ is T, S, or A;

and a light chain variable domain (V_L) comprising a light chain complementarity determining region LC-CDR1 comprising RSSQX₁LLX₂X₃X₄X₅YX₆YX₇D (SEQ ID NO: 70), wherein X₁ is S, R, or N, X₂ is A, H, or D, X₃ is S or T, X₄ is D or N, X₅ is G, A, or R, X₆ is N, I, T, E, or A, and X₇ is I, M, L, or V;

an LC-CDR2 comprising GX₁SX₂RAS (SEQ ID NO: 71), wherein X₁ is G or A, X₂ is N or K; and

an LC-CDR3 comprising X₁QHX₂X₃LPX₄T (SEQ ID NO: 72), wherein X₁ is L or M, X₂ is R or K, X₃ is A or V, and X₄ is P, or L.

8. An isolated anti-C5a antibody or antigen binding fragment thereof, comprising:

a V_H comprising an HC-CDR1 comprising an amino acid sequence having at least about 90% sequence identify with any one of SEQ ID NOs: 1-6; an HC-CDR2 comprising an amino acid sequence having at least about 90% sequence identify with any one of SEQ ID NOs: 7-29; and an HC-CDR3 comprising an amino acid sequence having at least about 90% sequence identify with any one of SEQ ID NOs: 30-38; and

a V_L comprising an LC-CDR1 comprising an amino acid sequence having at least about 90% sequence identify with any of SEQ ID NOs: 39-56; an LC-CDR2 comprising an amino acid sequence having at least about 90% sequence identify with any of SEQ ID NOs: 57-59; and an

LC-CDR3 comprising an amino acid sequence having at least about 90% sequence identify with any one of SEQ ID NOs: 60-66.

9. An isolated anti-C5a antibody or antigen binding fragment thereof, comprising a V_H comprising an HC-CDR1, an HC-CDR2, and an HC-CDR3 of a V_H comprising the amino acid sequence of any one of SEQ ID NOs: 73-111; and a V_L comprising an LC-CDR1, an LC-CDR2, and an LC-CDR3 of a V_L comprising the amino acid sequence of any one of SEQ ID NOs: 112-140.

10. The isolated anti-C5a antibody or antigen binding fragment of any one of claims 1-9, comprising:

(i) a V_H comprising an HC-CDR1 comprising an amino acid sequence having at least about 90% sequence identify with SEQ ID NO: 1, an HC-CDR2 comprising an amino acid sequence having at least about 90% sequence identify with SEQ ID NO: 7, and an HC-CDR3 comprising an amino acid sequence having at least about 90% sequence identify with SEQ ID NO: 30; and a V_L comprising an LC-CDR1 comprising an amino acid sequence having at least about 90% sequence identify with SEQ ID NO: 39, an LC-CDR2 comprising an amino acid sequence having at least about 90% sequence identify with SEQ ID NO: 57, and an LC-CDR3 comprising an amino acid sequence having at least about 90% sequence identify with SEQ ID NO: 60;

(ii) a V_H comprising an HC-CDR1 comprising an amino acid sequence having at least about 90% sequence identify with SEQ ID NO: 2, an HC-CDR2 comprising an amino acid sequence having at least about 90% sequence identify with SEQ ID NO: 8, and an HC-CDR3 comprising an amino acid sequence having at least about 90% sequence identify with SEQ ID NO: 31; and a V_L comprising an LC-CDR1 comprising an amino acid sequence having at least about 90% sequence identify with SEQ ID NO: 40, an LC-CDR2 comprising an amino acid sequence having at least about 90% sequence identify with SEQ ID NO: 57, and an LC-CDR3 comprising an amino acid sequence having at least about 90% sequence identify with SEQ ID NO: 61;

- (iii) a V_H comprising an HC-CDR1 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 2, an HC-CDR2 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 10, and an HC-CDR3 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 32; and a V_L comprising an LC-CDR1 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 42, an LC-CDR2 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 57, and an LC-CDR3 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 61;
- (iv) a V_H comprising an HC-CDR1 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 2, an HC-CDR2 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 11, and an HC-CDR3 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 32; and a V_L comprising an LC-CDR1 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 41, an LC-CDR2 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 57, and an LC-CDR3 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 64;
- (v) a V_H comprising an HC-CDR1 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 2, an HC-CDR2 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 9, and an HC-CDR3 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 32; and a V_L comprising an LC-CDR1 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 43, an LC-CDR2 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 57, and an LC-CDR3 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 63;
- (vi) a V_H comprising an HC-CDR1 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 2, an HC-CDR2 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 11, and an HC-CDR3 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID

NO: 35; and a V_L comprising an LC-CDR1 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 44, an LC-CDR2 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 57, and an LC-CDR3 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 60;

(vii) a V_H comprising an HC-CDR1 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 6, an HC-CDR2 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 18, and an HC-CDR3 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 36; and a V_L comprising an LC-CDR1 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 42, an LC-CDR2 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 57, and an LC-CDR3 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 61;

(viii) a V_H comprising an HC-CDR1 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 5, an HC-CDR2 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 21, and an HC-CDR3 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 32; and a V_L comprising an LC-CDR1 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 42, an LC-CDR2 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 57, and an LC-CDR3 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 61;

(ix) a V_H comprising an HC-CDR1 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 2, an HC-CDR2 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 10, and an HC-CDR3 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 32; and a V_L comprising an LC-CDR1 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 53, an LC-CDR2 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 59, and an LC-CDR3

comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 65;

(x) a V_H comprising an HC-CDR1 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 2, an HC-CDR2 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 23, and an HC-CDR3 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 32; and a V_L comprising an LC-CDR1 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 42, an LC-CDR2 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 57, and an LC-CDR3 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 61;

(xi) a V_H comprising an HC-CDR1 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 2, an HC-CDR2 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 23, and an HC-CDR3 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 32; and a V_L comprising an LC-CDR1 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 56, an LC-CDR2 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 57, and an LC-CDR3 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 61;

(xii) a V_H comprising an HC-CDR1 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 6, an HC-CDR2 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 18, and an HC-CDR3 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 36; and a V_L comprising an LC-CDR1 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 52, an LC-CDR2 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 58, and an LC-CDR3 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 61;

(xiii) a V_H comprising an HC-CDR1 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 6, an HC-CDR2 comprising an amino acid sequence

having at least about 90% sequence identity with SEQ ID NO: 18, and an HC-CDR3 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 36; and a V_L comprising an LC-CDR1 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 53, an LC-CDR2 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 59, and an LC-CDR3 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 65;

(xiv) a V_H comprising an HC-CDR1 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 5, an HC-CDR2 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 21, and an HC-CDR3 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 32; and a V_L comprising an LC-CDR1 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 52, an LC-CDR2 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 58, and an LC-CDR3 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 61; or

(xv) a V_H comprising an HC-CDR1 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 5, an HC-CDR2 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 21, and an HC-CDR3 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 32; and a V_L comprising an LC-CDR1 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 53, an LC-CDR2 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 59, and an LC-CDR3 comprising an amino acid sequence having at least about 90% sequence identity with SEQ ID NO: 65.

11. The isolated anti-C5a antibody or antigen binding fragment of any one of claims 1-10, comprising:

a V_H comprising an amino acid sequence having at least about 90% sequence identity with any one of SEQ ID NOs: 73-111; and

a V_L comprising an amino acid sequence having at least about 90% sequence identity with any one of SEQ ID NOs: 112-140.

12. The isolated anti-C5a antibody or antigen binding fragment of claim 11, comprising:

- 5 (i) a V_H comprising the amino acid sequence of SEQ ID NO: 73 or a variant thereof having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 73; and a V_L comprising the amino acid sequence of SEQ ID NO: 112 or a variant thereof having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 112;
- (ii) a V_H comprising the amino acid sequence of SEQ ID NO: 75 or a variant thereof having at
10 least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 75; and a V_L comprising the amino acid sequence of SEQ ID NO: 114 or a variant thereof having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 114;
- (iii) a V_H comprising the amino acid sequence of SEQ ID NO: 100 or a variant thereof having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 100; and a V_L
15 comprising the amino acid sequence of SEQ ID NO: 135 or a variant thereof having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 135;
- (iv) a V_H comprising the amino acid sequence of SEQ ID NO: 79 or a variant thereof having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 79; and a V_L comprising the amino acid sequence of SEQ ID NO: 118 or a variant thereof having at least
20 about 90% sequence identity to the amino acid sequence of SEQ ID NO: 118;
- (v) a V_H comprising the amino acid sequence of SEQ ID NO: 85 or a variant thereof having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 85; and a V_L comprising the amino acid sequence of SEQ ID NO: 117 or a variant thereof having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 117;
- 25 (vi) a V_H comprising the amino acid sequence of SEQ ID NO: 88 or a variant thereof having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 88; and a V_L comprising the amino acid sequence of SEQ ID NO: 126 or a variant thereof having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 126;
- (vii) a V_H comprising the amino acid sequence of SEQ ID NO: 93 or a variant thereof having
30 at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 93; and a V_L

comprising the amino acid sequence of SEQ ID NO: 116 or a variant thereof having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 116;

(viii) a V_H comprising the amino acid sequence of SEQ ID NO: 97 or a variant thereof having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 97; and a V_L

5 comprising the amino acid sequence of SEQ ID NO: 116 or a variant thereof having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 116;

(ix) a V_H comprising the amino acid sequence of SEQ ID NO: 77 or a variant thereof having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 77; and a V_L comprising the amino acid sequence of SEQ ID NO: 132 or a variant thereof having at least
10 about 90% sequence identity to the amino acid sequence of SEQ ID NO: 132.

(x) a V_H comprising the amino acid sequence of SEQ ID NO: 102 or a variant thereof having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 102; and a V_L comprising the amino acid sequence of SEQ ID NO: 135 or a variant thereof having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 135;

15 (xi) a V_H comprising the amino acid sequence of SEQ ID NO: 109 or a variant thereof having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 109; and a V_L comprising the amino acid sequence of SEQ ID NO: 138 or a variant thereof having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 138;

(xii) a V_H comprising the amino acid sequence of SEQ ID NO: 110 or a variant thereof having
20 at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 110; and a V_L comprising the amino acid sequence of SEQ ID NO: 139 or a variant thereof having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 139;

(xiii) a V_H comprising the amino acid sequence of SEQ ID NO: 110 or a variant thereof having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 110; and a V_L
25 comprising the amino acid sequence of SEQ ID NO: 140 or a variant thereof having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 140;

(xiv) a V_H comprising the amino acid sequence of SEQ ID NO: 111 or a variant thereof having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 111; and a V_L comprising the amino acid sequence of SEQ ID NO: 139 or a variant thereof having at least
30 about 90% sequence identity to the amino acid sequence of SEQ ID NO: 139; or

(xv) a V_H comprising the amino acid sequence of SEQ ID NO: 111 or a variant thereof having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 111; and a V_L comprising the amino acid sequence of SEQ ID NO: 140 or a variant thereof having at least about 90% sequence identity to the amino acid sequence of SEQ ID NO: 140.

5

13. An isolated anti-C5a antibody or antigen binding fragment that specifically binds to C5a competitively with the isolated anti-C5a antibody or antigen binding fragment of any one of claims 1-12, or specifically binds to the same epitope as the isolated anti-C5a antibody or antigen binding fragment of any one of claims 1-12.

10

14. The isolated anti-C5a antibody or antigen binding fragment according to any one of claims 1-13, wherein the anti-C5a antibody or antigen binding fragment comprises an Fc fragment.

15 15. The isolated anti-C5a antibody or antigen binding fragment of claim 14, wherein the anti-C5a antibody or antigen binding fragment is a full-length IgG antibody.

16. The isolated anti-C5a antibody or antigen binding fragment of claim 15, wherein the anti-C5a antibody or antigen binding fragment is a full-length IgG1 or IgG4 antibody.

20

17. The isolated anti-C5a antibody or antigen binding fragment of any one of claims 1-16, wherein the anti-C5a antibody or antigen binding fragment is chimeric, human, or humanized.

18. The isolated anti-C5a antibody or antigen binding fragment according to any one of
25 claims 1-13, wherein the anti-C5a antibody or antigen binding fragment is selected from the group consisting of a Fab, a Fab', a F(ab)'₂, a Fab'-SH, a single-chain Fv (scFv), an Fv fragment, a dAb, a Fd, a nanobody, a diabody, and a linear antibody.

19. An isolated nucleic acid molecule that encodes the anti-C5a antibody or antigen binding fragment according to any one of claims 1-18.

20. A vector comprising the nucleic acid molecule of claim 19.

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21. An isolated host cell comprising the anti-C5a antibody or antigen binding fragment of any one of claims 1-18, the nucleic acid of claim 19, or the vector of claim 20.

22. A method of producing an anti-C5a antibody or antigen binding fragment, comprising:

10 a) culturing the host cell of claim 21 effective to express the anti-C5a antibody or antigen binding fragment; and

b) obtaining the expressed anti-C5a antibody or antigen binding fragment from the host cell.

15 23. A pharmaceutical composition comprising the anti-C5a antibody or antigen binding fragment according to any one of claims 1-18, the nucleic acid of claim 19, the vector of claim 20, or the isolated host cell of claim 21, and a pharmaceutically acceptable carrier.

20 24. A method of treating a disease or condition in an individual in need thereof, comprising administering to the individual an effective amount of the pharmaceutical composition of claim 23.

25 25. The method of claim 24, wherein the disease or condition is selected from the group consisting of inflammatory response syndrome (SIRS), sepsis, severe sepsis, septic shock, ischemia/reperfusion related injuries, acute lung injury, pneumonia, acute and chronic graft rejection in transplant patients, graft versus host reactions, renal glomerular diseases, glomerulonephritis, entities of renal failure, rheumatoid arthritis, auto-immune diseases, Bechterew's disease, lupus-type diseases, inflammatory bowel disease, Crohn's disease, tumor growth, and solid organ cancer.