

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.
- 5 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 that specifically binds to an epitope of human C5a within, consisting of or comprising the sequence as follows:
- (i) DGACVNNDTCEQRAARISLGPR;
- (ii) NDETCEQRAARISLGPR; or
- (iii) DETCEQRAAR.
- 15 4. The isolated anti-C5a antibody or antigen binding fragment that specifically binds to a peptide consisting of or comprising the sequence as follows:
- (i) DGACVNNDTCEQRAARISLGPR;
- (ii) NDETCEQRAARISLGPR; or
- (iii) DETCEQRAAR.
- 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 K_d from about 0.1 pM to about 1nM.
- 25 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.
- 30 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 X_1YYX_2Q (SEQ ID NO: 67), wherein X_1 is D, or N, and X_2 is M, or I;
- an HC-CDR2 comprising $LIRX_1KX_2X_3GX_4TX_5X_6X_7AASX_8KG$ (SEQ ID NO: 68),
 5 wherein X_1 is K, or N, X_2 is A, or V, X_3 is V, N, or I, X_4 is G, E, F, H, I, Q, or R, X_5 is T, V, or A, X_6 is Q, E, T, or S, X_7 is Y or F, and X_8 is V or L; and
- an HC-CDR3 comprising $RX_1GPPGLX_2$ (SEQ ID NO: 69), wherein X_1 is A, L, or V, and X_2 is T, S, or A;
- and a light chain variable domain (V_L) comprising a light chain complementarity
 10 determining region LC-CDR1 comprising $RSSQX_1LLX_2X_3X_4X_5YX_6YX_7D$ (SEQ ID NO: 70), wherein X_1 is S, R, or N, X_2 is A, H, or D, X_3 is S or T, X_4 is D or N, X_5 is G, A, or R, X_6 is N, I, T, E, or A, and X_7 is I, M, L, or V;
- an LC-CDR2 comprising GX_1SX_2RAS (SEQ ID NO: 71), wherein X_1 is G or A, X_2 is N or K; and
- 15 an LC-CDR3 comprising $X_1QHX_2X_3LPX_4T$ (SEQ ID NO: 72), wherein X_1 is L or M, X_2 is R or K, X_3 is A or V, and X_4 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
 20 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
 25 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.
- 30 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:

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- (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;
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- (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;
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- (iii) 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: 10, and an HC-CDR3 comprising an amino acid sequence having at least about 90% sequence identify with SEQ ID NO: 32; and a V_L comprising an LC-CDR1 comprising an amino acid sequence having at least about 90% sequence identify with SEQ ID NO: 42, an LC-CDR2 comprising an amino acid sequence having at least about 90% sequence identify with SEQ ID NO: 57, and an LC-
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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

- 5 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;
- 10 (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;
- 15 (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;
- 20 (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
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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;

- 5 (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-
10 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
- 15 (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-
20 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.

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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
30 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;
- 10 (ii) a V_H comprising the amino acid sequence of SEQ ID NO: 75 or a variant thereof having at 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;
- 15 (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 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;
- 20 (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 about 90% sequence identity to the amino acid sequence of SEQ ID NO: 118;
- 25 (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;
- 30 (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 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 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 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;
- (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 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 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 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.
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.
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. 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.
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 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.

- 5 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.
- 10 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:
a) culturing the host cell of claim 21 effective to express the anti-C5a antibody or antigen binding fragment; and
15 b) obtaining the expressed anti-C5a antibody or antigen binding fragment from the host cell.
- 20 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.
- 25 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.
- 30 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.