

CLAIMS

What is claimed is:

1. An antibody that specifically binds to human C5.
wherein the antibody comprises:
 - a) a heavy chain variable (VH) region and a light chain variable (VL) region, wherein the VH region comprises:
 - i) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 3;
 - ii) a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 4; and
 - iii) a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 5; and wherein the VL region comprises:
 - i) a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 8;
 - ii) a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 9; and
 - iii) a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 10;
 - b) a VH region and a VL region, wherein the VH region comprises:
 - i) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 13;
 - ii) a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 14; and
 - iii) a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 15; andwherein the VL region comprises:
 - i) a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 18;
 - ii) a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 19; and
 - iii) a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 20;
 - c) a VH region comprising the amino acid sequence of SEQ ID NO: 22, and a VL region comprising the amino acid sequence of SEQ ID NO: 27;
 - d) a VH region and a VL region, wherein the VH region comprises:
 - i) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 32;
 - ii) a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 33; and
 - iii) a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 34; andwherein the VL region comprises:
 - i) a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 37;
 - ii) a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 38; and
 - iii) a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 39;
 - e) a VH region and a VL region, wherein the VH region comprises:

i) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 42;
ii) a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 43; and
iii) a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 44; and
wherein the VL region comprises:
i) a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 47;
ii) a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 48; and
iii) a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 49; or
f) a VH region and a VL region, wherein the VH region comprises:
i) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 52;
ii) a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 53; and
iii) a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 54; and
wherein the VL region comprises:
i) a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 57;
ii) a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 58; and
iii) a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 59.

2. The antibody of claim 1, wherein the antibody is a chimeric antibody, comprises
a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 3; a VH-CDR2
comprising the amino acid sequence of SEQ ID NO: 4; a VH-CDR3 comprising
the amino acid sequence of SEQ ID NO: 5; a VL-CDR1 comprising the amino
acid sequence of SEQ ID NO: 8; a VL-CDR2 comprising the amino acid
sequence of SEQ ID NO: 9; and a VL-CDR3 comprising the amino acid
sequence of SEQ ID NO:10..

3. The antibody of claim 1, wherein the antibody comprises ~~at least one of the CDRs~~
~~selected from the group consisting of:~~a VH-CDR1 comprising the amino acid
~~sequence of:~~ SEQ ID NO:133; ~~a VH-CDR2:~~ comprising the amino acid
~~sequence of~~ SEQ ID NO:144; ~~a VH-CDR3 comprising the amino acid sequence~~
~~of:~~ SEQ ID NO:155; ~~a VL-CDR1 comprising the amino acid sequence of:~~ SEQ
ID NO:188; ~~a VL-CDR2:~~ comprising the amino acid sequence of SEQ ID
NO:199; and ~~a VL-CDR3:~~ comprising the amino acid sequence of SEQ ID
NO:2040.

4. The antibody of claim 1, wherein the antibody comprises ~~the CDRs:~~a VH-CDR1:
comprising the amino acid sequence of SEQ ID NO:323; ~~a VH-CDR2:~~
comprising the amino acid sequence of SEQ ID NO:334; ~~a VH-CDR3:~~
comprising the amino acid sequence of SEQ ID NO:345; ~~a VL-CDR1:~~
comprising the amino acid sequence of SEQ ID NO:378; ~~a VL-CDR2:~~

comprising the amino acid sequence of SEQ ID NO:389; and a VL-CDR3:
comprising the amino acid sequence of SEQ ID NO:3910,7, or a variant or
variants thereof

5. The antibody of claim 1, wherein the antibody comprises a VH-CDR1 comprising
the amino acid sequence of SEQ ID NO: 42; a VH-CDR2 comprising the amino
acid sequence of SEQ ID NO: 43; a VH-CDR3 comprising the amino acid
sequence of SEQ ID NO: 44; a VL-CDR1 comprising the amino acid sequence
of SEQ ID NO: 47; a VL-CDR2 comprising the amino acid sequence of SEQ ID
NO: 48; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:
49,heavy chain comprising the amino acid sequence of SEQ ID NO:2, or a
variant thereof
6. The antibody of claim 1, wherein the antibody comprises a VH-CDR1 comprising
the amino acid sequence of SEQ ID NO: 52; a VH-CDR2 comprising the amino
acid sequence of SEQ ID NO: 53; a VH-CDR3 comprising the amino acid
sequence of SEQ ID NO: 54; a VL-CDR1 comprising the amino acid sequence
of SEQ ID NO: 57; a VL-CDR2 comprising the amino acid sequence of SEQ ID
NO: 58; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO:
59,light chain comprising the amino acid sequence of SEQ ID NO:7, or a variant
thereof
7. The antibody of any one of claims 1-6, wherein the antibody comprises a VH
region comprising an amino acid sequence selected from the group consisting
of:heavy chain comprising the amino acid sequence of SEQ ID NO:2 and a light
chain comprising the amino acid sequence of SEQ ID NO:7, or a variant or
variants thereof
 - i) an amino acid sequence having at least about 95% identity to SEQ ID NO: 2;
 - ii) an amino acid sequence having at least about 95% identity to SEQ ID NO: 12;
 - iii) an amino acid sequence of SEQ ID NO: 22;
 - iv) an amino acid sequence having at least about 95% identity to SEQ ID NO: 31;
 - v) an amino acid sequence having at least about 95% identity to SEQ ID NO: 41;
 - vi) an amino acid sequence having at least about 95% identity to SEQ ID NO: 51;
8. The antibody of any one of claims 1-7, wherein the antibody comprises a VL region
comprising an amino acid sequence selected from the group consisting of:at least one of
the CDRs selected from the group consisting of: VH-CDR1: SEQ ID NO:13; VH-CDR2:
SEQ ID NO:14; VH-CDR3: SEQ ID NO:15; VL-CDR1: SEQ ID NO:18; VL-CDR2:
SEQ ID NO:19; and VL-CDR3: SEQ ID NO:20, or a variant or variants thereof

- i) an amino acid sequence having at least about 95% identity to SEQ ID NO: 7;
- ii) an amino acid sequence having at least about 95% identity to SEQ ID NO: 17;
- iii) an amino acid sequence of SEQ ID NO: 27;
- iv) an amino acid sequence having at least about 95% identity to SEQ ID NO: 36;
- v) an amino acid sequence having at least about 95% identity to SEQ ID NO: 46;
- vi) an amino acid sequence having at least about 95% identity to SEQ ID NO: 56.

9. The antibody of any one of claims 1-8, wherein the antibody comprises: ~~the CDRs: VH-CDR1: SEQ ID NO:13; VH-CDR2: SEQ ID NO:14; VH-CDR3: SEQ ID NO:15; VL-CDR1: SEQ ID NO:18; VL-CDR2: SEQ ID NO:19; and VL-CDR3: SEQ ID NO:20, or a variant or variants thereof~~

- (a) a VH region comprising an amino acid sequence having at least about 95% identity to SEQ ID NO: 2, and a VL region comprising an amino acid sequence having at least about 95% identity to SEQ ID NO: 7;
- (b) a VH region comprising an amino acid sequence having at least about 95% identity to SEQ ID NO: 12, and a VL region comprising an amino acid sequence having at least about 95% identity to SEQ ID NO: 17;
- (c) a VH region comprising the amino acid sequence of SEQ ID NO: 22, and a VL region comprising the amino acid sequence of SEQ ID NO: 27;
- (d) a VH region comprising an amino acid sequence having at least about 95% identity to SEQ ID NO: 31, and a VL region comprising an amino acid sequence having at least about 95% identity to SEQ ID NO: 36;
- (e) a VH region comprising an amino acid sequence having at least about 95% identity to SEQ ID NO: 41, and a VL region comprising an amino acid sequence having at least about 95% identity to SEQ ID NO: 46;
- (f) a VH region comprising an amino acid sequence having at least about 95% identity to SEQ ID NO: 51, and a VL region comprising an amino acid sequence having at least about 95% identity to SEQ ID NO: 56;
- (g) a VH region comprising an amino acid sequence having at least about 95% identity to SEQ ID NO: 63, and a VL region comprising an amino acid sequence having at least about 95% identity to SEQ ID NO: 73; and
- (h) a VH region comprising an amino acid sequence having at least about 95% identity to SEQ ID NO: 68, and a VL region comprising an amino acid sequence having at least about 95% identity to SEQ ID NO: 7

10. The antibody of any one of claims 1, 2, and 7-9, wherein the antibody comprises a ~~heavy chain comprising the amino acid sequence of SEQ ID NO:12, or a variant~~

~~thereof~~ VH region comprising the amino acid sequence of SEQ ID NO: 2, and a VL region comprising the amino acid sequence of SEQ ID NO: 7.

11. The antibody of any one of claims 1, 3, and 7-9 wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO:17, or a variant thereof VH region comprising the amino acid sequence of SEQ ID NO: 12, and a VL region comprising the amino acid sequence of SEQ ID NO: 17.
12. The antibody of any one of claims 1 and 7-9, wherein the antibody comprises a VH region comprising the amino acid sequence of SEQ ID NO: 22, and a VL region comprising the amino acid sequence of SEQ ID NO: 27, ~~heavy chain comprising the amino acid sequence of SEQ ID NO:12 and a light chain comprising the amino acid sequence of SEQ ID NO:17, or a variant or variants thereof~~
13. The antibody of any one of claims 1, 4, and 7-9, wherein the antibody comprises a VH region comprising the amino acid sequence of SEQ ID NO: 31, and a VL region comprising the amino acid sequence of SEQ ID NO: 36, ~~at least one of the CDRs selected from the group consisting of: VH-CDR1: SEQ ID NO:23; VH-CDR2: SEQ ID NO:24; VH-CDR3: SEQ ID NO:25; VL-CDR1: SEQ ID NO:28; and VL-CDR2: SEQ ID NO:29, or a variant or variants thereof~~
14. The antibody of any one of claims 1, 5, and 7-9, wherein the antibody comprises a VH region comprising the amino acid sequence of SEQ ID NO: 41, and a VL region comprising the amino acid sequence of SEQ ID NO: 46, ~~the CDRs: VH-CDR1: SEQ ID NO:23; VH-CDR2: SEQ ID NO:24; VH-CDR3: SEQ ID NO:25; VL-CDR1: SEQ ID NO:28; and VL-CDR2: SEQ ID NO:29, or a variant or variants thereof~~
15. The antibody of any one of claims 1 and 6-9, wherein the antibody comprises a VH region comprising the amino acid sequence of SEQ ID NO: 51, and a VL region comprising the amino acid sequence of SEQ ID NO: 56, ~~heavy chain comprising the amino acid sequence of SEQ ID NO:22, or a variant thereof~~
16. ~~The antibody of claim 1, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO:27, or a variant thereof~~
17. ~~The antibody of claim 1, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:22 and a light chain comprising the amino acid sequence of SEQ ID NO:27, or a variant or variants thereof~~
18. ~~16.~~ The antibody of any one of claims 1-15, wherein the antibody is selected from the group consisting of full-length antibody, Fab, Fab', F(ab)₂, F(ab')₂,

~~scFv, and combinations thereof, comprises at least one of the CDRs selected from the group consisting of: VH CDR1: SEQ ID NO:32; VH CDR2: SEQ ID NO:33; VH CDR3: SEQ ID NO:34; VL CDR1: SEQ ID NO:37; VL CDR2: SEQ ID NO:38, VL CDR3: SEQ ID NO:39, or a variant or variants thereof~~

~~19.17. The antibody of any one of claims 1-16, wherein the antibody is a chimeric antibody, comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:31, or a variant thereof~~

~~20. The antibody of claim 1, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO:36, or a variant thereof~~

~~21. The antibody of claim 1, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:31 and a light chain comprising the amino acid sequence of SEQ ID NO:36, or a variant or variants thereof~~

~~22. The antibody of claim 1, wherein the antibody comprises at least one of the CDRs selected from the group consisting of: VH CDR1: SEQ ID NO:42; VH CDR2: SEQ ID NO:43; VH CDR3: SEQ ID NO:44; VL CDR1: SEQ ID NO:47; VL CDR2: SEQ ID NO:48, VL CDR3: SEQ ID NO:49, or a variant or variants thereof~~

~~23. The antibody of claim 1, wherein the antibody comprises the CDRs: VH CDR1: SEQ ID NO:42; VH CDR2: SEQ ID NO:43; VH CDR3: SEQ ID NO:44; VL CDR1: SEQ ID NO:47; VL CDR2: SEQ ID NO:48, VL CDR3: SEQ ID NO:49, or a variant or variants thereof~~

~~24. The antibody of claim 1, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 41, or a variant thereof~~

~~25. 18. The antibody of claim 1, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO:46, or a variant thereof~~
~~A cell comprising the antibody of claim 1~~

~~26. 19. The antibody of claim 1, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:41 and a light chain comprising the amino acid sequence of SEQ ID NO:46, or a variant or variants~~

~~thereof~~ The cell of claim 18, wherein the cell produces the antibody of any one of the claims 1-17.

~~27.~~ 20. The cell of claim 18, wherein the cell is a hybridoma, antibody of claim 1, wherein the antibody comprises at least one of the CDRs selected from the group consisting of: VH CDR1: SEQ ID NO:52; VH CDR2: SEQ ID NO:53; VH CDR3: SEQ ID NO:54; VL CDR1: SEQ ID NO:57; VL CDR2: SEQ ID NO:58, VL CDR3: SEQ ID NO:59, or a variant or variants thereof

~~28.~~ The antibody of claim 1, wherein the antibody comprises the CDRs: VH CDR1: SEQ ID NO:52; VH CDR2: SEQ ID NO:53; VH CDR3: SEQ ID NO:54; VL CDR1: SEQ ID NO:57; VL CDR2: SEQ ID NO:58, VL CDR3: SEQ ID NO:59, or a variant or variants thereof

~~29.~~ 21. The antibody of claim 1, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:51, or a variant thereof Use of the antibody of any one of claims 1-17 in the manufacture of a medicament for treating a complement pathway-mediated disease or disorder in an individual.

~~30.~~ 22. The antibody of claim 1, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO:56, or a variant thereof use of claim 21, wherein the complement pathway-mediated disease or disorder is selected from the group consisting of: macular degeneration (MD), age-related macular degeneration (AMD), ischemia reperfusion injury, arthritis, rheumatoid arthritis, lupus, ulcerative colitis, stroke, post-surgery systemic inflammatory syndrome, asthma, allergic asthma, chronic obstructive pulmonary disease (COPD), paroxysmal nocturnal hemoglobinuria (PNH) syndrome, myasthenia gravis, neuromyelitis optica (NMO), multiple sclerosis, delayed graft function, antibody-mediated rejection, atypical hemolytic uremic (aHUS) syndrome, central retinal vein occlusion (CRVO), central retinal artery occlusion (CRAO), epidermolysis bullosa, sepsis, organ transplantation, inflammation, inflammation associated with cardiopulmonary bypass surgery and kidney dialysis, C3 glomerulopathy, membranous nephropathy, IgA nephropathy, glomerulonephritis, anti-neutrophil cytoplasmic antibody (ANCA)-mediated glomerulonephritis, lupus nephritis, ANCA-mediated vasculitis, Shiga toxin induced HUS, antiphospholipid antibody-induced pregnancy loss, and any combinations thereof.

~~31.~~ 23. The antibody of claim 1, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:51 and a light chain

comprising the amino acid sequence of SEQ ID NO:56, or a variant or variants thereof Use of the antibody of any one of claims 1-17 in the manufacture of a medicament for reducing the activity of a complement system of an individual.

~~32.~~ 24. The use of any one of claims 21-23, wherein:

i) the antibody is for enteral administration, parenteral administration, or a combination thereof; and/or

ii) the individual is a human.

~~33. ——— A method of treating a complement pathway-mediated disease or disorder in an individual, comprising the step of administering to said individual the anti-05 antibody of any one of claims 1-32.~~

~~34. ——— The method of claim 33, wherein the disease or disorder is at least selected from the group consisting of: macular degeneration (MD), age-related macular degeneration (AMD), ischemia reperfusion injury, arthritis, rheumatoid arthritis, lupus, ulcerative colitis, stroke, post surgery systemic inflammatory syndrome, asthma, allergic asthma, chronic obstructive pulmonary disease (COPD), paroxysmal nocturnal hemoglobinuria (PNH) syndrome, myasthenia gravis, neuromyelitis optica, (NMO), multiple sclerosis, delayed graft function, antibody-mediated rejection, atypical hemolytic uremic (aHUS) syndrome, central retinal vein occlusion (CRVO), central retinal artery occlusion (CRAO), epidermolysis bullosa, sepsis, organ transplantation, inflammation (including, but not limited to, inflammation associated with cardiopulmonary bypass surgery and kidney dialysis), C3 glomerulopathy, membranous nephropathy, IgA nephropathy, glomerulonephritis (including, but not limited to, anti-neutrophil cytoplasmic antibody (ANCA)-mediated glomerulonephritis, lupus nephritis, and combinations thereof), ANCA-mediated vasculitis, Shiga toxin induced HUS, and antiphospholipid antibody-induced pregnancy loss, or any combinations thereof.~~

~~35. A method of reducing the activity of a complement system of an individual, wherein the method comprises administering an antibody to the individual via a route of administration selected from the group consisting of enteral administration, parenteral administration, and a combination thereof, and wherein the antibody is the antibody of any one of claims 1-32.~~

~~36. The method of claim 35, wherein the antibody is an antibody fragment selected from the group consisting of a Fab, Fab', F(ab)2, F(ab')2, scFv, and combinations thereof~~

~~37. A cell comprising the antibody of at least one of claims 1-32.~~

~~38. The cell of claim 37, wherein the cell produces the antibody of at least one of claims 1-32.~~

~~39. The cell of claim 37, wherein the cell is a hybridoma.~~

