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PTL 8: WO 02/30985

PTL 9: WO 2004/007553

PTL 10: WO 2010/015608

PTL 11: WO 2009/125825

PTL 12: WO 2011/122011

PTL 13: WO 2011/111007

Non-Patent Literature

[0019] NPL 1: Holers et al., Immunol. Rev. 223:300-316 (2008)

NPL 2: Dmytrijuk et al., The Oncologist 13(9):993-1000 (2008)

NPL 3: Yeung et al., J Immunol. 182(12): 7663-7671 (2009)

NPL 4: Datta-Mannan et al., J Biol. Chem. 282(3):1709-1717 (2007)

NPL 5: Dall'Acqua et al., J. Immunol. 169(9):5171-5180 (2002)

Summary of Invention

Technical Problem

[0020] An objective of the invention is to provide anti-C~~5~~~~S~~ antibodies and methods of using the same.

Solution to Problem

[0021] The invention provides anti-~~CS~~-C~~5~~ antibodies and methods of using the same.

[0022] In one aspect, the present invention refers to an anti-C5 antibody comprising: (a) a VH sequence of SEQ ID NO: 106 and a VL sequence of SEQ ID NO: 111; (b) a VH sequence of SEQ ID NO: 107 and a VL sequence of SEQ ID NO: 111; (c) a VH sequence of SEQ ID NO: 108 and a VL sequence of SEQ ID NO: 111; (d) a VH sequence of SEQ ID NO: 109 and a VL sequence of SEQ ID NO: 111; (e) a VH sequence of SEQ ID NO: 109 and a VL sequence of SEQ ID NO: 112; (f) a VH sequence of SEQ ID NO: 109 and a VL sequence of SEQ ID NO: 113; or (g) a VH sequence of SEQ ID NO: 110 and a VL sequence of SEQ ID NO: 113. In another aspect, the present invention refers to an isolated nucleic acid encoding the antibody as described herein. In another aspect, the present invention refers to a host cell comprising the nucleic acid as described herein. In another aspect, the present invention refers to method of producing an antibody comprising culturing the host cell as described herein so that the antibody is produced. In another aspect, the present invention refers to a pharmaceutical formulation comprising the antibody as described herein and a pharmaceutically acceptable carrier. In some examples, an isolated anti-C5 antibody of the present disclosure binds to an epitope within the beta chain of C5. In some examples, an isolated anti-C~~5~~~~S~~ antibody of the present disclosure binds to an epitope within the MG1-MG2 domain of the beta chain of C5. In some examples, an isolated anti-C~~5~~~~S~~ antibody of the present

disclosure binds to an epitope within a fragment consisting of amino acids 33-124 of the beta chain (SEQ ID NO: 40) of C5. In some examples, an isolated anti-C5 antibody of the present disclosure binds to an epitope within the beta chain (SEQ ID NO: 40) of C5 which comprises at least one fragment selected from the group consisting of amino acids 47-57, 70-76, and 107-110. In some examples, an isolated anti-C5 antibody of the present disclosure binds to an epitope within a fragment of the beta chain (SEQ ID NO: 40) of C5 which comprises at least one amino acid residue selected from the group consisting of Glu48, Asp51, His70, His72, Lys109, and His110 of SEQ ID NO: 40. In further examples, the antibody binds to C5 with a higher affinity at neutral pH than at acidic pH. In further examples, the antibody binds to C5 with a higher affinity at pH7.4 than at pH5.8. In another example, an isolated anti-C5 antibody of the present disclosure binds to the same epitope as an antibody described in Table 2. In further examples, the antibody binds to the same epitope as an antibody described in Table 2 with a higher affinity at

pH7.4 than at pH5.8. In a further example, the anti-C5 antibody of the present disclosure binds to the same epitope as an antibody described in Tables 7 or 8. In further examples, the antibody binds to the same epitope as an antibody described in Tables 7 or 8 with a higher affinity at pH7.4 than at pH5.8.

- [0023] In certain examples, an anti-C5 antibody of the present disclosure competes for binding C5 with an antibody comprising a VH and VL pair selected from: (a) a VH of SEQ ID NO:1 and a VL of SEQ ID NO:11; (b) a VH of SEQ ID NO: 5 and a VL of SEQ ID NO:15; (c) a VH of SEQ ID NO:4 and a VL of SEQ ID NO:14; (d) a VH of SEQ ID NO: 6 and a VL of SEQ ID NO: 16; (e) a VH of SEQ ID NO:2 and a VL of SEQ ID NO:12; (f) a VH of SEQ ID NO: 3 and a VL of SEQ ID NO: 13; (g) a VH of SEQ ID NO:9 and a VL of SEQ ID NO:19; (h) a VH of SEQ ID NO:7 and a VL of SEQ ID NO: 17; (i) a VH of SEQ ID NO:8 and a VL of SEQ ID NO:18; and (j) a VH of SEQ ID NO:10 and a VL of SEQ ID NO:20. In further examples, the anti-C5 antibody binds to C5 with a higher affinity at neutral pH than at acidic pH. In further examples, the anti-C5 antibody binds to C5 with a higher affinity at pH7.4 than at pH5.8.
- [0024] In some examples, an isolated anti-C5 antibody of the present disclosure has a characteristic selected from the group consisting of: (a) the antibody contacts amino acids D51 and K109 of C5 (SEQ ID NO:39); (b) the affinity of the antibody for C5 (SEQ ID NO:39) is greater than the affinity of the antibody for a C5 mutant consisting of an E48A substitution of SEQ ID NO:39; or (c) the antibody binds to a C5 protein consisting of the amino acid sequence of SEQ ID NO:39 at pH7.4, but does not bind to a C5 protein consisting of the amino acid sequence of SEQ ID NO:39 with a H72Y substitution at pH7.4. In further examples, the antibody binds to C5 with a higher affinity at neutral pH than at acidic pH. In further examples, the antibody binds to C5 with a higher affinity at pH7.4 than at pH5.8.
- [0025] In some examples, an isolated anti-C5 antibody of the present disclosure inhibits activation of C5. In some examples, an isolated anti-C5 antibody of the present disclosure inhibits activation of C5 variant R885H. In some examples, an isolated anti-C5 antibody of the present disclosure is a monoclonal antibody. In some examples, an isolated anti-C5 antibody of the present disclosure is a human, humanized, or chimeric antibody. In some examples, an isolated anti-C5 antibody of the present disclosure is an antibody fragment that binds to C5. In some examples, an isolated anti-C5 antibody of the present disclosure is a full length IgG1 or IgG4 antibody.
- [0026] In some examples, an isolated anti-C5 antibody of the present disclosure comprises (a) a HVR-H3 comprising the amino acid sequence DX₁GYX₂X₃PTHAMX₄X₅, wherein X₁ is G or A, X₂ is V, Q or D, X₃ is T or Y, X₄ is Y or H, X₅ is L or Y