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Summary

[0020]

In one aspect, the present disclosure provides a method of producing an anti-C5 antibody comprising immunizing a non-human animal against a polypeptide, wherein the polypeptide comprises the MG1-MG2 domain (SEQ ID NO: 43) of the beta chain of C5, wherein the anti-C5 antibody binds to an epitope within the domain with a higher affinity at pH7.4 than at pH5.8.

In another aspect, the present disclosure provides a method of producing an anti-C5 antibody comprising immunizing a non-human animal against a polypeptide, wherein the polypeptide comprises the region corresponding to amino acids at positions 19-180 of the beta chain (SEQ ID NO: 40) of C5, wherein the anti-C5 antibody binds to an epitope within a fragment consisting of the amino acids 19-180 with a higher affinity at pH7.4 than at pH5.8.

In another aspect, the present disclosure provides a method of producing an anti-C5 antibody comprising immunizing a non-human animal against a polypeptide, wherein the polypeptide comprises the region corresponding to amino acids at positions 33 to 124 of the beta chain (SEQ ID NO: 40) of C5, wherein the anti-C5 antibody binds to an epitope within a fragment consisting of the amino acids 33-124 with a higher affinity at pH7.4 than at pH5.8.

In another aspect, the present disclosure provides a method of producing an anti-C5 antibody comprising immunizing a non-human animal against a polypeptide, wherein the polypeptide comprises the region corresponding to amino acids at positions 33-124 of the beta chain (SEQ ID NO: 40) of C5, wherein the anti-C5 antibody binds to an epitope comprising at least one fragment selected from the group consisting of amino acids 47-57, 70-76, and 107-110 in the beta chain with a higher affinity at pH7.4 than at pH5.8.

In another aspect, the present disclosure provides a method of producing an anti-C5 antibody comprising immunizing a non-human animal against a polypeptide, wherein the polypeptide comprises at least one fragment selected from amino acids 47-57, 70-76, and 107-110 of the beta chain (SEQ ID NO: 40) of C5, wherein the anti-C5 antibody binds to the at least one fragment with a higher affinity at pH7.4 than at pH5.8.

In yet another aspect, the present disclosure provides a method of producing an anti-C5 antibody comprising immunizing a non-human animal against a polypeptide, wherein the polypeptide comprises a fragment of the beta chain (SEQ ID NO: 40) of C5 which comprises at least one amino acid selected from Glu48, Asp51, His70, His72, Lys109, and His110, wherein the anti-C5 antibody binds to the at least one amino acid with a higher affinity at pH7.4 than at pH5.8.

Also described herein are anti-C5 antibodies and methods of using the same.

[0021]

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-C5 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-C5 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

Claims

1. A method of producing an anti-C5 antibody comprising immunizing a non-human animal against a polypeptide, wherein the polypeptide comprises the MG1-MG2 domain (SEQ ID NO: 43) of the beta chain of C5, wherein the anti-C5 antibody binds to an epitope within the domain with a higher affinity at pH7.4 than at pH5.8.

2. A method of producing an anti-C5 antibody comprising immunizing a non-human animal against a polypeptide, wherein the polypeptide comprises the region corresponding to amino acids at positions 19-180 of the beta chain (SEQ ID NO: 40) of C5, wherein the anti-C5 antibody binds to an epitope within a fragment consisting of the amino acids 19-180 with a higher affinity at pH7.4 than at pH5.8.

3. A method of producing an anti-C5 antibody comprising immunizing a non-human animal against a polypeptide, wherein the polypeptide comprises the region corresponding to amino acids at positions 33 to 124 of the beta chain (SEQ ID NO: 40) of C5, wherein the anti-C5 antibody binds to an epitope within a fragment consisting of the amino acids 33-124 with a higher affinity at pH7.4 than at pH5.8.

4. A method of producing an anti-C5 antibody comprising immunizing a non-human animal against a polypeptide, wherein the polypeptide comprises the region corresponding to amino acids at positions 33-124 of the beta chain (SEQ ID NO: 40) of C5, wherein the anti-C5 antibody binds to an epitope comprising at least one fragment selected from the group consisting of amino acids 47-57, 70-76, and 107-110 in the beta chain with a higher affinity at pH7.4 than at pH5.8.

5. A method of producing an anti-C5 antibody comprising immunizing a non-human animal against a polypeptide, wherein the polypeptide comprises at least one fragment selected from amino acids 47-57, 70-76, and 107-110 of the beta chain (SEQ ID NO: 40) of C5, wherein the anti-C5 antibody binds to the at least one fragment with a higher affinity at pH7.4 than at pH5.8.

6. A method of producing an anti-C5 antibody comprising immunizing a non-human animal against a polypeptide, wherein the polypeptide comprises a fragment of the beta chain (SEQ ID NO: 40) of C5 which comprises at least one amino acid selected from Glu48, Asp51, His70, His72, Lys109, and His110, wherein the anti-C5 antibody binds to the at least one amino acid with a higher affinity at pH7.4 than at pH5.8.

7. The method of any one of claims 1 to 6, which further comprises confirming whether the anti-C5 antibody has a higher affinity at pH7.4 than at pH5.8.

8. The method of any one of claims 1 to 7, wherein the anti-C5 antibody binds to C5 with at least 2 or more times higher affinity at pH7.4 than at pH5.8.

9. The method of any one of claims 1 to 8, wherein the anti-C5 antibody is an isolated monoclonal antibody.

10. The method of any one of claims 1 to 9, wherein the anti-C5 antibody inhibits activation of C5.

11. The method of any one of claims 1 to 10, wherein the anti-C5 antibody inhibits activation of C5 variant R885H.

12. The method of any one of claims 1 to 11, wherein the anti-C5 antibody is a human, humanized, or chimeric antibody.

13. The method of any one of claims 1 to 12, wherein the anti-C5 antibody is an antibody fragment that binds to C5.

14. The method of any one of claims 1 to 12, wherein the anti-C5 antibody is derived from a full length IgG1 or IgG4 antibody.

15. The method of any one of claims 1 to 14, wherein the anti-C5 antibody binds to C5 with at least 5 or more times higher affinity at pH7.4 than at pH5.8.

16. The method of any one of claims 1 to 15, wherein the anti-C5 antibody binds to C5 with at least 20 or more times higher affinity at pH7.4 than at pH5.8.