

## SUMMARY

**[0006]** In one aspect, the present disclosure refers to an antibody that specifically binds to human FCMR, the antibody comprising a vhCDR1 comprising SEQ ID NO:13, a vhCDR2 comprising SEQ ID NO:14, a vhCDR3 comprising SEQ ID NO:15, a vlCDR1 comprising SEQ ID NO:16, a vlCDR2 comprising SEQ ID NO:17, and a vlCDR3 comprising SEQ ID NO:18. In one example, the present disclosure relates to novel anti-FCMR antibodies. In some examples, the anti-FCMR antibodies include a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:1 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:2. In some examples, the anti-FCMR antibodies include a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:3 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:4. In some examples, the anti-FCMR antibodies include a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:5 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:6. In some examples, the anti-FCMR antibodies include a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:7 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:8. In some examples, the anti-FCMR antibodies include a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:9 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:10. In some examples, the anti-FCMR antibodies include a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:11 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:12.

**[0007]** In another example, the present disclosure refers to an antibody that specifically binds to human FCMR, the antibody comprising: a) a vhCDR1 comprising SEQ ID NO:13, a vhCDR2 comprising SEQ ID NO:14, a vhCDR3 comprising SEQ ID NO:15, a vlCDR1 comprising SEQ ID NO:16, a vlCDR2 comprising SEQ ID NO:17, and a vlCDR3 comprising SEQ ID NO:18; b) a vhCDR1 comprising SEQ ID NO:19, a vhCDR2 comprising SEQ ID NO:20, a vhCDR3 comprising SEQ ID NO:21, a vlCDR1 comprising SEQ ID NO:22, a vlCDR2 comprising SEQ ID NO:23, and a vlCDR3 comprising SEQ ID NO:24; c) a vhCDR1 comprising SEQ ID NO:25, a vhCDR2 comprising SEQ ID NO:26, a vhCDR3 comprising SEQ ID NO:27, a vlCDR1 comprising SEQ ID NO:28, a vlCDR2 comprising SEQ ID NO:29, and a vlCDR3 comprising SEQ ID NO:30; d) a vhCDR1 comprising SEQ ID NO:31, a vhCDR2 comprising SEQ ID NO:32, a vhCDR3 comprising SEQ ID NO:33, a vlCDR1 comprising SEQ ID NO:34, a vlCDR2 comprising SEQ ID NO:35, and a vlCDR3 comprising SEQ ID NO:36; e) a vhCDR1 comprising SEQ ID NO:37, a vhCDR2 comprising SEQ ID NO:38, a vhCDR3 comprising SEQ ID NO:39, a vlCDR1 comprising SEQ ID NO:40, a vlCDR2 comprising SEQ ID NO:41, and a vlCDR3 comprising SEQ ID NO:42; or f) a vhCDR1 comprising SEQ ID NO:43, a vhCDR2 comprising SEQ ID NO:44, a vhCDR3 comprising SEQ ID NO:45, a vlCDR1 comprising SEQ ID NO:46, a vlCDR2 comprising SEQ ID NO:47, and a vlCDR3 comprising SEQ ID NO:48. In some examples, the anti-FCMR antibodies include a vhCDR1 comprising SEQ ID NO:13, a vhCDR2 comprising SEQ ID NO:14, a vhCDR3 comprising SEQ ID NO:15, a vlCDR1 comprising SEQ ID NO:16, a vlCDR2 comprising SEQ ID NO:17, and a vlCDR3 comprising SEQ ID NO:18. In some

examples, the anti-FCMR antibodies include a vhCDR1 comprising SEQ ID NO:19, a vhCDR2 comprising SEQ ID NO:20, a vhCDR3 comprising SEQ ID NO:21, a vlCDR1 comprising SEQ ID NO:22, a vlCDR2 comprising SEQ ID NO:23, and a vlCDR3 comprising SEQ ID NO:24. In some examples, the anti-FCMR antibodies include a vhCDR1 comprising SEQ ID NO:25, a vhCDR2 comprising SEQ ID NO:26, a vhCDR3 comprising SEQ ID NO:27, a vlCDR1 comprising SEQ ID NO:28, a vlCDR2 comprising SEQ ID NO:29, and a vlCDR3 comprising SEQ ID NO:30. In some examples, the anti-FCMR antibodies include a vhCDR1 comprising SEQ ID NO:31, a vhCDR2 comprising SEQ ID NO:32, a vhCDR3 comprising SEQ ID NO:33, a vlCDR1 comprising SEQ ID NO:34, a vlCDR2 comprising SEQ ID NO:35, and a vlCDR3 comprising SEQ ID NO:36. In some examples, the anti-FCMR antibodies include a vhCDR1 comprising SEQ ID NO:37, a vhCDR2 comprising SEQ ID NO:38, a vhCDR3 comprising SEQ ID NO:39, a vlCDR1 comprising SEQ ID NO:40, a vlCDR2 comprising SEQ ID NO:41, and a vlCDR3 comprising SEQ ID NO:42. In some examples, the anti-FCMR antibodies include a vhCDR1 comprising SEQ ID NO:43, a vhCDR2 comprising SEQ ID NO:44, a vhCDR3 comprising SEQ ID NO:45, a vlCDR1 comprising SEQ ID NO:46, a vlCDR2 comprising SEQ ID NO:47, and a vlCDR3 comprising SEQ ID NO:48.

**[0008]** In some examples, the anti-FCMR antibodies described herein bind human FCMR.

**[0009]** In some examples, the anti-FCMR antibodies described herein include a constant region with an amino acid sequence at least 90% identical to a human IgG. In some examples, the IgG is selected from an IgG1, IgG2, IgG3 or IgG4. In some examples, the IgG is an IgG1. In some examples the IgG is an IgG2.

**[0010]** In another aspect, the present disclosure relates to a nucleic acid composition encoding any one of the anti-FCMR antibodies described herein.

**[0011]** In another aspect, the present disclosure refers to an expression vector composition comprising the nucleic acid composition as disclosed herein, wherein a first nucleic acid is contained in a first expression vector and a second nucleic acid is contained in a second expression vector. In another aspect, the present disclosure refers to an expression vector composition comprising the nucleic acid composition as disclosed herein, wherein a first nucleic acid and a second nucleic acid are contained in a single expression vector. Another example of the present disclosure relates to an expression vector composition that includes any one of the nucleic acid compositions described herein. In some examples, the first nucleic acid is contained in a first expression vector and the second nucleic acid is contained in a second expression vector. In some other examples, the first nucleic acid and the second nucleic acid are contained in a single expression vector.

**[0012]** Another aspect of the present disclosure relates to a host cell that includes any one of the expression vectors described herein. Also presented is a method of making anti-FCMR antibodies, and the method includes culturing the host cell under conditions wherein the antibodies expressed, and recovering the antibodies.

**[0013]** In another aspect, the present disclosure relates to a composition that includes any one of the anti-FCMR antibodies described herein, and a pharmaceutical acceptable carrier or diluent.

**[0013a]** In another aspect, the present disclosure refers to a method of making an antibody comprising culturing said host cell as disclosed herein under conditions wherein the antibody is expressed, and recovering the antibody.

**[0014]** In another example, the present disclosure refers to the use of the antibody as disclosed herein or the composition as disclosed herein in the manufacture of a medicament for modulating an immune response in a subject. Also described is a method of modulating an immune response in a subject, and the method includes administering to the subject an effective amount of any one of the anti-FCMR antibodies described herein, or any one of the compositions described herein. In some examples, the method inhibits an immune response in the subject and the method includes

administering to the subject an effective amount of an anti-FCMR antibody that serves as a FCMR antagonist, or a pharmaceutical composition thereof. In some examples, the method stimulates an immune response in the subject and the method includes administering to the subject an effective amount of an anti-FCMR antibody that serves as a FCMR agonist, or a pharmaceutical composition thereof.

**[0015]** In some examples, the method suppresses an immune response in the subject, and the method includes administering to the subject an effective amount of an anti-FCMR antibody.

**[0016]** In some examples, the method stimulates an immune response in the subject, and the method includes administering to the subject an effective amount of an anti-FCMR antibody.

**[0017]** In another aspect, the present disclosure refers to the use of the antibody as disclosed herein or the composition as disclosed herein in the manufacture of medicament for treating an FCMR-associated cancer in a subject in need thereof. In another example, the present disclosure relates to a method of treating cancer in a subject, and the method includes administering to the subject an effective amount of an anti-FCMR antibody described herein, or a composition thereof. In some examples, the cancer to be treated upregulates FCMR compared to the corresponding non-cancerous tissue. In some examples, the cancer to be treated can be a B cell malignancy. In some examples, the B cell malignancy is chronic lymphocytic leukemia. In some examples, an anti-FCMR antibody is used in combination with one or more additional anti-cancer therapeutic agents. In some examples, such anti-cancer therapeutic agents are other immune checkpoint inhibitors, such as a PD-1 inhibitor, a PD-L1 inhibitor, a CTLA-4 inhibitor, a TIM-3 inhibitor, and a LAG-3 inhibitor.

**[0018]** In another aspect, the present disclosure refers to the use of the antibody as disclosed herein or the composition as disclosed herein in the manufacture of a medicament for treating an FCMR-associated autoimmune disease in a subject in need thereof. In another example, the present disclosure relates to a method of treating an autoimmune disease in a subject, and the method includes administering to the subject an effective amount of an anti-FCMR antibody described herein, or a composition thereof. In some examples, an anti-FCMR antibody is used in combination with one or more additional anti-inflammatory therapeutic agents.

**[0019]** In another aspect, the present disclosure refers to the use of the antibody as disclosed herein or the composition as disclosed herein in the manufacture of a medicament for treating an FCMR-associated bacterial infection in a subject in need thereof. In another example, the present disclosure relates to a method of treating a bacterial infection in a subject, and the method includes administering to the subject an effective amount of an anti-FCMR antibody described herein, or a composition thereof. In some examples, an anti-FCMR antibody is used in combination with one or more antibiotic therapeutic agents.

**[0020]** In another aspect, the present disclosure refers to the use of the antibody as disclosed herein or the composition as disclosed herein in the manufacture of a medicament for treating an FCMR-associated viral infection in a subject in need thereof. In yet another aspect, the present disclosure refers to the use of the antibody as disclosed herein or the composition as disclosed herein in the manufacture of a medicament for modulating FCMR in a subject. In another example, the present disclosure relates to a method of treating a viral infection in a subject, and the method includes administering to the subject an effective amount of an anti-FCMR antibody described herein, or a composition thereof. In some examples, an anti-FCMR antibody is used in combination with one or more additional anti-viral therapeutic agents.

**[0020a]** In another aspect, the present disclosure refers to the use of the antibody as disclosed herein or the composition as disclosed herein in the manufacture of a medicament for use in combinatorial therapy for treating an FCMR-associated cancer in a subject in need thereof, wherein the antibody or composition is to be administered in combination with one or more additional cancer therapeutic agents.

**[0020b]** In another aspect, the present disclosure refers to the use of the antibody as disclosed herein or the composition as disclosed herein in the manufacture of a medicament for use in combinatorial therapy for treating an FCMR-associated autoimmune disease in a subject in need thereof, wherein the antibody or composition is to be administered in combination with one or more additional anti-inflammatory therapeutic agents.

**[0020c]** In another aspect, the present disclosure refers to the use of the antibody as disclosed herein or the composition as disclosed herein in the manufacture of a medicament for use in combinatorial therapy for treating an FCMR-associated bacterial infection in a subject in need thereof, wherein the antibody or composition is to be administered in combination with one or more additional antibiotic therapeutic agents.

**[0020d]** In another aspect, the present disclosure refers to the use of the antibody as disclosed herein or the composition as disclosed herein in the manufacture of a medicament for use in combinatorial therapy for treating an FCMR-associated viral infection in a subject in need thereof, wherein the antibody or composition is to be administered in combination with one or more additional anti-viral therapeutic agents.

**[0020e]** In another aspect, the present disclosure refers to the antibody as disclosed herein or the composition as disclosed herein for use as a medicament.

## **Claims**

### **What Is Claimed Is:**

1. An antibody that specifically binds to human FCMR, the antibody comprising a vhCDR1 comprising SEQ ID NO:13, a vhCDR2 comprising SEQ ID NO:14, a vhCDR3 comprising SEQ ID NO:15, a vlCDR1 comprising SEQ ID NO:16, a vlCDR2 comprising SEQ ID NO:17, and a vlCDR3 comprising SEQ ID NO:18.
2. The antibody according to claim 1, the antibody comprising: a heavy chain variable region comprising an amino acid sequence of SEQ ID NO:1 and a light chain variable region comprising an amino acid sequence of SEQ ID NO:2.
3. The antibody according to any one of the previous claims, wherein the antibody comprises a constant region with an amino acid sequence at least 90% identical to a human wildtype IgG1, IgG2, IgG3, or IgG4.
4. The antibody according to claim 3, wherein the IgG is an IgG2.
5. The antibody according to claim 3, wherein the IgG is an IgG1.
6. A nucleic acid composition encoding the antibody according to any of the previous claims.
7. An expression vector composition comprising the nucleic acid composition according to claim 6, wherein a first nucleic acid is contained in a first expression vector and a second nucleic acid is contained in a second expression vector.
8. An expression vector composition comprising the nucleic acid composition according to claim 6, wherein a first nucleic acid and a second nucleic acid are contained in a single expression vector.
9. A host cell comprising the expression vector composition of claim 7 or 8.
10. A method of making an antibody comprising culturing said host cell of claim 9 under conditions wherein the antibody is expressed, and recovering the antibody.
11. A composition comprising the antibody according to any one of claims 1-5 and a pharmaceutical acceptable carrier or diluent.
12. Use of the antibody according to any one of the claims 1-5 or the composition according to claim 6 in the manufacture of medicament for treating an FCMR-associated cancer in a subject in need thereof.
13. The use according to claim 12, wherein the cancer is a B cell malignancy.
14. The use according to claims 12 or 13, wherein the cancer is chronic lymphocytic

leukemia.

15. Use of the antibody according to any one of claims 1-5 or the composition according to claim 6 in the manufacture of a medicament for use in combinatorial therapy for treating an FCMR-associated cancer in a subject in need thereof, wherein the antibody or composition is to be administered in combination with one or more additional cancer therapeutic agents.

16. The use according to claim 15, wherein the additional cancer therapeutic agents are immune checkpoint inhibitors.

17. The use according to claim 15, wherein the immune checkpoint inhibitors are selected from the group consisting of a PD-1 inhibitor, a PD-L1 inhibitor, a CTLA-4 inhibitor, a TIM-3inhibitor, and a LAG-3 inhibitor.

18. Use of the antibody according to any one of the claims 1-5 or the composition according to claim 6 in the manufacture of a medicament for treating an FCMR-associated autoimmune disease in a subject in need thereof.

19. Use of the antibody according to any one of claims 1-5 or the composition according to claim 6 in the manufacture of a medicament for use in combinatorial therapy for treating an FCMR-associated autoimmune disease in a subject in need thereof, wherein the antibody or composition is to be administered in combination with one or more additional anti-inflammatory therapeutic agents.

20. Use of the antibody according to any one of the claims 1-5 or the composition according to claim 6 in the manufacture of a medicament for treating an FCMR-associated bacterial infection in a subject in need thereof.

21. Use of the antibody according to any one of claims 1-5 or the composition according to claim 6 in the manufacture of a medicament for use in combinatorial therapy for treating an FCMR-associated bacterial infection in a subject in need thereof, wherein the antibody or composition is to be administered in combination with one or more additional antibiotic therapeutic agents.

22. Use of the antibody according to any one of the claims 1-5 or the composition according to claim 6 in the manufacture of a medicament for treating an FCMR-associated viral infection in a subject in need thereof.

23. Use of the antibody according to any one of claims 1-5 or the composition according to claim 6 in the manufacture of a medicament for use in combinatorial therapy for treating an FCMR-associated viral infection in a subject in need thereof, wherein the antibody or composition is to be administered in combination with one or more additional anti-viral therapeutic agents.

24. The antibody according to any one claims 1-5 or the composition according to claim 6 for use as a medicament.