

CLAIMS

1. An isolated antibody that binds human CCR8, wherein the antibody comprises:

(i) a heavy chain complementarity determining region 1 (HCDR1) comprising the amino acid sequence of SEQ ID NO: 84 or 100, a heavy chain complementarity determining region 2 (HCDR2) comprising the amino acid sequence of SEQ ID NO: 85, a heavy chain complementarity determining region 3 (HCDR3) comprising the amino acid sequence of SEQ ID NO: 86, a light chain complementarity determining region 1 (LCDR1) comprising the amino acid sequence of SEQ ID NO: 87, a light chain complementarity determining region 2 (LCDR2) comprising the amino acid sequence of SEQ ID NO: 88, and a light chain complementarity determining region 3 (LCDR3) comprising the amino acid sequence of SEQ ID NO: 89;

(ii) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 12, an HCDR2 comprising the amino acid sequence of SEQ ID NO: 13, an HCDR3 comprising the amino acid sequence of SEQ ID NO: 14, an LCDR1 comprising the amino acid sequence of SEQ ID NO: 15, an LCDR2 comprising the amino acid sequence of SEQ ID NO: 16, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 17; or

(iii) an HCDR1 comprising the amino acid sequence of SEQ ID NO: 60, an HCDR2 comprising the amino acid sequence of SEQ ID NOS: 61, 72, or 78, an HCDR3 comprising the amino acid sequence of SEQ ID NO: 62, an LCDR1 comprising the amino acid sequence of SEQ ID NOS: 63, 73, or 79, an LCDR2 comprising the amino acid sequence of SEQ ID NO: 64, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 65.

2. The isolated antibody of claim 1, wherein the antibody comprises:

(i) a heavy chain variable region (VH) comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 92, and a light chain variable region (VL) comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 93;

(ii) a VH comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 96,

and a VL comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 97;

(iii) a VH comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 8, and a VL comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 9; or

(vii) a VH comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NOS: 56, 68, or 74, and a VL comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NOS: 57, 69, or 75.

3. The isolated antibody of claim 1, wherein the antibody comprises:

(i) a VH comprising the amino acid sequence of SEQ ID NO: 92, and a VL comprising the amino acid sequence of SEQ ID NO: 93;

(ii) a VH comprising the amino acid sequence of SEQ ID NO: 96, and a VL comprising the amino acid sequence of SEQ ID NO: 97;

(iii) a VH comprising the amino acid sequence of SEQ ID NO: 8, and a VL comprising the amino acid sequence of SEQ ID NO: 9; or

(iv) a VH comprising the amino acid sequence of SEQ ID NO: 56, 68, or 74, and a VL comprising the amino acid sequence of SEQ ID NO: 57, 69, or 75.

4. The isolated antibody of any one of claims 1 to 3, wherein the antibody is a monoclonal antibody.

5. The isolated antibody of any one of claims 1 to 3, wherein the antibody is a humanized antibody.

6. The isolated antibody of any one of claims 1 to 3, wherein the antibody is a full-length antibody.

7. The isolated antibody of any one of claims 1 to 6, wherein the antibody is an IgG1 or IgG3 antibody.

8. The isolated antibody of claims 1, wherein the antibody comprises:

(i) a heavy chain (HC) comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 94, and a light chain (LC) comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 95;

(ii) an HC comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 98, and an LC comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 99;

(iii) an HC comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 10, and an LC comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 11; or

(iv) an HC comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NOS: 58, 70, or 76, and an LC comprising an amino acid sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NOS: 59, 71, or 77.

9. The isolated antibody of claim 1, wherein the antibody comprises an HC comprising the amino acid sequence of SEQ ID NO: 94, and an LC comprising the amino acid sequence of SEQ ID NO: 95.

10. The isolated antibody of claim 1, wherein the antibody comprises an HC comprising the amino acid sequence of SEQ ID NO: 98, and an LC comprising the amino acid sequence of SEQ ID NO: 99.

11. The isolated antibody of claim 1, wherein the antibody comprises an HC comprising the amino acid sequence of SEQ ID NO: 10, and an LC comprising the amino acid sequence of SEQ ID NO: 11.

12. The isolated antibody of claim 1, wherein the antibody comprises an HC comprising the amino acid sequence of SEQ ID NOs: 58, 70, or 76, and an LC comprising the amino acid sequence of SEQ ID NO: 59, 71, or 77.
13. The isolated antibody of any one of claims 1 to 12, wherein the antibody comprises at least one modification that enhances cell killing.
14. The isolated antibody of claim 13, wherein the enhanced cell killing is enhanced antibody-dependent cellular cytotoxicity (ADCC) and/or complement-dependent cytotoxicity (CDC).
15. The isolated antibody of claim 13, wherein the at least one modification is afucosylation.
16. The isolated antibody of claim 13, wherein the at least one modification is one or more heavy chain constant regions mutations at one or more positions selected from L234, L235, G236, S239, F243, H268, D270, R292, S298, Y300, V305, K326, A330, I332, E333, K334, and P396.
17. The isolated antibody of claim 16, wherein the one or more heavy chain constant region mutations are one or more mutation selected from S239D, S239M, F243L, H268D, D270E, R292P, S298A, Y300L, V305I, K326D, A330L, A330M, I332E, E333A, K334A, K334E, and P396L.
18. The isolated antibody of claim 16, wherein the one or more heavy chain constant region mutations are selected from: F243L/R292P/Y300L/V305I/P396L, S239D/I332E, S239D/I332E/A330L, S298A/E333A/K334A, L234Y/L235Q/G236W/S239M/H268D/D270E/S298A, and D270E/K326D/A330M/K334E.
19. The isolated antibody of claim 13, wherein the at least one modification is galactosylation.
20. The isolated antibody of any one of claim 1 to 19, wherein the antibody binds human CCR8 with an affinity (K_D) of less than 10 nM, or less than 5 nM, or less than 1 nM, or less than 500

pM, or less than 250 pM, or less than 100 pM, or less than 75 pM, or less than 50 pM, or less than 25 pM.

21. The isolated antibody of any one of claims 1 to 19, wherein the antibody binds human CCR8 with an on-cell affinity (K_D) of less than 10 nM, or less than 5 nM, or less than 1 nM, or less than 500 pM, or less than 250 pM, or less than 100 pM, or less than 75, or less than 50 pM, or less than 25 pM.

22. The isolated antibody of claim 20 or 21, wherein the affinity (K_D) is determined by Kinetic Exclusion Assay.

23. An isolated nucleic acid that encodes any one of the amino acid sequences of the antibody of any one of claims 1 to 22.

24. A vector comprising the nucleic acid of claim 23.

25. A host cell comprising the vector of claim 24.

26. A host cell that expresses the antibody of any one of claims 1 to 22.

27. A method of producing an antibody that binds CCR8 comprising culturing the host cell of claim 25 or 26 under conditions suitable for expressing the antibody.

28. Use of the isolated antibody of any one of claims 1 to 22 for the preparation of a medicament in the treatment of cancer.

29. A method of selecting a subject with cancer for treatment with an antibody of any one of claims 1 to 22, comprising detecting CCR8 expression in a sample from the subject.

30. An isolated antibody that binds human CCR8, wherein:

i) the antibody comprises a HCDR3 comprising SEQ ID NO: 86 or a variant of SEQ ID NO: 86 comprising 1, 2, or 3 mutations, and wherein the antibody binds to human CCR8 and possesses ADCC activity; or

ii) the antibody comprises HCDR3 that is at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to SEQ ID NO:86, and wherein the antibody binds to human CCR8 and possesses ADCC activity.

31. An isolated nucleic acid encoding any one of the amino acid sequences of the antibody of claim 30.

32. A vector comprising the isolated nucleic acid of claim 31.

33. A host cell comprising the vector of claim 32.

34. A host cell that expresses the antibody of claim 30.

35. A method of producing an antibody that binds CCR8 comprising culturing the host cell of claim 33 or 34 under conditions suitable for expressing the antibody.

36. Use of the isolated antibody of claim 30 for the preparation of a medicament in the treatment of cancer.