

CLAIMS

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

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.

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; or

(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.

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; or

(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.

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 claim 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; or
 - (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.
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 any one of claims 1 to 10, wherein the antibody comprises at least one modification that enhances cell killing.

12. The isolated antibody of claim 11, wherein the enhanced cell killing is enhanced antibody-dependent cellular cytotoxicity (ADCC) and/or complement-dependent cytotoxicity (CDC).
13. The isolated antibody of claim 11, wherein the at least one modification is afucosylation.
14. The isolated antibody of any one of claims 1 to 13, wherein the antibody comprises 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: 92, 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: 93.
15. The isolated antibody of any one of claims 1 to 13, wherein the antibody comprises 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.
16. The isolated antibody of any one of claims 1 to 14, wherein the antibody comprises 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.
17. The isolated antibody of any one of claims 1 to 13 or 15, wherein the antibody comprises 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.
18. The isolated antibody of any one of claims 1 to 13, wherein the antibody comprises a heavy chain 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 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.

19. The isolated antibody of any one of claims 1 to 13, wherein the antibody comprises a heavy chain 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 a light chain 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.

20. The isolated antibody of any one of claims 1 to 13 or 18, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 94, and a light chain comprising the amino acid sequence of SEQ ID NO: 95.

21. The isolated antibody of any one of claims 1 to 13 or 19, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 98, and a light chain comprising the amino acid sequence of SEQ ID NO: 99.

22. The isolated antibody of claim 11, 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.

23. The isolated antibody of claim 22, 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.

24. The isolated antibody of claim 22, 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.

25. The isolated antibody of claim 11, wherein the at least one modification is galactosylation.

26. The isolated antibody of any one of claim 1 to 25, 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, wherein the affinity (K_D) is determined by Kinetic Exclusion Assay.

27. The isolated antibody of any one of claims 1 to 25, 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, wherein the affinity (K_D) is determined by Kinetic Exclusion Assay.

28. An isolated nucleic acid that encodes the amino acid sequence of the antibody of any one of claims 1 to 27.

29. A vector comprising the nucleic acid of claim 28.

30. A host cell comprising the vector of claim 29.

31. A host cell that expresses the antibody of any one of claims 1 to 27.

32. A method of producing an antibody that binds CCR8 comprising culturing the host cell of claim 30 or 31 under conditions suitable for expressing the antibody.

33. Use of the isolated antibody of any one of claims 1 to 27 for the preparation of a medicament in the treatment of cancer, wherein the isolated antibody is Fc-competent.

34. A method of selecting a subject with cancer for treatment with an antibody of any one of claims 1 to 27, comprising detecting CCR8 expression in a sample from the subject.

35. An isolated antibody that binds human CCR8, wherein
the antibody comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 84 or 100, an HCDR2 comprising the amino acid sequence of SEQ ID NO: 85, an HCDR3

comprising any one of SEQ ID NOS: 104, 106-108, 110-11 and 115-119, an LCDR1 comprising the amino acid sequence of SEQ ID NO: 87, an LCDR2 comprising the amino acid sequence of SEQ ID NO: 88, and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 89, and wherein the antibody binds to human CCR8 and possesses ADCC activity.

36. An isolated nucleic acid encoding the amino acid sequence of the antibody of claim 35.

37. A vector comprising the isolated nucleic acid of claim 36.

38. A host cell comprising the vector of claim 37.

39. A host cell that expresses the antibody of claim 35.

40. A method of producing an antibody that binds CCR8 comprising culturing the host cell of claim 38 or 39 under conditions suitable for expressing the antibody.

41. Use of the isolated antibody of claim 35 for the preparation of a medicament in the treatment of cancer, wherein the isolated antibody is Fc-competent.