

CLAIMS

1. An anti-human leukocyte antigen G (HLA-G) antibody or an antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment comprises:

5 (a) a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (HC CDR1) of SEQ ID NO: 5, a heavy chain complementarity determining region 2 (HC CDR2) of SEQ ID NO: 6, and a heavy chain complementarity determining region 3 (HC CDR3) of SEQ ID NO: 7; and

(b) a light chain variable region (VL) comprising a light chain complementarity determining region 1 (LC CDR1) of SEQ ID NO: 8, a light chain complementarity determining region 2 (LC CDR2) of
10 SEQ ID NO: 9 and a light chain complementarity determining region 3 (LC CDR3) of SEQ ID NO: 10.

2. The antibody or antigen-binding fragment of claim 1, wherein the VH comprises SEQ ID NO: 1 and the VL comprises SEQ ID NO: 2.

15 3. The antibody or antigen-binding fragment of claim 1 or 2, wherein the antibody is a full-length immunoglobulin G comprising two heavy chains and two light chains.

4. The antibody or antigen-binding fragment of claim 1 or 3, wherein the antibody or antigen-binding fragment is humanized or chimeric.

20 5. The antibody or antigen-binding fragment of claim 1, wherein the VH, the VL, or both the VH and VL comprise human immunoglobulin framework region sequences.

6. The antibody or antigen-binding fragment of any one of claims 1-5, wherein the antibody
25 comprises an immunoglobulin constant region or a portion of an immunoglobulin constant region.

7. The antigen-binding fragment of any one of claims 1-5, wherein the antigen-binding fragment is a scFv, a Fv, a Fab, a Fab', or a F(ab')₂.

30 8. The antibody or antigen-binding fragment of any one of claims 1-7, wherein the antibody is monoclonal.

9. The antibody or antigen-binding fragment of any one of claims 1-8, wherein the antibody or antigen-binding fragment is conjugated to a toxic agent.

10. A chimeric antigen receptor (CAR) comprising:
 - (a) an extracellular domain comprising an antigen binding domain that specifically binds to HLA-G, wherein the antigen binding domain comprises:
 - (i) a VH comprising a heavy chain complementarity determining region 1 (HC CDR1) of SEQ ID NO: 5, a heavy chain complementarity determining region 2 (HC CDR2) of SEQ ID NO: 6, and a heavy chain complementarity determining region 3 (HC CDR3) of SEQ ID NO: 7; and
 - (ii) a VL comprising a light chain complementarity determining region 1 (LC CDR1) of SEQ ID NO: 8, a light chain complementarity determining region 2 (LC CDR2) of SEQ ID NO: 9 and a light chain complementarity determining region 3 (LC CDR3) of SEQ ID NO: 10;
 - (b) a transmembrane domain; and
 - (c) an intracellular domain.
11. The CAR of claim 10, wherein the VH comprises SEQ ID NO: 1 and the VL comprises SEQ ID NO: 2.
12. The CAR of claim 10 or 11, wherein the antigen binding domain is a scFv.
13. The CAR of any one of claims 10-12, wherein the antigen binding domain comprises SEQ ID NO: 31.
14. The CAR of any one of claims 10-13, wherein the transmembrane domain is a CD28 transmembrane domain; and wherein the intracellular domain comprises a 4-1BB costimulatory signaling region and a CD3 zeta endodomain.
15. The CAR of claim 14,
 - wherein the CD28 transmembrane domain comprises SEQ ID NO: 20,
 - wherein the 4-1BB costimulatory signaling region comprises SEQ ID NO: 21, and
 - wherein the CD3 zeta endodomain comprises SEQ ID NO: 22.
16. The CAR of claim 14 or 15, wherein the intracellular domain further comprises a CD28 costimulatory domain.
17. The CAR of claim any one of claims 10-16, further comprising a hinge domain connecting the antigen binding domain to the transmembrane domain.

18. The CAR of claim 17, wherein the hinge domain is (i) a human IgG4 hinge domain, (ii) a human IgG4 hinge domain and a CH3 human IgG4 domain, (iii) a mutated CH2 human IgG4 domain, a human IgG4 hinge domain and a CH3 human IgG4 hinge domain, (iv) a CD28 hinge or (v) a CD8a hinge domain.

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19. The CAR of any one of claims 10-18, wherein the CAR comprises SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34 or SEQ ID NO: 85.

20. A nucleic acid molecule encoding the CAR of any one of claims 10-19.

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21. An expression vector comprising the nucleic acid molecule of claim 20.

22. A cell comprising the nucleic acid molecule of claim 20 or the expression vector of claim 21.

15 23. A cell comprising the CAR of any one of claims 10-19.

24. The cell of claim 23, wherein the cell is a T cell, a B cell, a NK cell, a NKT cell, a monocyte cell or a dendritic cell.

20 25. A pharmaceutical composition comprising the cell of any one of claims 22-24, and a pharmaceutically acceptable carrier.

26. The cell of any one of claims 22-24 or the pharmaceutical composition of claim 25 for use in the treatment of cancer, wherein the cell is a T cell or a NKT cell; wherein the transmembrane domain is a CD28 transmembrane domain; and wherein the intracellular domain comprises a 4-1BB costimulatory signaling region and a CD3 zeta endodomain.

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27. Use of the cell of any one of claims 22-24 or the pharmaceutical composition of claim 25 in the manufacture of a medicament for the treatment of cancer, wherein the cell is a T cell or a NKT cell; wherein the transmembrane domain is a CD28 transmembrane domain; and wherein the intracellular domain comprises a 4-1BB costimulatory signaling region and a CD3 zeta endodomain.

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