

Patent Claims

1. An isolated antibody that bind to human HLA-G; and that inhibits ILT2 binding to HLAG on JEG-3 cells (ATCC HTB36) and restores HLA-G specific suppressed TNF alpha release by monocytes co-cultured with JEG-3 cells.
- 5 2. An isolated antibody that bind to human HLA-G wherein the antibody comprises
 - A) (a) a VH domain comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:1, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:2, and (iii) HVR-H3 comprising an amino acid sequence selected from
10 SEQ ID NO:3; and (b) a VL domain comprising (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:4; (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:5 and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:6; or
 - B) (a) a VH domain comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:9, (ii) HVR-H2 comprising the amino acid sequence of SEQ
15 ID NO:10, and (iii) HVR-H3 comprising an amino acid sequence selected from SEQ ID NO:11; and (b) a VL domain comprising (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:12; (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:13 and (iii) HVR-L3 comprising the amino acid
20 sequence of SEQ ID NO:14; or
 - C) (a) a VH domain comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:17, (ii) HVR-H2 comprising the amino acid sequence of SEQ ID NO:18, and (iii) HVR-H3 comprising an amino acid sequence selected from
25 SEQ ID NO:19; and (b) a VL domain comprising (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:20; (ii) HVR-L2 comprising the amino acid sequence of SEQ ID NO:21 and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:22; or
 - D) (a) a VH domain comprising (i) HVR-H1 comprising the amino acid sequence of SEQ ID NO:25, (ii) HVR-H2 comprising the amino acid sequence of SEQ
30 ID NO:26, and (iii) HVR-H3 comprising an amino acid sequence selected from SEQ ID NO:27; and (b) a VL domain comprising (i) HVR-L1 comprising the amino acid sequence of SEQ ID NO:28; (ii) HVR-L2 comprising the amino

acid sequence of SEQ ID NO:29 and (iii) HVR-L3 comprising the amino acid sequence of SEQ ID NO:30.

3. The antibody according to claim 2, wherein the antibody comprises

A)

5 iv) comprises a VH sequence of SEQ ID NO:7 and a VL sequence of SEQ ID NO:8;

v) or humanized variant of the VH and VL of the antibody under i); or

vi) comprises a VH sequence of SEQ ID NO:33 and a VL sequence of SEQ ID NO:34; or

10 B)

comprises a VH sequence of SEQ ID NO:15 and a VL sequence of SEQ ID NO:16; or

C)

15 comprises a VH sequence of SEQ ID NO:23 and a VL sequence of SEQ ID NO:24; or

D)

comprises a VH sequence of SEQ ID NO:31 and a VL sequence of SEQ ID NO:32.

4. An isolated antibody that binds to human HLA-G, wherein the antibody

20 a) binds to the same epitope as an antibody which comprises a VH sequence of SEQ ID NO:7 and a VL sequence of SEQ ID NO:8;

or b) binds to the same epitope as an antibody which comprises a VH sequence of SEQ ID NO:31 and a VL sequence of SEQ ID NO:32.

25 5. The anti-HLA-G antibody according to any one of claims 1 to 4, wherein the antibody

- a) does not crossreact with a modified human HLA-G β 2M MHC I complex comprising SEQ ID NO:44; and/ or
- b) does not crossreact with human HLA-A2 β 2M MHC I complex comprising SEQ ID NO:39 and SEQ ID NO: 37; and/ or
- 5 c) does not crossreact with a mouse H2Kd β 2M MHC I complex comprising SEQ ID NO:45; and/ or
- d) does not crossreact with rat RT1A β 2M MHC I complex comprising SEQ ID NO:47; and/ or
- 10 e) inhibits ILT2 binding to monomeric HLA-G β 2M MHC I complex; and/or
- f) inhibits ILT2 binding to trimeric HLA-G β 2M MHC I complex; and/or
- g) inhibits ILT2 binding to monomeric and/or dimeric and/or trimeric HLA-G β 2M MHC I complex by more than 50%; and/ or
- h) inhibits ILT2 binding to JEG3 cells (ATCC No. HTB36); and/or
- 15 i) binds to (HLA-G on) JEG3 cells (ATCC No. HTB36), and inhibits ILT2 binding to (HLA-G on) JEG3 cells (ATCC No. HTB36) ; and/or
- j) inhibits CD8a binding to HLAG by more than 80%.
- 6. The antibody according to any one of the preceding claims, wherein the antibody is of IgG1 isotype.
- 20 7. The antibody according claim 6, wherein the antibody is of IgG1 isotype with mutations L234A, L235A and P329G (numbering according to the EU index of Kabat).
- 8. Isolated nucleic acid encoding the antibody according to any one of the preceding claims.
- 25 9. A host cell comprising the nucleic acid of claim 8.
- 10. A method of producing an antibody comprising culturing the host cell of claim 8 so that the antibody is produced.

11. The method of claim 10, further comprising recovering the antibody from the host cell.
12. A pharmaceutical formulation comprising the antibody according any one of claims 1 to 7 and a pharmaceutically acceptable carrier.
- 5 13. The antibody according any one of claims 1 to 7 for use as a medicament.
14. The antibody according any one of claims 1 to 7 for use in treating cancer.
15. Use of the antibody according any one of claims 1 to 7 in the manufacture of a medicament.