

CLAIMS

1. An antibody or an antigen-binding fragment thereof that binds to TIGIT, comprising

(i) HCDR1, HCDR2 and HCDR3 sequences of a heavy chain variable region set forth in SEQ ID NOs: 84, 85, 86, or 87, and LCDR1, LCDR2 and LCDR3 sequences of a light chain variable region set forth in SEQ ID NO: 104,

(ii) HCDR1, HCDR2 and HCDR3 sequences of a heavy chain variable region set forth in SEQ ID NOs: 88, 89, or 90, and LCDR1, LCDR2 and LCDR3 sequences of a light chain variable region set forth in SEQ ID NOs: 105 or 106,

(iii) HCDR1, HCDR2 and HCDR3 sequences of a heavy chain variable region set forth in SEQ ID NOs: 91, 92, or 93, and LCDR1, LCDR2 and LCDR3 sequences of a light chain variable region set forth in SEQ ID NO: 107,

(iv) HCDR1, HCDR2 and HCDR3 sequences of a heavy chain variable region set forth in SEQ ID NOs: 94, 95, 96, or 97, and LCDR1, LCDR2 and LCDR3 sequences of a light chain variable region set forth in SEQ ID NO: 108,

(v) HCDR1, HCDR2 and HCDR3 sequences of a heavy chain variable region set forth in SEQ ID NOs: 98, 99, or 100, and LCDR1, LCDR2 and LCDR3 sequences of a light chain variable region set forth in SEQ ID NO: 109, or

(vi) HCDR1, HCDR2 and HCDR3 sequences of a heavy chain variable region set forth in SEQ ID NOs: 101, 102, or 103, and LCDR1, LCDR2 and LCDR3 sequences of a light chain variable region set forth in SEQ ID NO: 110.

2. An antibody or an antigen-binding fragment thereof that binds to TIGIT, comprising three heavy chain complementarity determining regions (HCDRs) and three light chain complementarity determining regions (LCDRs), wherein

(a) HCDR1 comprises an amino acid sequence set forth in SEQ ID NOs: 1, 2, 3, 4, or 5, HCDR2 comprises an amino acid sequence set forth in SEQ ID NOs: 6, 7, 8, 9, or 10, HCDR3 comprises an amino acid sequence set forth in SEQ ID NOs: 11, 12, 13, 14, or 15, LCDR1 comprises an amino acid sequence set forth in SEQ ID NO: 16, LCDR2 comprises an amino acid sequence set forth in SEQ ID NO: 17, and LCDR3 comprises an amino acid sequence set forth in SEQ ID NO: 18;

(b) HCDR1 comprises an amino acid sequence set forth in SEQ ID NOs: 19, 20, or 21, HCDR2 comprises an amino acid sequence set forth in SEQ ID NOs: 22, 23, or 24, HCDR3 comprises an amino acid sequence set forth in SEQ ID NO: 25, LCDR1 comprises an amino acid sequence set forth in SEQ ID NO: 26, LCDR2 comprises an amino acid sequence set forth in SEQ ID NO: 27, and LCDR3 comprises an amino acid sequence set forth in SEQ ID NOs: 28, 29, or 30;

(c) HCDR1 comprises an amino acid sequence set forth in SEQ ID NOs: 31, 32, or 33, HCDR2 comprises an amino acid sequence set forth in SEQ ID NOs: 34, 35, 36, or 37, HCDR3 comprises an amino acid sequence set forth in SEQ ID NOs: 38, 39, or 40, LCDR1 comprises an amino acid sequence set forth in SEQ ID NO: 41, LCDR2 comprises an amino acid sequence set forth in SEQ ID NO: 42, and LCDR3 comprises an amino acid sequence set forth in SEQ ID NO: 43;

(d) HCDR1 comprises an amino acid sequence set forth in SEQ ID NOs: 44, 45, 46, or 47, HCDR2 comprises an amino acid sequence set forth in SEQ ID NOs: 48, 49, 50, 51, or 52, HCDR3 comprises an amino acid sequence set forth in SEQ ID NOs: 53, 54, 55, or 56, LCDR1 comprises an amino acid sequence set forth in SEQ ID NO: 57, LCDR2 comprises an amino acid sequence set forth in SEQ ID NO: 58, and LCDR3 comprises an amino acid sequence set forth in SEQ ID NO: 59; or

(e) HCDR1 comprises an amino acid sequence set forth in SEQ ID NOs: 60, 61, or 62, HCDR2 comprises an amino acid sequence set forth in SEQ ID NOs: 6, 63, 64, or 65, HCDR3 comprises an amino acid sequence set forth in SEQ ID NOs: 66, 67, or 68, LCDR1 comprises an amino acid sequence set forth in SEQ ID NO: 69, LCDR2 comprises an amino acid sequence set forth in SEQ ID NO: 17, and LCDR3 comprises an amino acid sequence set forth in SEQ ID NO: 70;

(f) HCDR1 comprises an amino acid sequence set forth in SEQ ID NOs: 71, 72, 73, or 74, HCDR2 comprises an amino acid sequence set forth in SEQ ID NOs: 22, 75, 76, or 77, HCDR3 comprises an amino acid sequence set forth in SEQ ID NOs: 78, 79, or 80, LCDR1 comprises an amino acid sequence set forth in SEQ ID NO: 81, LCDR2 comprises an amino acid sequence set forth in SEQ ID NO: 82, and LCDR3 comprises an amino acid sequence set forth in SEQ ID NO: 83;

(g) HCDR1 comprises an amino acid sequence set forth in SEQ ID NOs: 178, 179, 180, or 181, HCDR2 comprises an amino acid sequence set forth in SEQ ID NOs: 6, 7, 8, or 9, HCDR3 comprises an amino acid sequence set forth in SEQ ID NOs: 182, 183, 184, or 185, LCDR1 comprises an amino acid sequence set forth in SEQ ID NO: 16, LCDR2 comprises an amino acid sequence set forth in SEQ ID NO: 17, and LCDR3 comprises an amino acid sequence set forth in SEQ ID NO: 18;

(h) HCDR1 comprises an amino acid sequence set forth in SEQ ID NOs: 186 or 187, HCDR2 comprises an amino acid sequence set forth in SEQ ID NOs: 22 or 23, HCDR3 comprises an amino acid sequence set forth in SEQ ID NO: 188, LCDR1 comprises an amino acid sequence set forth in SEQ ID NO: 26, LCDR2 comprises an amino acid sequence set forth in SEQ ID NO: 27, and LCDR3 comprises an amino acid sequence set forth in SEQ ID NOs: 28 or 29;

(i) HCDR1 comprises an amino acid sequence set forth in SEQ ID NOs: 189 or 190, HCDR2 comprises an amino acid sequence set forth in SEQ ID NOs: 34, 35 or 36, HCDR3 comprises an amino acid sequence set forth in SEQ ID NOs: 191 or 192, LCDR1 comprises an amino acid sequence set forth in SEQ ID NO: 41, LCDR2 comprises an amino acid sequence set forth in SEQ ID NO: 42, and LCDR3 comprises an amino acid sequence set forth in SEQ ID NO: 43;

(j) HCDR1 comprises an amino acid sequence set forth in SEQ ID NOs: 193, 194, or 195, HCDR2 comprises an amino acid sequence set forth in SEQ ID NOs: 48, 49, 50, or 51, HCDR3 comprises an amino acid sequence set forth in SEQ ID NOs: 196, 197, or 198, LCDR1 comprises an amino acid sequence set forth in SEQ ID NO: 57, LCDR2 comprises an amino acid sequence set forth in SEQ ID NO: 58, and LCDR3 comprises an amino acid sequence set forth in SEQ ID NO: 59;

(k) HCDR1 comprises an amino acid sequence set forth in SEQ ID NOs: 199 or 200, HCDR2 comprises an amino acid sequence set forth in SEQ ID NOs: 6, 63 or 64, HCDR3 comprises an amino acid sequence set forth in SEQ ID NOs: 201 or 202, LCDR1 comprises an amino acid

sequence set forth in SEQ ID NO: 69, LCDR2 comprises an amino acid sequence set forth in SEQ ID NO: 17, and LCDR3 comprises an amino acid sequence set forth in SEQ ID NO: 70; or

(l) HCDR1 comprises an amino acid sequence set forth in SEQ ID NOs: 203, 204, or 205, HCDR2 comprises an amino acid sequence set forth in SEQ ID NOs: 22, 75, or 76, HCDR3 comprises an amino acid sequence set forth in SEQ ID NOs: 206 or 207, LCDR1 comprises an amino acid sequence set forth in SEQ ID NO: 81, LCDR2 comprises an amino acid sequence set forth in SEQ ID NO: 82, and LCDR3 comprises an amino acid sequence set forth in SEQ ID NO: 83.

3. The antibody or the antigen-binding fragment thereof according to claims 1 or 2, comprising

(i) a heavy chain variable region comprising an amino acid sequence having at least 80%, 85%, or 90% sequence identity to an amino acid sequence set forth in SEQ ID NO: 84, 85, 86, or 87, and/or a light chain variable region comprising an amino acid sequence having at least 80%, 85%, or 90% sequence identity to an amino acid sequence set forth in SEQ ID NO: 104,

(ii) a heavy chain variable region comprising an amino acid sequence having at least 80%, 85%, or 90% sequence identity to an amino acid sequence set forth in SEQ ID NOs: 88, 89, or 90, and/or a light chain variable region comprising an amino acid sequence having at least 80%, 85%, or 90% sequence identity to an amino acid sequence set forth in SEQ ID NOs: 105 or 106,

(iii) a heavy chain variable region comprising an amino acid sequence having at least 80%, 85%, or 90% sequence identity to an amino acid sequence set forth in SEQ ID NOs: 91, 92, or 93, and/or a light chain variable region comprising an amino acid sequence having at least 80%, 85%, or 90% sequence identity to an amino acid sequence set forth in SEQ ID NO: 107,

(iv) a heavy chain variable region comprising an amino acid sequence having at least 80%, 85%, or 90% sequence identity to an amino acid sequence set forth in SEQ ID NOs: 94, 95, 96, or 97, and/or a light chain variable region comprising an amino acid sequence having at least 80%, 85%, or 90% sequence identity to an amino acid sequence set forth in SEQ ID NO: 108,

(v) a heavy chain variable region comprising an amino acid sequence having at least 80%, 85%, or 90% sequence identity to an amino acid sequence set forth in SEQ ID NOs: 98, 99, or 100, and/or a light chain variable region comprising an amino acid sequence having at least 80%, 85%, or 90% sequence identity to an amino acid sequence set forth in SEQ ID NO: 109, or

(vi) a heavy chain variable region comprising an amino acid sequence having at least 80%, 85%, or 90% sequence identity to an amino acid sequence set forth in SEQ ID NOs: 101, 102, or 103, and/or a light chain variable region comprising an amino acid sequence having at least 80%, 85%, or 90% sequence identity to an amino acid sequence set forth in SEQ ID NO: 110.

4. The antibody or the antigen-binding fragment thereof according to any one of claims 1 to 3, comprising a heavy chain variable region and a light chain variable region selected from:

(i) a heavy chain variable region comprising an amino acid sequence set forth in SEQ ID NOs: 84, 85, 86, or 87, and a light chain variable region comprising an amino acid sequence set forth in SEQ ID NO: 104,

(ii) a heavy chain variable region comprising an amino acid sequence set forth in SEQ ID NOs: 88, 89, or 90, and a light chain variable region comprising an amino acid sequence set forth in

SEQ ID NOs: 105 or 106,

(iii) a heavy chain variable region comprising an amino acid sequence set forth in SEQ ID NOs: 91, 92, or 93, and a light chain variable region comprising an amino acid sequence set forth in SEQ ID NO: 107,

(iv) a heavy chain variable region comprising an amino acid sequence set forth in SEQ ID NOs: 94, 95, 96, or 97, and a light chain variable region comprising an amino acid sequence set forth in SEQ ID NO: 108,

(v) a heavy chain variable region comprising an amino acid sequence set forth in SEQ ID NOs: 98, 99, or 100, and a light chain variable region comprising an amino acid sequence set forth in SEQ ID NO: 109, or

(vi) a heavy chain variable region comprising an amino acid sequence set forth in SEQ ID NOs: 101, 102, or 103, and a light chain variable region comprising an amino acid sequence set forth in SEQ ID NO: 110.

5. The antibody or the antigen-binding fragment thereof according to any one of the preceding claims, wherein the antibody is an antibody in the form of IgG1, IgG2, or IgG4, or an antigen-binding fragment thereof, preferably an IgG4 Fc region comprising S228P, F234A, and L235A mutations.

6. The antibody or the antigen-binding fragment thereof according to any one of the preceding claims, wherein the antibody is a fully humanized antibody, a humanized antibody, or a chimeric antibody.

7. The antibody or the antigen-binding fragment thereof according to any one of the preceding claims, wherein the antigen-binding fragment is an antibody fragment selected from: Fab, Fab', Fab'-SH, Fv, single chain antibodies such as scFv, (Fab')₂ fragments, single domain antibodies, diabodies (dAbs), or linear antibodies.

8. The antibody or the antigen-binding fragment thereof according to any one of the preceding claims, wherein the antibody has one or more of the following properties:

(i) capacity of binding to human TIGIT with high affinity;

(ii) activity of cross-immunoreaction with monkey and/or murine TIGIT;

(iii) effectively binding to TIGIT on cell surface;

(iv) blocking the binding of TIGIT to its ligand CD155;

(v) relieving the inhibitory effect of binding of TIGIT to CD155 on a downstream IL-2 signaling pathway;

(vi) increasing IL-2 production in T cells;

(vii) anti-tumor activity, *e.g.*, inhibiting tumor growth;

(viii) having better tumor inhibitory effect in combination with anti-PD-1 antibody, *e.g.*, better inhibiting tumor growth.

9. An isolated nucleic acid encoding the anti-TIGIT antibody or the antigen-binding fragment

thereof according to any one of the preceding claims.

10. A vector comprising the nucleic acid according to claim 9, wherein, preferably, the vector is an expression vector.

11. A host cell comprising the nucleic acid according to claim 9 or the vector according to claim 10, wherein, preferably, the host cell is prokaryotic or eukaryotic, and more preferably, a yeast cell or mammalian cell (*e.g.*, a 293 cell or a CHO cell).

12. A method for preparing an anti-TIGIT antibody or an antigen-binding fragment thereof, comprising cultivating the host cell according to claim 11 under conditions suitable for expressing a nucleic acid encoding the anti-TIGIT antibody or the antigen-binding fragment thereof according to any one of claims 1-8, and optionally isolating the antibody or the antigen-binding fragment thereof, wherein optionally, the method further comprises isolating the anti-TIGIT antibody or the antigen-binding fragment thereof from the host cell.

13. An immunoconjugate comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1-8 conjugated to a therapeutic or diagnostic agent.

14. A multispecific antibody comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1-8, wherein, preferably, the multispecific antibody is a bispecific antibody.

15. A pharmaceutical composition comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1-8, and optionally a pharmaceutical adjuvant.

16. The pharmaceutical composition according to claim 15, comprising a second therapeutic agent, wherein, preferably, the second therapeutic agent is selected from an anti-PD-1 antibody or an anti-PD-L1 antibody.

17. A method for preventing or treating a tumor or an infectious disease in a subject, comprising: administering to the subject an effective amount of the anti-TIGIT antibody or the antigen-binding fragment thereof according to any one of claims 1-8, or the pharmaceutical composition according to claims 15 or 16, wherein, preferably, the tumor is a gastrointestinal cancer, such as colon cancer.

18. A method for blocking binding of TIGIT to CD155 so as to reduce or eliminate the immunosuppressive effect of TIGIT in a subject, comprising: administering to the subject an effective amount of the anti-TIGIT antibody or the antigen-binding fragment thereof according to any one of claims 1-8, or the pharmaceutical composition according to claims 15 or 16.

19. A method for detecting TIGIT in a sample, comprising:

(a) contacting the sample with the antibody or the antigen-binding fragment thereof according to any one of claims 1-8; and

(b) detecting a complex formed by the antibody or the antigen-binding fragment and TIGIT, wherein, optionally, the antibody is detectably labeled.