

CLAIMS

1. 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;

(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: 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: 70, and LCDR3 comprises an amino acid sequence set forth in SEQ ID NO: 71;

(f) HCDR1 comprises an amino acid sequence set forth in SEQ ID NOs: 72, 73, or 74, HCDR2 comprises an amino acid sequence set forth in SEQ ID NOs: 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.

2. The antibody or the antigen-binding fragment thereof according to claim 1, 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.

3. The antibody or the antigen-binding fragment thereof according to claim 1, 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.

4. The antibody or the antigen-binding fragment thereof according to claim 1, wherein the antibody is an antibody in the form of IgG1, IgG2, or IgG4, or an antigen-binding fragment thereof, optionally wherein the antibody has an IgG4 Fc region comprising S228P, F234A, and L235A mutations.

5. The antibody or the antigen-binding fragment thereof according to claim 1, wherein the antibody is a fully humanized antibody, a humanized antibody, or a chimeric antibody.

6. The antibody or the antigen-binding fragment thereof according to claim 1, wherein the antigen-binding fragment is an antibody fragment selected from: Fab, Fab', Fab'-SH, Fv, single chain antibody, scFv, (Fab')₂ fragment, diabody (dAb), or linear antibody.
7. The antibody or the antigen-binding fragment thereof according to claim 1, 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; and
 - (viii) having better tumor inhibitory effect in combination with anti-PD-1 antibody.
8. An isolated nucleic acid encoding the anti-TIGIT antibody or the antigen-binding fragment thereof according to claim 1.
9. A vector comprising a nucleic acid encoding the anti-TIGIT antibody or the antigen-binding fragment thereof according to claim 1, optionally wherein the vector is an expression vector.
10. A host cell comprising a nucleic acid encoding the anti-TIGIT antibody or the antigen-binding fragment thereof according to claim 1, optionally wherein the host cell is prokaryotic or eukaryotic, further optionally wherein the host cell is a yeast cell or mammalian cell, and further optionally wherein the host cell is a 293 cell or a CHO cell.
11. A method for preparing an anti-TIGIT antibody or an antigen-binding fragment thereof according to claim 1, the method comprising cultivating a host cell comprising a nucleic acid encoding the anti-TIGIT antibody or the antigen-binding fragment thereof under conditions suitable for expressing the nucleic acid, 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.
12. An immunoconjugate comprising the antibody or the antigen-binding fragment thereof according to claim 1 conjugated to a therapeutic or diagnostic agent.
13. A multispecific antibody comprising the antibody or the antigen-binding fragment thereof according to claim 1, wherein, optionally, the multispecific antibody is a bispecific antibody.
14. A pharmaceutical composition comprising the antibody or the antigen-binding fragment thereof according to claim 1, and optionally a pharmaceutical adjuvant.
15. The pharmaceutical composition according to claim 14, comprising the antibody or the antigen-binding fragment thereof and an anti-PD-1 antibody.
16. The pharmaceutical composition according to claim 14, comprising a second therapeutic

agent.

17. Use of the antibody or the antigen-binding fragment thereof according to any one of claims 1-7, or the pharmaceutical composition according to any one of claims 14 to 16, in the manufacture of a medicament for the treatment of a tumor or an infectious disease in a subject, wherein, preferably, the tumor is a gastrointestinal cancer, such as colon cancer.

18. The use according to claim 17, wherein the antibody or the antigen-binding fragment thereof is in combination with an anti-PD-1 antibody.

19. Use of the antibody or the antigen-binding fragment thereof according to any one of claims 1-7, or the pharmaceutical composition according to any one of claims 14 to 16, in the manufacture of a medicament for blocking binding of TIGIT to CD155 so as to reduce or eliminate the immunosuppressive effect of TIGIT in a subject.

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

(a) contacting the sample with the antibody or the antigen-binding fragment thereof according to any one of claims 1-7; and

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

21. The antibody or the antigen-binding fragment thereof according to claim 1, comprising

- HCDR1 comprising an amino acid sequence set forth in SEQ ID NO: 200,
- HCDR2 comprising an amino acid sequence set forth in SEQ ID NO: 64,
- HCDR3 comprises an amino acid sequence set forth in SEQ ID NO: 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.

22. The antibody or the antigen-binding fragment thereof according to claim 1, comprising

- HCDR1 comprising an amino acid sequence set forth in SEQ ID NO: 189,
- HCDR2 comprising an amino acid sequence set forth in SEQ ID NO: 35,
- HCDR3 comprises an amino acid sequence set forth in SEQ ID NO: 191,
- 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.