

In one aspect, the present disclosure provides an antibody or antigen binding fragment thereof that binds to mature human TIGIT, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises a heavy chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO:88, a heavy chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO:89, a heavy chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:90, and the light chain variable region comprises a light chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO:91, a light chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO:92, and a light chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:93.

In one aspect, the present disclosure provides an antibody or antigen binding fragment thereof that binds to mature human TIGIT, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises a heavy chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO:88, a heavy chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO: 134, a heavy chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:90, and the light chain variable region comprises a light chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO:91, a light chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO:92, and a light chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:93.

5 fragments as defined herein, or any one of the polypeptides as defined herein. In one
embodiment, the disclosure provides isolated nucleic acids encoding anyone of the polypeptides
of SEQ ID NOs: 1-30, 37-52, 57-64 or 88-133, wherein said polypeptides can optionally
comprise a leader sequence. The disclosure also provides expression vectors comprising a
nucleic acid encoding anyone of the polypeptides of SEQ ID NOs: 1-30, 37-52, 57-83 or 88-167
10 (wherein said polypeptides can optionally comprise a leader sequence). In another aspect, the
disclosure provides an expression vector comprising the isolated nucleic acid as disclosed herein.
These isolated nucleic acids and the expression vectors comprising them may be used to express
the antibodies of the disclosure or antigen binding fragments thereof in recombinant host cells.
Thus, the disclosure also provides host cells comprising isolated nucleic acids encoding anyone
15 of the polypeptides of SEQ ID NOs: 1-30, 37-52, 57-83 or 88-151 (wherein said polypeptides
can optionally comprise a leader sequence). In another aspect, the disclosure provides a host
cell comprising the antibody or antigen binding fragment thereof, polypeptide, polynucleotide or
expression vector as disclosed herein. In one embodiment, the host cell is Chinese hamster ovary
cell. In one embodiment, the host cell is a yeast cell, for example a *Pichia* cell or a *Pichia*
20 *pastoris* host cell.

In another aspect, the disclosure also provides pharmaceutical compositions comprising
an antibody or antigen binding fragment thereof of the disclosure and a pharmaceutically
acceptable carrier or diluent.

5 NO: 62. In one embodiment, the anti-TIGIT antibody or antigen binding fragment thereof comprises: (i) a heavy chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO: 88; (ii) a heavy chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO: 89, 134 or 135; (iii) a heavy chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO: 90; (iv) a light chain variable region CDR1 comprising the amino acid
10 sequence of SEQ ID NO: 91; (v) a light chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO: 92; and (vi) a light chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO: 93. In one embodiment, the anti-TIGIT antibody or antigen binding fragment thereof comprises: (i) a heavy chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO: 88; (ii) a heavy chain variable region CDR2 comprising the
15 amino acid sequence of SEQ ID NO: 134; (iii) a heavy chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO: 90; (iv) a light chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO: 91; (v) a light chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO: 92; and (vi) a light chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO: 93.

20 The disclosure also provides a method of producing an anti-TIGIT antibody or antigen binding fragment of the disclosure comprising: culturing a host cell comprising a polynucleotide encoding a heavy chain and/or light chain of an antibody of the disclosure (or an antigen binding fragment thereof) under conditions favorable to expression of the polynucleotide; and optionally, recovering the antibody or antigen binding fragment from the host cell and/or culture medium. In
25 another aspect, the disclosure provides a method of producing an antibody or antigen binding fragment thereof comprising: culturing a host cell comprising a polynucleotide encoding the heavy chain and the light chain of any one of the antibodies or antigen binding fragments as defined herein under conditions favorable to expression of the polynucleotide; and optionally, recovering the antibody or antigen binding fragment thereof from the host cell and/or culture
30 medium. In one embodiment, the polynucleotide encoding the heavy chain and the polynucleotide encoding the light chain are in a single vector. In another embodiment, the polynucleotide encoding the heavy chain and the polynucleotide encoding the light chain are in different vectors. In one embodiment, the polynucleotide encoding the heavy chain and the polynucleotide encoding the light chain encode an antibody or antigen binding fragment
35 comprising: (i) a heavy chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO: 1; (ii) a heavy chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO: 2; (iii) a heavy chain variable region CDR3 comprising the amino acid

5 The disclosure also provides a method of increasing the anti-tumor activity of an anti-TIGIT antibody comprising: obtaining a parental anti-TIGIT antibody and increasing the effector function of the parental anti-TIGIT antibody; wherein the activity of the resulting anti-TIGIT antibody is increased as compared to the parental anti-TIGIT antibody. As used herein, a “parental anti-antibody” refers to antibody having a wild-type Fc region and/or wild type glycosylation (i.e., glycosylation pattern resulting from expression of the polypeptide in a non-engineered mammalian host cell). The effector function of a parental antibody can be increased by mutating its Fc region or by altering its glycosylation, for example by making the antibody afucosylated (as discussed in further detail below). In one embodiment, the effector function of a parental anti-TIGIT antibody is increased by making mutations in the Fc region of the parental anti-TIGIT antibody. In another embodiment, the effector function of a parental anti-TIGIT antibody is increased by removing the fucose residues from the antibody, or expressing the antibody in a host cell that has been genetically engineered to remove the activity of the enzyme that adds fucose to glycoproteins.

 In another aspect, the disclosure provides an antibody or antigen binding fragment thereof as disclosed herein, for use to treat cancer.

 In another aspect, the disclosure provides use of the antibody or antigen binding fragment thereof as disclosed herein in the manufacture of a medicament for the treatment of cancer.

CLAIMS

1. An antibody or antigen binding fragment thereof that binds to mature human TIGIT, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises a heavy chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO:88, a heavy chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO:89, a heavy chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:90, and the light chain variable region comprises a light chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO:91, a light chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO:92, and a light chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:93.
2. An antibody or antigen binding fragment thereof that binds to mature human TIGIT, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises a heavy chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO:88, a heavy chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO: 134, a heavy chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:90, and the light chain variable region comprises a light chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO:91, a light chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO:92, and a light chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:93.
3. The antibody or antigen binding fragment thereof of claim 1, wherein the antibody or antigen binding fragment thereof comprises
 - a. a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:128 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:132;
 - b. a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:127 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:130;
 - c. a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:128 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:133;

- 5 d. a heavy chain variable region comprising at least 90% identity to SEQ ID NO:128
and a light chain variable region comprising at least 90% identity to SEQ ID NO:
132; wherein any sequence variations occur in the framework regions of the antibody;
- e. a heavy chain variable region comprising at least 90% identity to SEQ ID NO:127
and a light chain variable region comprising at least 90% identity to SEQ ID NO:
10 130, wherein any sequence variations occur in the framework regions of the antibody;
or
- f. a heavy chain variable region comprising at least 90% identity to SEQ ID NO:128
and a light chain variable region comprising at least 90% identity to SEQ ID NO:
133, wherein any sequence variations occur in the framework regions of the antibody.
- 15 4. The antibody or antigen binding fragment thereof of claim 3, which is an antibody, wherein
the heavy chain variable region of the antibody comprises the amino acid sequence of SEQ
ID NO: 128 and the light chain variable region of the antibody comprises the amino acid
sequence of SEQ ID NO: 132.
5. The antibody or antigen binding fragment thereof of claim 3, which is an antibody, wherein
20 the heavy chain variable region of the antibody comprises the amino acid sequence of SEQ
ID NO: 128 and the light chain variable region of the antibody comprises the amino acid
sequence of SEQ ID NO: 133.
6. The antibody or antigen binding fragment thereof of claim 3, which is an antibody, wherein
the heavy chain variable region of the antibody comprises the amino acid sequence of SEQ
25 ID NO: 127 and the light chain variable region of the antibody comprises the amino acid
sequence of SEQ ID NO: 130.
7. The antibody or antigen binding fragment thereof of any one of claims 1-6, wherein the
antibody binds to human TIGIT with a KD value of 1×10^{-9} M to 1×10^{-12} M as determined
by surface plasmon resonance.
- 30 8. The antibody or antigen binding fragment thereof of any of claims 1-3 or 7 which is an
antibody.
9. The antibody or antigen binding fragment thereof of any of the above claims, which is a
humanized antibody comprising two heavy chains and two light chains.
10. The antibody or antigen binding fragment thereof of any of the above claims, which is a
35 humanized antibody, wherein the antibody comprises a human IgG1 constant domain and a
human kappa constant domain.

- 5 11. The antibody or antigen binding fragment thereof of any of the above claims, which is a humanized antibody, wherein the antibody comprises a human IgG4 constant domain and a human kappa constant domain.
12. The antibody or antigen binding fragment thereof of claim 11, wherein the human IgG1 constant domain comprises SEQ ID NO: 86 and the human kappa constant domain comprises
10 SEQ ID NO: 56.
13. An antibody which comprises two heavy chain immunoglobulins and two light chain immunoglobulins, wherein the heavy chain immunoglobulin comprises (i) a heavy chain variable region comprising SEQ ID NO: 128 and (ii) an IgG1 constant domain comprising SEQ ID NO: 86 and wherein the light chain immunoglobulin comprises (i) a light chain
15 variable region comprising SEQ ID NO: 132 and (ii) a human kappa constant domain comprising SEQ ID NO: 56.
14. An antibody which comprises two heavy chain immunoglobulins and two light chain immunoglobulins, wherein the heavy chain immunoglobulin comprises (i) a heavy chain variable region comprising SEQ ID NO: 128 and (ii) an IgG1 constant domain comprising
20 SEQ ID NO: 86 and wherein the light chain immunoglobulin comprises (i) a light chain variable region comprising SEQ ID NO: 133 and (ii) a human kappa constant domain comprising SEQ ID NO: 56.
15. An antibody which comprises two heavy chain immunoglobulins and two light chain immunoglobulins, wherein the heavy chain immunoglobulin comprises (i) a heavy chain
25 variable region comprising SEQ ID NO: 127 and (ii) an IgG1 constant domain comprising SEQ ID NO: 86 and wherein the light chain immunoglobulin comprises (i) a light chain variable region comprising SEQ ID NO: 130 and (ii) a human kappa constant domain comprising SEQ ID NO: 56.
16. The antibody or antigen binding fragment thereof of any one of the above claims, which is an
30 antibody, wherein the antibody is produced in a Chinese hamster ovary (CHO) cell.
17. An isolated polypeptide comprising
an immunoglobulin heavy chain variable (V_H) domain of any one of SEQ ID NOs: 124-129;
and
an immunoglobulin light chain variable (V_L) domain of any one of SEQ ID NOs: 130-133.

- 5 18. An isolated nucleic acid encoding: any one of the antibodies or antigen binding fragments of claims 1-16, or any one of the polypeptides of claim 17.
19. An expression vector comprising the isolated nucleic acid of claim 18.
20. A host cell comprising the antibody or antigen binding fragment thereof of claims 1 to 16, the polypeptide of claim 17, the isolated nucleic acid of claim 18 or the expression vector of
10 claim 19.
21. The host cell of claim 20, which is a *Pichia* cell or a Chinese hamster ovary (CHO) cell.
22. A composition comprising the antibody or antigen binding fragment thereof of any one of claims 1-16 and a pharmaceutically acceptable carrier or diluent.
23. The composition of claim 22, further comprising an anti-PD1 antibody.
- 15 24. The composition of claim 22, further comprising an anti-PDL1 antibody.
25. The composition of claim 23, wherein the anti-PD1 antibody is pembrolizumab.
26. A method of producing an antibody or antigen binding fragment thereof comprising:
- 20 a. culturing a host cell comprising a polynucleotide encoding the heavy chain and the light chain of any one of the antibodies or antigen binding fragments of claims 1-15 under conditions favorable to expression of the polynucleotide; and
- b. optionally, recovering the antibody or antigen binding fragment thereof from the host cell and/or culture medium.
27. An antibody or antigen binding fragment thereof according to any one of claims 1-16, for use to treat cancer.
- 25 28. Use of the antibody or antigen binding fragment thereof of claims 1-16 in the manufacture of a medicament for the treatment of cancer.