

In one aspect, the present disclosure provides an antibody or antigen binding fragment 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 of 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.

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In one embodiment, the disclosure provides an antibody or antigen binding fragment thereof that binds to human TIGIT, comprising: a heavy chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO: 3, 79, 80, 81, 82, 83, 59, 90, 140, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166 or 167. In one embodiment, the antibody or
10 antigen binding fragment thereof optionally has at least one of the following characteristics: (i) binds to human TIGIT with a KD value of about 1×10^{-9} M to about 1×10^{-12} M as determined

5 variable region comprising SEQ ID NO:130 and a human kappa light chain (SEQ ID NO:56);
and each heavy chain comprises: a variable region comprising SEQ ID NO:127, a human IgG1
constant region (SEQ ID NO:86). In another aspect, there is provided 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
10 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.

In one embodiment, the anti-TIGIT antibody of the disclosure comprises a full tetrameric
structure having two light chains and two heavy chains, wherein each light chain comprises: a
15 variable region comprising SEQ ID NO:133 and a human kappa light chain (SEQ ID NO:56);
and each heavy chain comprises: a variable region comprising SEQ ID NO:128, a human IgG1
constant region (SEQ ID NO:86). In another aspect, there is provided 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
20 NO: 128 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: 133
and (ii) a human kappa constant domain comprising SEQ ID NO: 56.

In any of the above mentioned embodiments, the anti-TIGIT antibody or antigen binding
fragment thereof of the disclosure can be conjugated to at least one therapeutic agent. In one
25 embodiment, the wherein the therapeutic agent comprises a second antibody or fragment thereof,
an immunomodulator, a hormone, a cytotoxic agent, an enzyme, a radionuclide, a second
antibody conjugated to at least one immunomodulator, enzyme, radioactive label, hormone,
antisense oligonucleotide, or cytotoxic agent, or a combination thereof.

The disclosure also provides isolated polypeptides comprising the amino acid sequence
30 of any one of SEQ ID NOs: 1-30, 37-52, 57-83 or 88-151, or a fragment of any said sequences.
In another aspect, the disclosure provides 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.

The disclosure also provides isolated nucleic acids encoding anyone of the anti-TIGIT
35 antibodies or antigen binding fragments of the disclosure . In another aspect, the disclosure
provides an isolated nucleic acid encoding: any one of the antibodies or antigen binding

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, 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 of the disclosure and a pharmaceutically acceptable
carrier or diluent.

CLAIMS

1. An antibody or antigen binding fragment 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 of 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 of claim 1, wherein the antibody or antigen binding fragment comprises

- 5 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
10 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;

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- 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.

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- 5 4. The antibody of antigen binding fragment 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.
- 10 5. The antibody of antigen binding fragment 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: 133.
- 15 6. The antibody of antigen binding fragment 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: 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 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.
- 20 8. The antibody or antigen binding fragment of any of claims 1-3 or 7 which is an antibody.

- 5 9. The antibody or antigen binding fragment 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 of any of the above claims, which is a humanized antibody, wherein the antibody comprises a human IgG1 constant domain and a human kappa constant domain.
- 10 11. The antibody or antigen binding fragment 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 of claim 11, wherein the human IgG1 constant domain comprises SEQ ID NO: 86 and the human kappa constant domain comprises SEQ ID
15 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
20 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
25 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
30 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 of any one of the above claims, which is an
35 antibody, wherein the antibody is produced in a Chinese hamster ovary (CHO) cell.

- 5 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 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 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.

- 5 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 comprising:
- 10 a. culturing a host cell comprising a polynucleotide encoding the heavy chain and/or 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 from the host cell and/or culture medium.

- 5 27. An antibody or antigen binding fragment according to any one of claims 1-16, for use to treat cancer.
28. Use of the antibody or antigen binding fragment of claims 1-16 in the manufacture of a medicament for the treatment of cancer.