

- 5 In one aspect, the present disclosure provides an antibody or antigen binding fragment thereof that binds to human TIGIT, wherein the antibody or antigen binding fragment 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
- 10 NO: 147, and a heavy chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO: 153 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:

5 148, and a light chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:93.

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,  
10 157, 158, 159, 160, 161, 162, 163, 164, 165, 166 or 167. In one embodiment, the antibody or antigen binding fragment thereof optionally has at least one of the following characteristics: (i) binds to human TIGIT with a KD value of about  $1 \times 10^{-9}$  M to about  $1 \times 10^{-12}$  M as determined

5 CDR2 and CDR3 of any one of SEQ ID NOs: 130-133, wherein the light chain variable region comprises at least 90%, 95%, 96%, 97%, 98% or 99% identity to any one of SEQ ID NOs: 130-133. In another embodiment, the disclosure also provides an antibody or antigen binding fragment thereof that binds to human TIGIT comprising: (i) a heavy chain variable region comprising the CDR1, CDR2 and CDR3 of SEQ ID NOs: 128, wherein the heavy chain variable  
10 region comprises 90%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NOs: 128 and/or (ii) a light chain variable region comprising the CDR1, CDR2 and CDR3 of SEQ ID NOs: 132, wherein the light chain variable region comprises at least 90%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NOs: 132. In another embodiment, the disclosure also provides an antibody or antigen binding fragment thereof that binds to human TIGIT comprising: (i) a heavy chain  
15 variable region comprising the CDR1, CDR2 and CDR3 of SEQ ID NOs: 128, wherein the heavy chain variable region comprises at least 90%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NOs: 128 and/or (ii) a light chain variable region comprising the CDR1, CDR2 and CDR3 of SEQ ID NOs: 133, wherein the light chain variable region comprises at least 90%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NOs: 133. In another embodiment, the  
20 disclosure also provides an antibody or antigen binding fragment thereof that binds to human TIGIT comprising: (i) a heavy chain variable region comprising the CDR1, CDR2 and CDR3 of SEQ ID NOs: 127, wherein the heavy chain variable region comprises at least 90%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NOs: 127 and/or (ii) a light chain variable region comprising the CDR1, CDR2 and CDR3 of SEQ ID NOs: 130, wherein the light chain variable  
25 region comprises at least 90%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NOs: 130. In these embodiments, the allowed sequence variations occur in the framework regions of the variable chains. In some embodiments, the antibody or antigen binding fragment thereof binds to human TIGIT with a KD value of about  $1 \times 10^{-9}$  M to about  $1 \times 10^{-12}$  M as determined by surface plasmon resonance (e.g., BIACORE) or a similar technique (e.g. KinExa or OCTET).  
30 In another embodiment, the disclosure provides an antibody or antigen binding fragment thereof, comprising: a variable heavy chain comprising the amino acid sequence of SEQ ID NO: 7 and/or a variable light chain selected comprising the amino acid sequence of SEQ ID NO: 8, wherein the antibody or antigen binding fragment thereof binds to human TIGIT. In one embodiment, the antibody binds to human TIGIT with a KD value of about  $1 \times 10^{-9}$  M to about 1

5 domain (SEQ ID NO: 86) or a variant thereof, wherein the variant comprises up to 20 modified amino acid substitutions. In one embodiment, the antibody or antigen binding fragment thereof of the disclosure is an antibody comprising a human heavy chain IgG1 constant domain comprising the amino acid sequence of SEQ ID NO: 86. In one embodiment, the antibody or antigen binding fragment thereof of the disclosure comprises a human heavy chain IgG1 constant domain wherein the IgG1 constant domain is afucosylated. In one embodiment, the antibody or antigen binding fragment thereof of the disclosure comprises a human heavy chain IgG4 constant domain or a variant thereof, wherein the variant comprises up to 20 modified amino acid substitutions. In another embodiment, the antibody or antigen binding fragment thereof of the disclosure comprises a human heavy chain IgG4 constant domain, wherein the amino acid at position 228 (using EU numbering scheme) has been substituted from Ser to Pro. In one embodiment, the antibody or antigen binding fragment thereof of the disclosure comprises a human heavy chain IgG4 constant domain comprising the amino acid sequence of SEQ ID NO: 55.

In any of the above mentioned embodiments, the antibody or antigen binding fragment thereof of the disclosure can comprise any of the variable light chains described above and human light chain constant domain. In one embodiment, the antibody or antigen binding fragment thereof of the disclosure comprises a human kappa light chain constant domain or a variant thereof, wherein the variant comprises up to 20 modified amino acid substitutions. In another embodiment, the antibody or antigen binding fragment thereof of the disclosure comprises a human lambda light chain constant domain or a variant thereof, wherein the variant comprises up to 20 modified amino acid substitutions. In one embodiment, the antibody or antigen binding fragment thereof of the disclosure comprises a human kappa light chain constant domain comprising the amino acid sequence of 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 variable region comprising SEQ ID NO:132 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 NO: 128 and (ii) an IgG1 constant domain comprising SEQ ID NO: 86 and wherein the light

- 5 chain immunoglobulin comprises (i) a light chain variable region comprising SEQ ID NO: 132 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

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 the amino acid  
sequence of any one of SEQ ID NOs: 7-30, 37-52, 63-64, 94-95 or 124-133, 136-139, 143-146,  
149-151.

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, 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 pastoris* host cell.  
20 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.

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 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 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 another aspect, the disclosure provides a method of producing an antibody or antigen binding fragment comprising: 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 as defined herein 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 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 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 acid sequence of SEQ ID NO: 6. In another embodiment, the anti-TIGIT antibody or antigen binding fragment of the disclosure comprises: (i) a heavy chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO: 57; (ii) a heavy chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO: 58; (iii) a heavy chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO: 59; (iv) a light chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO: 60; (v) a light chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO: 61; and (vi) a light chain variable region CDR3 comprising the amino acid sequence of SEQ ID 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 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 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.

The disclosure also provides a vaccine comprising an antibody or antigen binding fragment of the disclosure. In one embodiment, the anti-TIGIT antibody or antigen binding fragment of the disclosure comprises: (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 sequence of SEQ ID NO: 3, 79, 80, 81, 82, 83 or 1401; (iv) a light chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO: 4; (v) a light chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO: 5, 65, 66, 67, 68, 69, 70, 71, 72, 73 or 141; and (vi) a light chain variable region CDR3 comprising the amino acid sequence

5 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: 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  
10 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 vaccine further comprises an antigen.

The disclosure provides a method for detecting the presence of a TIGIT peptide or a fragment thereof in a sample comprising contacting the sample with an antibody or antigen  
15 binding fragment thereof of the disclosure and detecting the presence of a complex between the antibody or fragment and the peptide; wherein detection of the complex indicates the presence of the TIGIT peptide. In one embodiment, the anti-TIGIT antibody or antigen binding fragment of the disclosure comprises: (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  
20 sequence of SEQ ID NO: 2; (iii) a heavy chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO: 3, 79, 80, 81, 82, 83 or 140; (iv) a light chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO: 4; (v) a light chain variable region CDR2 comprising the amino acid sequence of SEQ ID NO: 5, 65, 66, 67, 68, 69, 70, 71, 72, 73 or 141; and (vi) a light chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:  
25 6, 74, 75, 76, 77, 78 or 142. In one embodiment, the 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, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 134, 135 or 147; (iii) a heavy chain variable region CDR3 comprising the amino acid sequence  
30 of SEQ ID NO: 153; (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, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122 or 148; and (vi) a light chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO: 93. In one embodiment, the antibody or antigen binding fragment of the disclosure comprises: (i) a  
35 heavy chain variable region CDR1 comprising the amino acid sequence of SEQ ID NO: 1; (ii) a

- 5           The disclosure also provides a method of increasing the activity of an immune cell, comprising contacting the immune cell with any one of the antibodies or antigen binding fragments of the disclosure. In one embodiment, the disclosure provides a method of increasing the activity of an immune cell, comprising administering to a subject in need thereof an effective

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.

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

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

**BRIEF DESCRIPTION OF THE FIGURES**

**Figure 1** shows binding of antibody 14A6 to human and rhesus TIGIT (expressed in CHO-K1 cells).

**Figure 2** shows binding of antibody 28H5 to human and rhesus TIGIT (expressed in CHO-K1 cells).

10 **Figure 3** shows that antibodies 14A6 and 28H5 block hCD155 interaction with hTIGIT as determined by a cell-based ELISA blocking assay.

**Figure 4** shows binding of antibody 31C6 to human and rhesus TIGIT (expressed in CHO-K1 cells), and also shows that antibody 31C6 blocks hCD155 interaction with hTIGIT.

**Figure 5** shows the activity of antibodies 14A6 and 28H5 in an *in vitro* T cell assay.

15 **Figure 6** shows the activity of antibodies 14A6 and 31C6 *in vitro* T cell assay.

**Figure 7** shows expression of TIGIT, CD226, CD155 and CD96 in primary human T cell lines. At day 3, clone BC4-49 shows highest up-regulation of TIGIT (negative) and down-regulation of CD226 (positive)

5

## CLAIMS

1. An antibody or antigen binding fragment thereof that binds to human TIGIT, wherein the antibody or antigen binding fragment 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: 147, and a heavy chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO: 153, 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: 148, and a light chain variable region CDR3 comprising the amino acid sequence of SEQ ID NO:93.

- 5     2. The antibody or antigen binding fragment of claim 1, 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, 134 or 135, 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.
- 10
3. The antibody or antigen binding fragment of claim 1, 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.
- 15
- 20
4. 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: 94 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:95;
- b. 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;
- 10 c. 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;
- d. 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;
- 15

- 5 e. 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;
- f. 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
- g. 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:  
15 133, wherein any sequence variations occur in the framework regions of the antibody.

- 5 5. The antibody of antigen binding fragment of claim 4, 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 6. The antibody of antigen binding fragment of claim 4, 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 7. The antibody of antigen binding fragment of claim 4, 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.
8. The antibody or antigen binding fragment of any one of claims 1-7, wherein the antibody binds to human TIGIT with a KD value of about  $1 \times 10^{-9}$  M to about  $1 \times 10^{-12}$  M as determined by surface plasmon resonance.
- 20 9. The antibody or antigen binding fragment of any of claims 1-4 or 8 which is an antibody.

- 5 10. 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.
11. 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 12. 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.
13. The antibody of 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.
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 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.
15. 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.
16. 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.
17. 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.
18. An isolated polypeptide comprising the amino acid sequence of any one of SEQ ID NOs: 124-133.

5

19. An isolated nucleic acid encoding: any one of the antibodies or antigen binding fragments of claims 1-17, or any one of the polypeptides of claim 18.
20. An expression vector comprising the isolated nucleic acid of claim 19.
21. A host cell comprising the antibody, binding fragment, polypeptide, polynucleotide or  
10 expression vector of any of claims 1-20.
22. The host cell of claim 21, which is a *Pichia* cell or a Chinese hamster ovary (CHO) cell.
23. A composition comprising the antibody or antigen binding fragment of any one of claims 1-17 and a pharmaceutically acceptable carrier or diluent.
24. The composition of claim 23, further comprising an anti-PD1 antibody

- 5     25. The composition of claim 23, further comprising an anti-PDL1 antibody.
26. The composition of claim 24, wherein the anti-PD1 antibody is pembrolizumab.
27. 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 1-16 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    28. An antibody or antigen binding fragment according to any one of claims 1-17, for use to treat cancer.
29. Use of the antibody or antigen binding fragment of claims 1-17 in the manufacture of a medicament for the treatment of cancer.