

**Claims:**

1. An antibody or antigen binding fragment which is capable of binding to TIM-3, optionally isolated, having the amino acid sequences i) to vi):

- |               |                  |                    |
|---------------|------------------|--------------------|
| i) LC-CDR1:   | SGSSSNIGNNYVS    | (SEQ ID NO:10);    |
| ii) LC-CDR2:  | GNNWRPS          | (SEQ ID NO:11);    |
| iii) LC-CDR3: | EAWDYYVAAGY      | (SEQ ID NO:12),    |
|               | DSWDSADASGV      | (SEQ ID NO:13),    |
|               | DSWDYDYAAGV      | (SEQ ID NO:14),    |
|               | DSWDSYLAAGV      | (SEQ ID NO:15),    |
|               | ESWDYDYASGV      | (SEQ ID NO:16),    |
|               | DSWDSSDSSGV      | (SEQ ID NO:17),    |
|               | EAWDSAYAAGS      | (SEQ ID NO:18),    |
|               | DSWDAALSAGV      | (SEQ ID NO:19), or |
|               | ESWDAAAAAGY      | (SEQ ID NO:20);    |
| iv) HC-CDR1:  | GYYS             | (SEQ ID NO:61), or |
|               | GGSFSGYYWS       | (SEQ ID NO:30);    |
| v) HC-CDR2:   | EINHSGSTNYNPSLKS | (SEQ ID NO:31);    |
| vi) HC-CDR3:  | GYVAGSDA         | (SEQ ID NO:32),    |
|               | GYVAGFDD         | (SEQ ID NO:33),    |
|               | GYVAGFDS         | (SEQ ID NO:34),    |
|               | GYVAGYDY         | (SEQ ID NO:35),    |
|               | GYVAGSDA         | (SEQ ID NO:36),    |
|               | GYVAGFDS         | (SEQ ID NO:37),    |
|               | GYVAGDDY         | (SEQ ID NO:38),    |
|               | GYVAGYDY         | (SEQ ID NO:39), or |
|               | GYVAGSDA         | (SEQ ID NO:40).    |

2. The antibody, or antigen binding fragment, of claim 1, having:

(i) at least one light chain variable region incorporating the following CDRs:

- |          |               |                     |
|----------|---------------|---------------------|
| LC-CDR1: | SGSSSNIGNNYVS | (SEQ ID NO:10)      |
| LC-CDR2: | GNNWRPS       | (SEQ ID NO:11)      |
| LC-CDR3: | EAWDYYVAAGY   | (SEQ ID NO:12); and |

at least one heavy chain variable region incorporating the following CDRs:

- |          |                  |                    |
|----------|------------------|--------------------|
| HC-CDR1: | GYYS             | (SEQ ID NO:61), or |
|          | GGSFSGYYWS       | (SEQ ID NO:30)     |
| HC-CDR2: | EINHSGSTNYNPSLKS | (SEQ ID NO:31)     |
| HC-CDR3: | GYVAGSDA         | (SEQ ID NO:32);    |

OR

(ii) at least one light chain variable region incorporating the following CDRs:

- |          |               |                     |
|----------|---------------|---------------------|
| LC-CDR1: | SGSSSNIGNNYVS | (SEQ ID NO:10)      |
| LC-CDR2: | GNNWRPS       | (SEQ ID NO:11)      |
| LC-CDR3: | DSWDSADASGV   | (SEQ ID NO:13); and |

at least one heavy chain variable region incorporating the following CDRs:

- |          |                  |                    |
|----------|------------------|--------------------|
| HC-CDR1: | GYYS             | (SEQ ID NO:61), or |
|          | GGSFSGYYWS       | (SEQ ID NO:30)     |
| HC-CDR2: | EINHSGSTNYNPSLKS | (SEQ ID NO:31)     |

- OR
- HC-CDR3: GYVAGFDD (SEQ ID NO:33);
- (iii) at least one light chain variable region incorporating the following CDRs:
- LC-CDR1: SGSSSNIGNNYVS (SEQ ID NO:10)
- LC-CDR2: GNNWRPS (SEQ ID NO:11)
- LC-CDR3: DSWDYDYAAGV (SEQ ID NO:14); and
- at least one heavy chain variable region incorporating the following CDRs:
- HC-CDR1: GYYWS (SEQ ID NO:61), or  
GGSFSGYYWS (SEQ ID NO:30)
- HC-CDR2: EINHSGSTNYNPSLKS (SEQ ID NO:31)
- HC-CDR3: GYVAGFDS (SEQ ID NO:34);
- OR
- (iv) at least one light chain variable region incorporating the following CDRs:
- LC-CDR1: SGSSSNIGNNYVS (SEQ ID NO:10)
- LC-CDR2: GNNWRPS (SEQ ID NO:11)
- LC-CDR3: DSWDSYLAAGV (SEQ ID NO:15); and
- at least one heavy chain variable region incorporating the following CDRs:
- HC-CDR1: GYYWS (SEQ ID NO:61), or  
GGSFSGYYWS (SEQ ID NO:30)
- HC-CDR2: EINHSGSTNYNPSLKS (SEQ ID NO:31)
- HC-CDR3: GYVAGYDY (SEQ ID NO:35);
- OR
- (v) at least one light chain variable region incorporating the following CDRs:
- LC-CDR1: SGSSSNIGNNYVS (SEQ ID NO:10)
- LC-CDR2: GNNWRPS (SEQ ID NO:11)
- LC-CDR3: ESWDYDYASGV (SEQ ID NO:16); and
- at least one heavy chain variable region incorporating the following CDRs:
- HC-CDR1: GYYWS (SEQ ID NO:61), or  
GGSFSGYYWS (SEQ ID NO:30)
- HC-CDR2: EINHSGSTNYNPSLKS (SEQ ID NO:31)
- HC-CDR3: GYVAGSDA (SEQ ID NO:36);
- OR
- (vi) at least one light chain variable region incorporating the following CDRs:
- LC-CDR1: SGSSSNIGNNYVS (SEQ ID NO:10)
- LC-CDR2: GNNWRPS (SEQ ID NO:11)
- LC-CDR3: DSWDSSDSSGV (SEQ ID NO:17); and
- at least one heavy chain variable region incorporating the following CDRs:
- HC-CDR1: GYYWS (SEQ ID NO:61), or  
GGSFSGYYWS (SEQ ID NO:30)
- HC-CDR2: EINHSGSTNYNPSLKS (SEQ ID NO:31)
- HC-CDR3: GYVAGFDS (SEQ ID NO:37);
- OR
- (vii) at least one light chain variable region incorporating the following CDRs:
- LC-CDR1: SGSSSNIGNNYVS (SEQ ID NO:10)
- LC-CDR2: GNNWRPS (SEQ ID NO:11)
- LC-CDR3: EAWDSAYAAGS (SEQ ID NO:18); and
- at least one heavy chain variable region incorporating the following CDRs:

|          |                   |                    |
|----------|-------------------|--------------------|
| HC-CDR1: | GYYSWS            | (SEQ ID NO:61), or |
|          | GGSFSGYYWS        | (SEQ ID NO:30)     |
| HC-CDR2: | EINHSGSTNYPNPSLKS | (SEQ ID NO:31)     |
| HC-CDR3: | GYAGDDY           | (SEQ ID NO:38);    |

OR

(viii) at least one light chain variable region incorporating the following CDRs:

|          |               |                     |
|----------|---------------|---------------------|
| LC-CDR1: | SGSSSNIGNNYVS | (SEQ ID NO:10)      |
| LC-CDR2: | GNNWRPS       | (SEQ ID NO:11)      |
| LC-CDR3: | DSWDAALSAGV   | (SEQ ID NO:19); and |

at least one heavy chain variable region incorporating the following CDRs:

|          |                   |                    |
|----------|-------------------|--------------------|
| HC-CDR1: | GYYSWS            | (SEQ ID NO:61), or |
|          | GGSFSGYYWS        | (SEQ ID NO:30)     |
| HC-CDR2: | EINHSGSTNYPNPSLKS | (SEQ ID NO:31)     |
| HC-CDR3: | GYVAGYDY          | (SEQ ID NO:39);    |

OR

(ix) at least one light chain variable region incorporating the following CDRs:

|          |               |                     |
|----------|---------------|---------------------|
| LC-CDR1: | SGSSSNIGNNYVS | (SEQ ID NO:10)      |
| LC-CDR2: | GNNWRPS       | (SEQ ID NO:11)      |
| LC-CDR3: | ESWDAAAAGY    | (SEQ ID NO:20); and |

at least one heavy chain variable region incorporating the following CDRs:

|          |                   |                    |
|----------|-------------------|--------------------|
| HC-CDR1: | GYYSWS            | (SEQ ID NO:61), or |
|          | GGSFSGYYWS        | (SEQ ID NO:30)     |
| HC-CDR2: | EINHSGSTNYPNPSLKS | (SEQ ID NO:31)     |
| HC-CDR3: | GYVAGSDA          | (SEQ ID NO:40).    |

3. The antibody, or antigen binding fragment, of claim 1 or claim 2, wherein the antibody is cytotoxic.

4. The antibody, or antigen binding fragment, of any one of claims 1 to 3, wherein the antibody is effective to restore T-cell function in T-cells exhibiting T-cell exhaustion or T-cell anergy.

5. The antibody or antigen binding fragment according to any one of claims 1 to 4, comprising a heavy chain and a light chain variable region sequence, wherein:

the heavy chain sequence has at least 85% sequence identity to the heavy chain sequence of one of SEQ ID NOs: 21 to 29 (Figure 2), and

the light chain sequence has at least 85% sequence identity to the light chain sequence of one of: SEQ ID NO:1 to 9 (Figure 1).

6. An antibody or antigen binding fragment, optionally isolated, which is capable of binding to TIM-3, which is a bispecific antibody or a bispecific antigen binding fragment comprising (i) an antigen binding fragment according to any one of claims 1 to 5, and (ii) an antigen binding domain which is capable of binding to a target protein other than TIM-3.

7. The antibody, or antigen binding fragment, of claim 6, wherein the antigen binding domain which is capable of binding to a target protein other than TIM-3 is capable of binding to CD3 or a CD3 polypeptide.

8. An *in vitro* complex, optionally isolated, comprising an antibody, or antigen binding fragment, according to any one of claims 1 to 7 bound to TIM-3.
9. A composition comprising the antibody, or antigen binding fragment, of any one of claims 1 to 7 and at least one pharmaceutically-acceptable carrier.
10. An isolated nucleic acid encoding the antibody, or antigen binding fragment, of any of one of claims 1 to 7.
11. A vector comprising the nucleic acid of claim 10.
12. A host cell comprising the vector of claim 11.
13. A method for making an antibody, or antigen binding fragment, of any of one of claims 1 to 7 comprising culturing the host cell of claim 12 under conditions suitable for the expression of a vector encoding the antibody, or antigen binding fragment, and recovering the antibody, or antigen binding fragment.
14. An antibody or antigen binding fragment according to any of one of claims 1 to 7 for use in therapy, or in a method of medical treatment.
15. An antibody or antigen binding fragment according to any of one of claims 1 to 7 for use in the treatment of cancer, a T-cell dysfunctional disorder, or an infectious disease.
16. Use of an antibody or antigen binding fragment according to any of one of claims 1 to 7 in the manufacture of a medicament for use in the treatment of cancer, a T-cell dysfunctional disorder, or an infectious disease.
17. A method, *in vitro*, of killing a cell that expresses TIM-3 comprising administering an antibody or antigen binding fragment according to any one of claims 1 to 7 to a cell that expresses TIM-3.
18. A method, *in vitro*, of enhancing T-cell function comprising administering an antibody or antigen binding fragment according to any one of claims 1 to 7 to a dysfunctional T-cell.
19. A method comprising contacting a sample containing, or suspected to contain, TIM-3 with an antibody or antigen binding fragment according to any one of claims 1 to 7 and detecting the formation of a complex of antibody, or antigen binding fragment, and TIM-3.
20. A method of diagnosing a disease or condition in a subject, the method comprising contacting, *in vitro*, a sample from the subject with an antibody, or antigen binding fragment, according to any one of claims 1 to 7 and detecting the formation of a complex of antibody, or antigen binding fragment, and TIM-3.
21. A method of selecting or stratifying a subject for treatment with a modulator of TIM-3 signalling, the method comprising contacting, *in vitro*, a sample from the subject with an

antibody, or antigen binding fragment, according to any one of claims 1 to 7 and detecting the formation of a complex of antibody, or antigen binding fragment, and TIM-3.

22. Use of an antibody, or antigen binding fragment, according to any one of claims 1 to 7 for the detection of TIM-3 *in vitro*.

23. Use of an antibody, or antigen binding fragment, according to any one of claims 1 to 7 as an *in vitro* diagnostic agent.

24. A method for expanding a population of T cells, wherein T cells are contacted *in vitro* or *ex vivo* with an antibody or antigen binding fragment according to any one of claims 1 to 7.

25. A chimeric antigen receptor (CAR) comprising an antigen binding fragment according to any one of claims 1 to 7.