

CLAIMS:

1. An isolated antibody that specifically binds to human TIM-3, the antibody comprising a heavy chain variable region comprising complementarity determining regions CDRH1, CDRH2 and CDRH3 and a light chain variable region comprising complementarity determining regions CDRL1, CDRL2 and CDRL3, wherein CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 comprise the amino acid sequences set forth in SEQ ID NOs: 1, 2, 3, 14, 21, and 22; 4, 2, 3, 14, 21, and 22; 5, 2, 3, 14, 21, and 22; 6, 2, 3, 14, 21, and 22; 7, 2, 3, 14, 21, and 22; 8, 2, 3, 14, 21, and 22; 9, 2, 3, 14, 21, and 22; 10, 2, 3, 14, 21, and 22; 11, 2, 3, 14, 21, and 22; 12, 2, 3, 14, 21, and 22; or 1, 2, 3, 15, 18, and 22, respectively.
2. The isolated antibody of claim 1, wherein CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 comprise the amino acid sequences set forth in SEQ ID NOs: 5, 2, 3, 14, 21, and 22, respectively.
3. The isolated antibody of claim 1 or 2, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 55.
4. The isolated antibody of any one of claims 1-3, wherein:
 - (a) the heavy chain variable region comprises an amino acid sequence which is at least 75% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 24-35;
 - (b) the heavy chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 24-35;
 - (c) the light chain variable region comprises the amino acid sequence of SEQ ID NO: 56;
 - (d) the light chain variable region comprises an amino acid sequence which is at least 75% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 36-47; or
 - (e) the light chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 36-47.

5. The isolated antibody of any one of claims 1-4, wherein the antibody comprises:
 - (a) a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region and the light chain variable region, respectively, comprise the amino acid sequences set forth in SEQ ID NOs: 24 and 36; 24 and 38; 26 and 42; 24 and 42; 24 and 46; 24 and 43; 26 and 43; 26 and 46; 26 and 41; 24 and 41; 25 and 39; 24 and 47; 25 and 40; 26 and 47; 25 and 37; 25 and 45; 25 and 44; 25 and 46; 25 and 42; 25 and 41; 25 and 43; 25 and 47; 27 and 46; 28 and 46; 29 and 46; 30 and 46; 31 and 46; 32 and 46; 33 and 46; 34 and 46; or 35 and 46;
 - (b) a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region and the light chain variable region, respectively, comprise SEQ ID NO: 28 and 46; or
 - (c) a heavy chain comprising the amino acid sequence of SEQ ID NO: 58, 61 or 65, and/or a light chain comprising the amino acid sequence of SEQ ID NO: 69.

6. The isolated antibody of any one of claims 1-5, wherein the antibody comprises a heavy chain constant region, wherein the heavy chain constant region:
 - (a) is selected from the group consisting of human IgG₁, IgG₂, IgG₃, IgG₄, IgA₁, and IgA₂;
 - (b) is an IgG₁ heavy chain constant region;
 - (c) is an IgG₁ heavy chain constant region comprising a N297A mutation, numbered according to the EU numbering system;
 - (d) comprises the amino acid sequence of SEQ ID NO: 72;
 - (e) is an IgG₁ heavy chain constant region comprising a N297Q mutation, numbered according to the EU numbering system;
 - (f) is a non-fucosylated IgG₁;
 - (g) is an IgG₄ heavy chain constant region;
 - (h) is an IgG₄ heavy chain constant region comprising an S228P mutation, numbered according to the EU numbering system;
 - (i) comprises the amino acid sequence of SEQ ID NO: 74.

7. The isolated antibody of any one of claims 1-6, wherein the antibody comprises a human kappa or human lambda light chain constant region.

8. The isolated antibody of claim 7, wherein the light chain constant region is a human kappa light chain constant region.
9. The isolated antibody of claim 8, wherein the antibody comprises a light chain constant region comprising the amino acid sequence of SEQ ID NO: 76.
10. The isolated antibody of any one of claims 1-9, comprising a heavy chain and a light chain, wherein the heavy chain and the light chain, respectively, comprise the amino acid sequences set forth in SEQ ID NOs: 58 and 69; 61 and 69; or 65 and 69.
11. The isolated antibody of claim 10, wherein the heavy chain and the light chain, respectively, comprise the amino acid sequences set forth in SEQ ID NOs: 61 and 69.
12. The isolated antibody of claim 11, wherein the amino acid sequences of the heavy chain and the light chain, respectively, consist of the amino acid sequences set forth in SEQ ID NOs: 61 and 69.
13. The isolated antibody of any one of claims 1-12, wherein the antibody:
 - (a) is a human antibody,
 - (b) is antagonistic to human TIM-3,
 - (c) deactivates, reduces, or inhibits an activity of human TIM-3,
 - (d) inhibits binding of human TIM-3 to phosphatidylserine, and/or
 - (e) is internalized upon binding to cells expressing human TIM-3.
14. The isolated antibody of any one of claims 1-13, conjugated to a cytotoxic agent, cytostatic agent, toxin, radionuclide, or detectable label.
15. A pharmaceutical composition comprising the antibody of any one of claims 1-14 and a pharmaceutically acceptable carrier or excipient.

16. Use of the antibody or pharmaceutical composition of any one of claims 1-15 in the manufacture of a medicament for:
 - (a) the treatment of cancer in a subject in need thereof;
 - (b) increasing T cell activation in response to an antigen in a subject; or
 - (c) the treatment of an infectious disease in a subject in need thereof.
17. The antibody or pharmaceutical composition of any one of claims 1-15 for use in therapy.
18. An isolated polynucleotide encoding
 - a) a heavy chain variable region and a light chain variable region of the antibody of any one of claims 1-14;
 - b) a heavy chain and a light chain of the antibody of any one of claims 1-14; or
 - c) the amino acid sequence of any one of SEQ ID NOs: 55, 56, 24-47, 58, 61, 65, or 69.
19. A vector comprising the polynucleotide of claim 18.
20. A recombinant host cell comprising:
 - a) the polynucleotide of claim 18;
 - b) the vector of claim 19;
 - c) a first polynucleotide encoding a heavy chain variable region or a heavy chain of the antibody of any one of claims 1-14 and a second polynucleotide encoding a light chain variable region or a light chain of the antibody of any one of claims 1-14;
 - d) a first vector comprising a first polynucleotide encoding a heavy chain variable region or a heavy chain of the antibody of any one of claims 1-14 and a second vector comprising a second polynucleotide encoding a light chain variable region or light chain of the antibody of any one of claims 1-14.

21. A method of producing an antibody that binds to human TIM-3, the method comprising culturing a host cell comprising:
- a) a polynucleotide encoding a heavy chain variable region and a light chain variable region, or a heavy chain and a light chain, of the antibody of any one of claims 1-14;
 - b) a first polynucleotide encoding a heavy chain variable region or a heavy chain of the antibody of any one of claims 1-14 and a second polynucleotide encoding a light chain variable region or a light chain of the antibody of any one of claims 1-14;
 - c) a vector comprising a polynucleotide encoding a heavy chain variable region and a light chain variable region, or a heavy chain and a light chain, of the antibody of any one of claims 1-14; or
 - d) a first vector comprising a first polynucleotide encoding a heavy chain variable region or a heavy chain of the antibody of any one of claims 1-14 and a second vector comprising a second polynucleotide encoding a light chain variable region or light chain of the antibody of any one of claims 1-14, so that the antibody is produced.