

CLAIMS

1. An isolated antibody that specifically binds to human GITR, comprising:
 - (a) a heavy chain variable region (VH) comprising a VH complementarity determining regions (CDR) 1 comprising the amino acid sequence of SEQ ID NO: 13, a VH CDR2 comprising the amino acid sequence of SEQ ID NO: 14, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO: 15; and
 - (b) a light chain variable region (VL) comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO: 16, a VL CDR2 comprising the amino acid sequence of SEQ ID NO: 17, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO: 18.
2. The antibody of claim 1, wherein the VH comprises the amino acid sequence of SEQ ID NO: 206.
3. The antibody of claim 1, wherein the VL comprises the amino acid sequence of SEQ ID NO: 208.
4. The antibody of claim 1, wherein:
 - (a) the VH comprises the amino acid sequence of SEQ ID NO: 206; and
 - (b) the VL comprises the amino acid sequence of SEQ ID NO: 208.
5. The antibody of claim 4, wherein:
 - (a) the amino acid sequence of the VH consists of the amino acid sequence of SEQ ID NO: 206; and
 - (b) the amino acid sequence of the VL consists of the amino acid sequence of SEQ ID NO: 208.
6. The antibody of any one of the preceding claims, wherein the antibody further comprises a human immunoglobulin IgG₁ heavy chain constant region.
7. The antibody of any one of the preceding claims, wherein the antibody further comprises a human immunoglobulin IgG kappa light chain constant region.
8. The antibody of any one of the preceding claims, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 567.

9. The antibody of any one of the preceding claims, wherein the antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO: 576.
10. The antibody of any one of the preceding claims, wherein the antibody is produced by culturing a host cell comprising a nucleic acid molecule encoding the amino acid sequence of SEQ ID NO: 206 so that the nucleic acid molecule is expressed and the antibody is produced.
11. The antibody of claim 10, wherein the host cell further comprises a nucleic acid molecule encoding the amino acid sequence of SEQ ID NO: 576.
12. The antibody of any one of the preceding claims, wherein the antibody is produced by culturing a host cell comprising a nucleic acid molecule encoding the amino acid sequence of SEQ ID NO: 576 so that the nucleic acid molecule is expressed and the antibody is produced.
13. An isolated antibody that specifically binds to human GITR, wherein the antibody is produced by culturing a host cell comprising a first nucleic acid molecule encoding the amino acid sequence of SEQ ID NO: 206 and a second nucleic acid molecule encoding the amino acid sequence of SEQ ID NO: 208 so that the first nucleic acid molecule and the second nucleic acid molecule are expressed and the antibody is produced.
14. The antibody of any one of claims 10-13, wherein the host cell is a CHO cell.
15. The antibody of claim 13 or 14, wherein the first nucleic acid molecule and the second nucleic acid molecule are in a single vector.
16. The antibody of claim 13 or 14, wherein the first nucleic acid molecule is in a first vector and the second nucleic acid molecule is in a second vector.
17. An isolated antibody that specifically binds to human GITR, comprising:
 - (a) a heavy chain comprising the amino acid sequence of SEQ ID NO: 567; and
 - (b) a light chain comprising the amino acid sequence of SEQ ID NO: 576.
18. The antibody of claim 17, wherein:
 - (a) the amino acid sequence of the heavy chain consists of the amino acid sequence of SEQ ID NO: 567; and
 - (b) the amino acid sequence of the light chain consists of the amino acid sequence of SEQ ID NO: 576.

19. The antibody of any one of the preceding claims, wherein the antibody induces, activates or enhances an activity of human GITR, optionally in a cell independent of TCR triggering.
20. The antibody of any one of the preceding claims, wherein the antibody is a humanized antibody, or a chimeric antibody.
21. The antibody of any one of the preceding claims, wherein the antibody is bispecific.
22. A pharmaceutical composition comprising the antibody of any one of the preceding claims and a pharmaceutically acceptable carrier or excipient.
23. A pharmaceutical composition comprising an isolated antibody that specifically binds to human GITR, wherein the antibody comprises:
 - (a) a VH comprising the amino acid sequence of SEQ ID NO: 206; and
 - (b) a VL comprising the amino acid sequence of SEQ ID NO: 208,and a pharmaceutically acceptable carrier or excipient.
24. A pharmaceutical composition comprising an isolated antibody that specifically binds to human GITR, wherein the antibody comprises:
 - (a) a heavy chain comprising the amino acid sequence of SEQ ID NO: 567; and
 - (b) a VL comprising the amino acid sequence of SEQ ID NO: 208,and a pharmaceutically acceptable carrier or excipient.
25. A pharmaceutical composition comprising an isolated antibody that specifically binds to human GITR, wherein the antibody comprises:
 - (a) a light chain comprising the amino acid sequence of SEQ ID NO: 576; and
 - (b) a VH comprising the amino acid sequence of SEQ ID NO: 206,and a pharmaceutically acceptable carrier or excipient.
26. An isolated nucleic acid molecule encoding the VH of the antibody of any one of claims 1-12 or 19-21.
27. An isolated nucleic acid molecule encoding the VL of the antibody of any one of claims 1-12 or 19-21.

28. An isolated nucleic acid molecule encoding the VH and the VL of the antibody of any one of claims 1-12 or 19-21.
29. An isolated nucleic acid molecule encoding the heavy chain of the antibody of any one of claims 17-21.
30. An isolated nucleic acid molecule encoding the light chain of the antibody of any one of claims 17-21.
31. An isolated nucleic acid molecule encoding the heavy chain and the light chain of the antibody of any one of claims 17-21.
32. An isolated vector comprising the nucleic acid molecule of claim 26.
33. An isolated vector comprising the nucleic acid molecule of claim 27.
34. An isolated vector comprising the nucleic acid molecule of claim 28.
35. An isolated vector comprising the nucleic acid molecule of claim 29.
36. An isolated vector comprising the nucleic acid molecule of claim 30.
37. An isolated vector comprising the nucleic acid molecule of claim 31.
38. A population of vectors comprising a first vector comprising a nucleic acid encoding the VH of the antibody of any one of claims 1-12 or 19-21, and a second vector comprising a nucleic acid encoding the VL of the antibody of any one of claims 1-12 or 19-21.
39. A population of vectors comprising a first vector comprising a nucleic acid encoding the heavy chain of the antibody of any one of claims 17-21, and a second vector comprising a nucleic acid encoding the light chain of the antibody of any one of claims 17-21.
40. A host cell comprising the isolated nucleic acid molecule of any one of claims 26-28, the isolated vector of any one of claims 32-34, or the population of vectors of claim 38.
41. The host cell of claim 40, comprising:

- (a) the isolated nucleic acid of claim 26, wherein the isolated nucleic acid encodes the VH of the antibody of claim 1, and the isolated nucleic acid of claim 27, wherein the isolated nucleic acid encodes the VL of the antibody of claim 1;
 - (b) the isolated nucleic acid of claim 28, wherein the isolated nucleic acid encodes the VH and the VL of the antibody of claim 1;
 - (c) the isolated vector of claim 32, wherein the isolated vector comprises the nucleic acid molecule encoding the VH of the antibody of claim 1, and the isolated vector of claim 33, wherein the isolated vector comprises the nucleic acid molecule encoding the VL of the antibody of claim 1;
 - (d) the isolated vector of claim 34, wherein the isolated vector comprises the nucleic acid molecule encoding the VH and the VL of the antibody of claim 1; or
 - (e) the population of vectors of claim 38, wherein the population of vectors comprises a first vector comprising a nucleic acid encoding the VH of the antibody of claim 1, and a second vector comprising a nucleic acid encoding the VL of the antibody of claim 1.
42. The host cell of claim 40, wherein
- (a) the host cell contains a vector comprising a nucleic acid molecule encoding the VH and the VL of the antibody of any one of claims 1-12 or 19-21, or
 - (b) the host cell contains two different vectors, a first vector comprising a nucleic acid molecule encoding the VH of the antibody of any one of claims 1-12 or 19-21, and a second vector comprising a nucleic acid molecule encoding the VL of the antibody of any one of claims 1-12 or 19-21.
43. A host cell comprising the isolated nucleic acid molecule of any one of claims 29-31, the isolated vector of any one of claims 35-37, or the population of vectors of claim 39.
44. The host cell of claim 43, comprising:
- (a) the isolated nucleic acid of claim 29, wherein the isolated nucleic acid encodes the heavy chain of the antibody of claim 17, and the isolated nucleic acid of claim 30, wherein the isolated nucleic acid encodes the light chain of the antibody of claim 17;
 - (b) the isolated nucleic acid of claim 31, wherein the isolated nucleic acid encodes the heavy chain and the light chain of the antibody of claim 17;
 - (c) the isolated vector of claim 35, wherein the isolated vector comprises the nucleic acid molecule encoding the heavy chain of the antibody of claim 17, and the isolated vector of claim 36, wherein the isolated vector comprises the nucleic acid molecule encoding the light chain of the antibody of claim 17;

- (d) the isolated vector of claim 37, wherein the isolated vector comprises the nucleic acid molecule encoding the heavy chain and the light chain of the antibody of claim 17; or
 - (e) the population of vectors of claim 39, wherein the population of vectors comprises a first vector comprising a nucleic acid encoding the light chain of the antibody of claim 17, and a second vector comprising a nucleic acid encoding the heavy chain of the antibody of claim 17.
45. The host cell of claim 43, wherein
- (a) the host cell contains a vector comprising a nucleic acid molecule encoding the heavy chain and the light chain of the antibody of any one of claims 17-21, or
 - (b) the host cell contains two different vectors, a first vector comprising a nucleic acid molecule encoding the heavy chain of the antibody of any one of claims 17-21, and a second vector comprising a nucleic acid molecule encoding the light chain of the antibody of any one of claims 17-21.
46. The host cell of any of claims 40-45, wherein the host cell is a CHO cell.
47. A method of producing an antibody that binds to human GITR comprising culturing the host cell of any of claims 40-46, so that the nucleic acid molecule(s) is/are expressed and the antibody is produced.
48. The method of claim 47, comprising culturing the host cell of any one of claims 40-45, wherein the host cell is a CHO cell.
49. The method of claim 47, wherein a first host cell comprises a first vector comprising a nucleic acid molecule encoding the VH of the antibody of any one of claims 1-12 or 19-21, and a second host cell comprises a second vector comprising a nucleic acid molecule encoding the VL of the antibody of any one of claims 1-12 or 19-21, and wherein the VH expressed by the first cell associates with the VL expressed by the second cell to form the antibody.
50. The method of claim 47, wherein a first host cell comprises a first vector comprising a nucleic acid molecule encoding the heavy chain of the antibody of any one of claims 17-21, and a second host cell comprises a second vector comprising a nucleic acid molecule encoding the light chain of the antibody of any one of claims 17-21, and wherein the heavy chain expressed by the first cell associates with the light chain expressed by the second cell to form the antibody.

51. The antibody of any one of claims 1-21, or the pharmaceutical composition of any one of claims 22-25, for use in enhancing T cell activation.

52. The antibody of any one of claims 1-21, or the pharmaceutical composition of any one of claims 22-25, for use in the treatment of cancer.

53. The antibody or the pharmaceutical composition for use of claim 52, wherein the cancer is endometrial cancer, gastric cancer, stomach cancer, esophageal cancer, gastroesophageal junction carcinoma, head and neck squamous cell carcinoma, melanoma, non-small cell lung cancer, or renal cell carcinoma.

54. The antibody of any one of claims 1-21, or the pharmaceutical composition of any one of claims 22-25, for use in the treatment of a viral infection.