

CLAIMS

1. An anti-GITR agonist antibody or antibody fragment thereof comprising a HCDR3 consensus sequence (H/N)AYGHDGGFAMDY and further comprising:

- (a) a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO:22; a VHCDR2 amino acid sequence of SEQ ID NO:23; and a VHCDR3 amino acid sequence of SEQ ID NO:29; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO:30; a VLCDR2 amino acid sequence of SEQ ID NO:33; and a VLCDR3 amino acid sequence of SEQ ID NO:34;
- (b) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO:84; a VHCDR2 amino acid sequence of SEQ ID NO:80; a VHCDR3 amino acid sequence of SEQ ID NO:29; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO:85; a VLCDR2 amino acid sequence of SEQ ID NO:82; and a VLCDR3 amino acid sequence of SEQ ID NO:83;
- (c) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO:22; a VHCDR2 amino acid sequence of SEQ ID NO:24; and a VHCDR3 amino acid sequence of SEQ ID NO:29; and a VL amino acid sequence comprising a VLCDR1 of SEQ ID NO:31; a VLCDR2 amino acid sequence of SEQ ID NO:33; and a VLCDR3 amino acid sequence of SEQ ID NO:34;
- (d) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO:84; a VHCDR2 amino acid sequence of SEQ ID NO:80; a VHCDR3 amino acid sequence of SEQ ID NO:29; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO:86; a VLCDR2 amino acid sequence of SEQ ID NO:82; and a VLCDR3 amino acid sequence of SEQ ID NO:83;
- (e) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO:22, a VHCDR2 amino acid sequence of SEQ ID NO:25; and a VHCDR3 amino acid sequence of SEQ ID NO:29; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO:30; a VLCDR2 amino acid sequence of SEQ ID NO:33; and a VLCDR3 amino acid sequence of SEQ ID NO:34.
- (f) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO:22; a VHCDR2 amino acid sequence of SEQ ID NO:26; and a VHCDR3 amino acid sequence of SEQ ID NO:29; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO:30; a VLCDR2 amino acid sequence of SEQ ID NO:33; and a VLCDR3 of SEQ ID NO:34;
- (g) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO:84; a VHCDR2 amino acid

sequence of SEQ ID NO:80; a VHCDR3 amino acid sequence of SEQ ID NO:29; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO:85; a VLCDR2 amino acid sequence of SEQ ID NO:82; and a VLCDR3 amino acid sequence of SEQ ID NO:83;

(h) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO:22; a VHCDR2 amino acid sequence of SEQ ID NO:27; and a VHCDR3 amino acid sequence of SEQ ID NO:29; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO:30; a VLCDR2 amino acid sequence of SEQ ID NO:33; and a VLCDR3 amino acid sequence of SEQ ID NO:34;

(i) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO:22, a VHCDR2 amino acid sequence of SEQ ID NO:25, a VHCDR3 amino acid sequence of SEQ ID NO:109; and a VL comprising a VLCDR1 amino acid sequence of SEQ ID NO:30, a VLCDR2 amino acid sequence of SEQ ID NO:33, and a VLCDR3 amino acid sequence of SEQ ID NO:34; or

(j) a VH comprising a VHCDR1 amino acid sequence of SEQ ID NO:84, a VHCDR2 amino acid sequence of SEQ ID NO:80, a VHCDR3 amino acid sequence of SEQ ID NO:109; and a VL amino acid sequence comprising a VLCDR1 of SEQ ID NO:85, a VLCDR2 amino acid sequence of SEQ ID NO:82, and a VLCDR3 amino acid sequence of SEQ ID NO:83.

2. The antibody or antibody fragment of claim 1, wherein the VH comprises a heavy chain variable segment amino acid sequence of SEQ ID NO:16, and/or the VL comprises a light chain variable segment amino acid sequence of SEQ ID NO:17.

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

4. The antibody or antibody fragment of any one of claims 1-3, which is Fab, F(ab')₂, Fv, or a single chain Fv fragment (scFv); or which comprises a heavy chain constant region selected from IgG1, IgG2, IgG3 and IgG4, and optionally a light chain constant region chosen from the light chain constant regions of kappa or lambda.

5. The antibody or antibody fragment of claim 1-4, which comprises:

a VH comprising an amino acid sequence chosen from SEQ ID NO: 6, 8, 10, 12, 14, 99, or 105, or comprising an amino acid sequence at least 85% identical to any of SEQ ID NOs: 6, 8, 10, 12, 14, 99, or 105; and/or

a VL comprising an amino acid sequence chosen from SEQ ID NO: 7 or 9, or comprising an amino acid sequence at least 85% identical to any of SEQ ID NOs: 7 or 9.

6. The antibody or antibody fragment of any one of claims 1-5, which comprises: a VH comprising an amino acid sequence chosen from SEQ ID NO: 6, 8, 10, 12, 14, 99, or 105; and/or a VL comprising an amino acid sequence chosen from SEQ ID NO: 7 or 9.

7. The antibody or antibody fragment of any one of claims 1-6, which comprises:

a VH comprising the amino acid sequence of SEQ ID NO:6, and a VL comprising SEQ ID NO:7;

a VH comprising the amino acid sequence of SEQ ID NO:8, and a VL comprising the amino acid sequence of SEQ ID NO:9;

a VH comprising the amino acid sequence of SEQ ID NO:10, and a VL comprising the amino acid sequence of SEQ ID NO:7;

a VH comprising the amino acid sequence of SEQ ID NO:12, and a VL comprising the amino acid sequence of SEQ ID NO:7;

a VH comprising the amino acid sequence of SEQ ID NO:14, and a VL comprising the amino acid sequence of SEQ ID NO:7;

a VH comprising the amino acid sequence of SEQ ID NO:99, and a VL comprising the amino acid sequence of SEQ ID NO:7; or

a VH comprising the amino acid sequence of SEQ ID NO:105, and a VL comprising the amino acid sequence of SEQ ID NO:7.

8. The antibody or antibody fragment of any one of claims 1-7, which comprises a heavy chain comprising an amino acid sequence of SEQ ID NO:65, SEQ ID NO:69, SEQ ID NO:73, SEQ ID NO:75, SEQ ID NO:77, SEQ ID NO:100 and SEQ ID NO:106; and/or a light chain comprising an amino acid sequence of SEQ ID NO:66 or SEQ ID NO:70.

9. The antibody or antibody fragment of any one of claims 1-8, which comprises:

a heavy chain comprising the amino acid sequence of SEQ ID NO:65; and a light chain comprising the amino acid sequence of SEQ ID NO:66;

a heavy chain comprising the amino acid sequence of SEQ ID NO:69; and a light chain comprising the amino acid sequence of SEQ ID NO:70;

a heavy chain comprising the amino acid sequence of SEQ ID NO:73; and a light chain comprising the amino acid sequence of SEQ ID NO:66;

a heavy chain comprising the amino acid sequence of SEQ ID NO:75; and a light chain comprising the amino acid sequence of SEQ ID NO:66;

a heavy chain comprising the amino acid sequence of SEQ ID NO:77; and a light chain comprising the amino acid sequence of SEQ ID NO:66;

a heavy chain comprising the amino acid sequence of SEQ ID NO:100; and a light chain comprising the amino acid sequence of SEQ ID NO:66;

a heavy chain comprising the amino acid sequence of SEQ ID NO: 106; and a light chain comprising the amino acid sequence of SEQ ID NO:66;

10. The antibody or antibody fragment of any one of claims 1-9, which comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:100; and a light chain comprising the amino acid sequence of SEQ ID NO:66.

11. The antibody or antibody fragment of any one of any one of claims 1-10, which is cross-linked to a second anti-GITR agonist antibody or antibody fragment.

12. The antibody or antibody fragment of any one of any one of claims 1-11, wherein the antibody or antibody fragment is glycosylated or aglycosylated.

13. A pharmaceutical composition comprising the antibody or antibody fragment of any of claims 1-12 and a pharmaceutically acceptable carrier.

14. A polynucleotide encoding the antibody or antibody fragment VH and VL of any of claims 1-13.

15. An expression vector comprising the polynucleotide of claim 14.

16. A host cell comprising the polynucleotide of claim 14 or the expression vector of claim 15.

17. A method of producing the antibody molecule or antibody fragment of any one of claims 1-12, using the host cell of claim 16.

18. The antibody or antibody fragment of any one of claims 1-12 for use in or treating a cancer or an infectious disease in an individual in need thereof.

19. The use of an antibody or antibody fragment, of any one of claims 1-12 in the manufacture of a medicament for treating a cancer or an infectious disease wherein the cancer is selected from the group consisting of epithelial cancers, carcinomas, sarcomas and lymphomas.

20. The use of an antibody or antibody fragment, of any one of claims 1-12 in the manufacture of a medicament or for treating a cancer or an infectious disease wherein the cancer is selected from the group consisting of: renal cancer, lung cancer including non-small cell lung cancer (NSCLC), glioma, fibrosarcoma, pancreatic cancer, melanomas, breast cancer, bronchial cancer, colorectal cancer, prostate cancer, stomach cancer, ovarian cancer, urinary bladder cancer, brain or central nervous system cancer, peripheral nervous system cancer, esophageal cancer, cervical cancer, uterine or endometrial cancer, cancer of the oral cavity or pharynx, liver cancer, testicular cancer, biliary tract cancer, small bowel or appendix cancer, salivary gland cancer, thyroid gland cancer, adrenal gland cancer, osteosarcoma, chondrosarcoma, cancer of hematological tissues, and head and neck squamous cell carcinoma (HNSCC).

21. The use of claim 19 or claim 20, wherein the medicament is to be co-administered with a chemotherapeutic agent or a cytotoxin.

22. The use of claim 19 or claim 20, wherein upon administration, the T cell response is a CD8+ cytotoxic T lymphocyte (CTL) T cell response or a CD4+ helper T cell (Th) response.

23. The use as claimed in any one of claims 19-22, wherein the antibody or antibody fragment induces an elevated Teff:Treg ratio at tumor sites.