

CLAIMS

What is claimed is:

1. An isolated anti-IL-2 antibody comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein said VH comprises heavy chain complementarity determining regions (HCDRs) HCDR1, HCDR2 and HCDR3, said VL comprises light chain complementarity determining regions (LCDRs) LCDR1, LCDR2 and LCDR3, wherein said CDRs have the amino acid sequences of
 - (a) the HCDR1 comprises the amino acid sequence of SEQ ID NO:38, the HCDR2 comprises the amino acid sequence of SEQ ID NO:39, the HCDR3 comprises the amino acid sequence of SEQ ID NO:40, the LCDR1 comprises the amino acid sequence of SEQ ID NO:41, the LCDR2 comprises the amino acid sequence of SEQ ID NO:42, the LCDR3 comprises the amino acid sequence of SEQ ID NO:43;
 - (b) the HCDR1 comprises the amino acid sequence of SEQ ID NO:44, the HCDR2 comprises the amino acid sequence of SEQ ID NO:45, the HCDR3 comprises the amino acid sequence of SEQ ID NO:46, the LCDR1 comprises the amino acid sequence of SEQ ID NO:47, the LCDR2 comprises the amino acid sequence of SEQ ID NO:48, the LCDR3 comprises the amino acid sequence of SEQ ID NO:49;
 - (c) the HCDR1 comprises the amino acid sequence of SEQ ID NO:50, the HCDR2 comprises the amino acid sequence of SEQ ID NO:51, the HCDR3 comprises the amino acid sequence of SEQ ID NO:52, the LCDR1 comprises the amino acid sequence of SEQ ID NO:53, the LCDR2 comprises the amino acid sequence of SEQ ID NO:54, the LCDR3 comprises the amino acid sequence of SEQ ID NO:55;
 - (d) the HCDR1 comprises the amino acid sequence of SEQ ID NO:56, the HCDR2 comprises the amino acid sequence of SEQ ID NO:57, the HCDR3 comprises the amino acid sequence of SEQ ID NO:58, the LCDR1 comprises the amino acid sequence of SEQ ID NO:59, the LCDR2 comprises the amino acid sequence of SEQ ID NO:60, the LCDR3 comprises the amino acid sequence of SEQ ID NO:61; or
 - (e) the HCDR1 comprises the amino acid sequence of SEQ ID NO:62, the HCDR2 comprises the amino acid sequence of SEQ ID NO:63, the HCDR3 comprises the amino acid sequence of SEQ ID NO:64, the LCDR1 comprises the amino acid

sequence of SEQ ID NO:65, the LCDR2 comprises the amino acid sequence of SEQ ID NO:66, the LCDR3 comprises the amino acid sequence of SEQ ID NO:67.

2. The antibody of claim 1, wherein the VH and VL have the amino acid sequences of
 - (a) the VH comprises the amino acid sequence of SEQ ID NO:10, the VL comprises the amino acid sequence of SEQ ID NO:11;
 - (b) the VH comprises the amino acid sequence of SEQ ID NO:12, the VL comprises the amino acid sequence of SEQ ID NO:13;
 - (c) the VH comprises the amino acid sequence of SEQ ID NO:14, the VL comprises the amino acid sequence of SEQ ID NO:15;
 - (d) the VH comprises the amino acid sequence of SEQ ID NO:16, the VL comprises the amino acid sequence of SEQ ID NO:17;
 - (e) the VH comprises the amino acid sequence of SEQ ID NO:18, the VL comprises the amino acid sequence of SEQ ID NO:19;
 - (f) the VH comprises the amino acid sequence of SEQ ID NO:20, the VL comprises the amino acid sequence of SEQ ID NO:21;
 - (g) the VH comprises the amino acid sequence of SEQ ID NO:22, the VL comprises the amino acid sequence of SEQ ID NO:23;
 - (h) the VH comprises the amino acid sequence of SEQ ID NO:24, the VL comprises the amino acid sequence of SEQ ID NO:25;
 - (i) the VH comprises the amino acid sequence of SEQ ID NO:26, the VL comprises the amino acid sequence of SEQ ID NO:27; or
 - (j) the VH comprises the amino acid sequence of SEQ ID NO:36, the VL comprises the amino acid sequence of SEQ ID NO:37.
3. The antibody of claim 1, wherein the antibody comprises an IgG, IgA, IgM, IgE, IgD, a Fv, a scFv, a Fab, a F(ab')₂, a minibody, a diabody, a triabody, a nanobody, or a single domain antibody.
4. The antibody of claim 1, wherein said antibody comprises a heavy chain comprising a mutation that reduces binding to Fcγ receptor.

5. The antibody of claim 4, said antibody comprising a heavy chain sequence and a light chain sequence,
 - (a) said heavy chain sequence set forth in SEQ ID NO: 68 and said light chain sequence set forth in SEQ ID NO: 69;
 - (b) said heavy chain sequence set forth in SEQ ID NO: 70 and said light chain sequence set forth in SEQ ID NO: 71; or
 - (c) said heavy chain sequence set forth in SEQ ID NO: 72 and said light chain sequence set forth in SEQ ID NO: 73.
6. A composition comprising the antibody of claim 1 and a pharmaceutically acceptable carrier.
7. The composition of claim 6, wherein the composition is formulated to be at a pH between about pH 5.0 - 6.0 and comprises a buffer selected from a histidine buffer and a citrate buffer.
8. The composition of claim 7, said composition further comprising at least one of sucrose, methionine, or PS80, or any combination thereof.
9. The composition of claim 6, further comprising IL-2.
10. An isolated polynucleotide sequence encoding the heavy chain variable region of an anti-IL-2 antibody, wherein the VH amino acid sequences is set forth in the amino acid sequence of SEQ ID NO:10, 12, 14, 16, 18, 20, 22, 24, 26, or 36.
11. A vector comprising the polynucleotide sequence of claim 10.
12. A host cell comprising the vector of claim 11.
13. An isolated polynucleotide sequence encoding the light chain variable region of an anti-IL-2 antibody, wherein the VL amino acid sequences is set forth in the amino acid sequence

of SEQ ID NO: 11, 13, 15, 17, 19, 21, 23, 25, 27, or 37.

14. A vector comprising the polynucleotide sequence of claim 13.
15. A host cell comprising the vector of claim 14.
16. An isolated polynucleotide sequence encoding an anti-IL-2 scFv, wherein the polynucleotide sequence is set forth in SEQ ID NO: 1, 2, 3, 4, 5, 31, 32, 33, 34, or 35.
17. A vector comprising the polynucleotide sequence of claim 16.
18. A host cell comprising the vector of claim 17.
19. A method of treating a disease or a condition in a subject, comprising the step of administering to the subject a composition comprising the anti-IL-2 antibody of claim 1, wherein said antibody promotes differential growth of subsets of immune cells and decreases undesirable effects caused by IL-2, thereby treating said disease or condition in said subject.
20. The method of claim 19, wherein said composition comprises the anti-IL-2 antibody and IL-2, or the anti-IL-2 antibody complexed with IL-2.
21. The method of claim 19, wherein the disease comprises a viral infection, a bacterial infection, or a cancer.
22. The method of claim 19, wherein said condition comprises a weak immune system and said treatment prophylactically boosts the immune system.
23. The method of claim 19, wherein said condition comprises a genetic predisposition that increases likelihood of cancer in said subject.
24. The method of claim 23, wherein said genetic predisposition comprises a change in expression or activity of a gene product, said gene comprising a tumor suppressor gene or

a mismatch repair (MMR) gene, or a combination thereof.

25. The method of claim 23, wherein said genetic predisposition comprises a change in expression or activity of a gene product, said gene comprising BRCA1, BRAC2, MLH1, MSH2, MSH6, PMS1, PMS2, TP53, or CHEK2, or a combination thereof.
26. The method of claim 19, wherein the immune cells comprise one or more of naïve T cells, memory T cells, CD8⁺ T cells, NK cells, or Natural Killer T cells.
27. The method of claim 19, wherein said undesirable effect caused by IL-2 comprises one or more of activation of regulatory T cells, apoptosis of CD25⁺ T effector cells, IL-2 induced pulmonary edema, IL-2 induced pneumonia, or IL-2-induced vascular leakage.
28. The method of claim 19, wherein said anti-IL-2 antibody inhibits IL-2 binding to CD25.
29. The method of claim 19, wherein said subject is further treated with one or more immune checkpoint inhibitors targeting one or more immune checkpoints.
30. The method of claim 29, wherein said subject is treated with said immune checkpoint inhibitors concurrently, before, or after treatment with said anti-IL-2 antibody.
31. The method of claim 29, wherein said immune checkpoint comprises PD-1, PDL-1, CTLA-4, TIGIT, TIM-3, B7-H3, CD73, LAG3, CD27, CD70, 4-1BB, GITR, OX40, SIRP-alpha (CD47), CD39, ILDR2, VISTA, BTLA, or VTCN-1, or a combination thereof.
32. The method of claim 21, wherein the viral infection is caused by SARS CoV-2; norovirus; rotavirus; hepatitis virus A, B, C, D, or E; rabies virus; West Nile virus; enterovirus; echovirus; coxsackievirus; herpes simplex virus (HSV); HSV-2; varicella-zoster virus; mosquito-borne viruses; arbovirus; St. Louis encephalitis virus; California encephalitis virus; lymphocytic choriomeningitis virus; human immunodeficiency virus (HIV); poliovirus; zika virus; rubella virus; cytomegalovirus; human papillomavirus (HPV);

enterovirus D68; severe acute respiratory syndrome (SARS) coronavirus; Middle East respiratory syndrome coronavirus; Epstein-Barr virus; influenza virus; respiratory syncytial virus; polyoma viruses including JC virus; BK virus); Ebola virus; Dengue virus; or any combination thereof.

33. A method of immunizing a subject, wherein said immunization comprises administration of a vaccine comprising an adjuvant, said adjuvant comprising an IL-2 antibody adjuvant, said anti-IL-2 antibody comprising the anti-IL-2 antibody of claim 1.
34. The method of claim 33, wherein said IL-2 antibody adjuvant comprises the anti-IL-2 antibody and IL-2, or comprises an anti-IL-2 antibody complexed with IL-2.
35. The method of claim 33, wherein said subject has a weakened immune system.
36. The method of claim 33, wherein said subject has a genetic predisposition that increases likelihood of cancer in said subject.
37. The method of claim 36, wherein said genetic predisposition comprises a change in expression or activity of a gene product, said gene comprising a tumor suppressor gene or a mismatch repair (MMR) gene, or a combination thereof.
38. The method of claim 36, wherein said genetic predisposition comprises a change in expression or activity of a gene product, said gene comprising BRCA1, BRAC2, MLH1, MSH2, MSH6, PMS1, PMS2, TP53, or CHEK2, or a combination thereof.