

WHAT IS CLAIMED IS:

1. A genetically modified T-cell genetically modified to express:
 - a) a recombinant arginine transporter and
 - b) a chimeric antigen receptor having at least one antigen-specific targeting region that specifically binds a cell surface antigen present on a target cell population, a transmembrane domain, and an intracellular signaling domain.
2. An expression vector comprising an isolated nucleic acid encoding a) an antigen-specific targeting region, b) a transmembrane domain, c) optionally at least one co-stimulatory domain, d) an intracellular signaling domain and e) an arginine transporter.
3. A genetically modified T-cell modified to express a chimeric antigen receptor encoded by the expression vector of claim 2.
4. The genetically modified T-cell of claim 1 or 3, wherein the arginine transporter is selected from the group consisting of CAT-1, CAT-2, CAT-3, CAT-4, y^+LAT1 and 4F2hc, y^+LAT2 and 4F2hc, $b^{0,+}AT$ and rBAT, and ATB $^{0,+}$.
5. The genetically modified T-cell of any one of claims 1, 3, or 4, wherein the genetically modified T-cell comprises a nucleic acid sequence selected from the group consisting of: SEQ ID NO:180, 184-188, 204, 205, 210, 214, 215, 220-222, 227-230, 234-236, 242, and 246, or a fragment or a variant thereof.
6. The genetically modified T-cell of claims 1, 3 or 4, wherein the genetically modified T-cell comprises a nucleic acid expressing a sequence having about 90%, 95%, or 99% percent identity to one of SEQ ID NO: 180, 184-188, 204, 205, 210, 214, 215, 220-222, 227-230, 234-236, 242, and 246.
7. A pharmaceutically acceptable composition comprising the genetically modified T-cell of any one of claims 1 or 3-6, and a pharmaceutically acceptable excipient.

8. A priming medium comprising the genetically modified T-cell of any one of claims 1 or 3-6, and L-arginine.
9. A pharmaceutical composition comprising a chimeric antigen receptor T cell (CAR-T cell) which expresses a recombinant arginine transporter and a chimeric antigen receptor protein.
10. The pharmaceutical composition of claim 9, wherein the arginine transporter is CAT-1.
11. The pharmaceutical composition of claim 9, wherein the arginine transporter is CAT-2.
12. The pharmaceutical composition of claim 9, wherein the arginine transporter is CAT-3.
13. The pharmaceutical composition of claim 9, wherein the arginine transporter is CAT-4.
14. The pharmaceutical composition of claim 9, wherein the arginine transporter is y^{+} LAT1 and 4F2hc.
15. The pharmaceutical composition of claim 9, wherein the arginine transporter is y^{+} LAT2 and 4F2hc.
16. The pharmaceutical composition of claim 9, wherein the arginine transporter is $b^{0,+}$ AT and rBAT.
17. The pharmaceutical composition of claim 9, wherein the arginine transporter is $ATB^{0,+}$.
18. The pharmaceutical composition of claim 9, wherein the pharmaceutical composition is packaged as a kit.
19. A method of treating a solid tumor cancer in a patient in need thereof, comprising administering to the patient an effective amount of the pharmaceutical composition of claim 7 or 9.
20. A method of treating a hematological cancer in a patient in need thereof, comprising administering to the patient an effective amount of the pharmaceutical composition of claim 7 or 9.

21. A method of modulating intracellular arginine levels to effect a T cell-mediated immune response in a patient in need thereof, comprising administering to the patient an effective amount of the pharmaceutical composition of claim 7 or 9.
22. A method for treating a condition in a human patient in need thereof, comprising: administering to the human patient a therapeutically effective amount of a composition comprising a chimeric antigen receptor T cell (CAR-T cell) which expresses a recombinant arginine transporter and a chimeric antigen receptor protein.
23. A method of modulating a T cell-mediated immune response to a target cell population expressing a cell surface antigen in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of T-cells that are a) genetically modified to express a chimeric antigen receptor wherein the chimeric antigen receptor comprises: at least one antigen-specific targeting region that specifically binds the cell surface antigen present on the target cell population, a transmembrane domain, an intracellular signaling domain, and b) genetically modified to express a recombinant arginine transporter.
24. The method of claim 22 or 23, wherein the T-cells are cultured in a culture medium comprising arginine before administering.
25. The method according to any one of claims 22-24, wherein the arginine transporter is CAT-1.
26. The method according to any one of claims 22-24, wherein the arginine transporter is CAT-2.
27. The method according to any one of claims 22-24, wherein the arginine transporter is CAT-3.
28. The method according to any one of claims 22-24, wherein the arginine transporter is CAT-4.

29. The method according to any one of claims 22-24, wherein the arginine transporter is y⁺LAT1 and 4F2hc.
30. The method according to any one of claims 22-24, wherein the arginine transporter is y⁺LAT2 and 4F2hc.
31. The method according to any one of claims 22-24, wherein the arginine transporter is b^{0,+}AT and rBAT.
32. The method according to any one of claims 22-24, wherein the arginine transporter is ATB^{0,+}.
33. The method of any one of claims 22-24, comprising administering the T-cell of any one of claims 1 and 3-6.
34. The method according to any one of claims 22-32, further comprising administering a second therapeutic agent to the human patient.
35. The method according to claim 34, wherein the second therapeutic agent an anti-PD-1, anti-PD-L1, or an anti-CTLA-4 antibody.
36. The method according to claim 34 or 35, wherein the administering of the second therapeutic agent is performed before, during or after the administering of the composition comprising the CAR-T cell.
37. The method according to claim 34 or 35, wherein the administering of the second therapeutic agent is performed before, during or after the administering of the therapeutically effective amount of T-cells.
38. The method according to any one of claims 22-37, wherein the composition comprising the CAR-T cells is administered to the human patient once every week, once every 2 weeks, once every 3 weeks, or once every 4 weeks.

39. The method according to any one of claims 22-37, comprising administering 10^7 to 10^{10} CAR-T cells per kilogram of the patient.
40. A method of making a genetically modified CAR-T cell that expresses a recombinant arginine transporter, comprising:
transfecting a T-cell with a DNA construct comprising a nucleotide sequence for a specific chimeric antigen receptor and for an arginine transporter thereby producing a genetically modified CAR-T cell that expresses both the chimeric antigen receptor and the arginine transporter;
and
culturing the genetically modified CAR-T cell in a culture medium comprising arginine.
41. The method of claim 40, wherein said culturing comprises culturing the genetically modified CAR-T cell in the culture medium until the intracellular arginine level of the CAR-T cell accumulates to a certain level.
42. A genetically modified T-cell genetically modified to express a recombinant arginine transporter.
43. The genetically modified T-cell of claim 42, wherein the arginine transporter is selected from the group consisting of CAT-1, CAT-2, CAT-3, CAT-4, y^+LAT1 and 4F2hc, y^+LAT2 and 4F2hc, $b^{0,+}AT$ and rBAT, and $ATB^{0,+}$.
44. The genetically modified T-cell of claim 42 or 43, wherein the genetically modified T-cell comprises a nucleic acid sequence selected from the group consisting of: SEQ ID NO:180, 184-188, 204, 205, 210, 214, 215, 220-222, 227-230, 234-236, 242, and 246, or a fragment or a variant thereof.
45. The genetically modified T-cell of claim 42 or 43, wherein the genetically modified T-cell comprises a nucleic acid expressing a sequence having about 90%, 95%, or 99% percent identity to one of SEQ ID NO: 180, 184-188, 204, 205, 210, 214, 215, 220-222, 227-230, 234-236, 242, and 246.

46. A pharmaceutically acceptable composition comprising the genetically modified T-cell of any one of claims 42-45, and a pharmaceutically acceptable excipient.
47. A priming medium comprising the genetically modified T-cell of any one of claims 42-45, and L-arginine.
48. A pharmaceutical composition comprising a T cell which expresses a recombinant arginine transporter protein.
49. The pharmaceutical composition of claim 48, wherein the arginine transporter is CAT-1.
50. The pharmaceutical composition of claim 48, wherein the arginine transporter is CAT-2.
51. The pharmaceutical composition of claim 48, wherein the arginine transporter is CAT-3.
52. The pharmaceutical composition of claim 48, wherein the arginine transporter is CAT-4.
53. The pharmaceutical composition of claim 48, wherein the arginine transporter is y^{+} LAT1 and 4F2hc.
54. The pharmaceutical composition of claim 48, wherein the arginine transporter is y^{+} LAT2 and 4F2hc.
55. The pharmaceutical composition of claim 48, wherein the arginine transporter is $b^{0,+}$ AT and rBAT.
56. The pharmaceutical composition of claim 48, wherein the arginine transporter is $ATB^{0,+}$.
57. The pharmaceutical composition of claim 48, wherein the pharmaceutical composition is packaged as a kit.
58. A method of treating a solid tumor cancer in a patient in need thereof, comprising administering to the patient an effective amount of the pharmaceutical composition of claim 46 or 48.

59. A method of treating a hematological cancer in a patient in need thereof, comprising administering to the patient an effective amount of the pharmaceutical composition of claim 46 or 48.
60. A method of modulating intracellular arginine levels to effect a T cell-mediated immune response in a patient in need thereof, comprising administering to the patient an effective amount of the pharmaceutical composition of claim 46 or 48.
61. A method for treating a condition in a human patient in need thereof, comprising: administering to the human patient a therapeutically effective amount of a composition comprising a T cell which expresses a recombinant arginine transporter.
62. The method of claim 61, wherein the T-cells are cultured in a culture medium comprising arginine before administering.
63. The method of claim 61 or 62, wherein the arginine transporter is CAT-1.
64. The method of claim 61 or 62, wherein the arginine transporter is CAT-2.
65. The method of claim 61 or 62, wherein the arginine transporter is CAT-3.
66. The method of claim 61 or 62, wherein the arginine transporter is CAT-4.
67. The method of claim 61 or 62, wherein the arginine transporter is y^+ LAT1 and 4F2hc.
68. The method of claim 61 or 62, wherein the arginine transporter is y^+ LAT2 and 4F2hc.
69. The method of claim 61 or 62, wherein the arginine transporter is $b^{0,+}$ AT and rBAT.
70. The method of claim 61 or 62, wherein the arginine transporter is $ATB^{0,+}$.
71. The method of claim 61 or 62, comprising administering the T-cell of any one of claims 42-45.

72. The method according to any one of claims 58-71, further comprising administering a second therapeutic agent to the human patient.
73. The method according to claim 72, wherein the second therapeutic agent is an anti-PD-1, anti-PD-L1, or an anti-CTLA-4 antibody.
74. The method according to claim 72 or 73, wherein the administering of the second therapeutic agent is performed before, during or after the administering of the composition comprising the T cell.
75. The method according to claim 72 or 73, wherein the administering of the second therapeutic agent is performed before, during or after the administering of the therapeutically effective amount of T-cells.
76. A method of making a genetically modified T cell that expresses a recombinant arginine transporter, comprising:
transfecting a T-cell with a DNA construct comprising a nucleotide sequence for an arginine transporter thereby producing a genetically modified T cell that expresses the arginine transporter; and
culturing the genetically modified T cell in a culture medium comprising arginine.
77. The method of claim 76, wherein said culturing comprises culturing the genetically modified T cell in the culture medium until the intracellular arginine level of the T cell accumulates to a certain level.
78. A method of increasing T cell survival in a low arginine environment, the method comprising: administering a T cell comprising a recombinant arginine transporter to a low arginine environment.
79. The method of claim 78, wherein prior to the administering step, the method comprises transfecting the T cell with a DNA construct comprising a nucleotide sequence encoding the recombinant arginine transporter.

80. The method of claim 78 or claim 79, wherein the T-cell comprises a chimeric antigen receptor and/or a DNA construct comprising a nucleotide sequence encoding a chimeric antigen receptor.
81. The method of any one of claims 78-80, wherein prior to the administering step, the method comprises culturing the T cell in a culture medium comprising arginine.
82. The method of claim 81, wherein the culturing comprises culturing the T cell in the culture medium until the intracellular arginine level of the T cell accumulates to a certain level.
83. The method of any one of claims 78-82, wherein the arginine transporter is selected from the group consisting of CAT-1, CAT-2, CAT-3, CAT-4, y^+LAT1 and 4F2hc, y^+LAT2 and 4F2hc, $b^{0,+}AT$ and rBAT, and $ATB^{0,+}$.
84. The method of any one of claims 78-82, wherein the DNA construct comprising a nucleotide sequence encoding the recombinant arginine transporter comprises a nucleic acid sequence selected from the group consisting of: SEQ ID NO:180, 184-188, 204, 205, 210, 214, 215, 220-222, 227-230, 234-236, 242, and 246, or a fragment or a variant thereof.
85. The method of any one of claims 78-82, wherein the DNA construct comprising a nucleotide sequence encoding the recombinant arginine transporter comprises a nucleic acid expressing a sequence having about 90%, 95%, or 99% percent identity to one of SEQ ID NO: 180, 184-188, 204, 205, 210, 214, 215, 220-222, 227-230, 234-236, 242, and 246.
86. The method of any one of claims 78-85, wherein the low arginine environment is a cell culture medium.
87. The method of any one of claims 78-85, wherein the low arginine environment is a tumor microenvironment.