CLAIMS

What is Claimed:

1. A chimeric antigen receptor that binds to C-type-lectin-like-1 ("CLL-1 "), wherein the chimeric antigen receptor is a polypeptide comprising a single chain Fv (scFv) that binds CLL-1, a transmembrane domain, and an intracellular activating domain that is a signaling domain of CD3 zeta, and wherein the scFv comprises a heavy chain variable (VH) and light chain variable region (VL) pair that is selected from the group consisting of:

(a) a VH region comprising complementary determining regions ("CDRs") 1, 2, and 3 with amino acid sequences SEQ ID NO: 17, SEQ ID NO: 18, and SEQ ID NO: 19, respectively, and a VL region comprising CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO: 22, SEQ ID NO: 23, and SEQ ID NO: 24, respectively;;

(b) a VH region comprising CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO: 51, SEQ ID NO: 52, and SEQ ID NO: 53, respectively, and a VL region comprising CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO: 56, SEQ ID NO: 57, and SEQ ID NO: 58, respectively;

(c) a VH region comprising CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO: 73, SEQ ID NO: 74, and SEQ ID NO: 75, respectively, and a VL region comprising CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO: 78, SEQ ID NO: 79, and SEQ ID NO: 80, respectively; and

(d) a VH region comprising CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO: 95, SEQ ID NO: 96, and SEQ ID NO: 97, respectively, and a VL region comprising CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO: 100, SEQ ID NO: 101, and SEQ ID NO: 102, respectively.

2. The chimeric antigen receptor according to claim 1, wherein the signaling domain of CD3 zeta comprises the amino acid sequence set forth in SEQ ID NO: 10.

3. The chimeric antigen receptor according to claim 1 further comprising at least one costimulatory domain signaling region.

4. The chimeric antigen receptor according to claim 3, wherein the costimulatory domain signaling region is a signaling region of CD28, OX-40, 4-1BB/CD137, CD27, or ICOS.

5. The chimeric antigen receptor according to claim 4, wherein the costimulatory domain signaling region comprises SEQ ID NO: 8.

6. The chimeric antigen receptor according to claim 5, wherein the chimeric antigen receptor comprises SEQ ID NO: 2.

7. The chimeric antigen receptor according to claim 1, wherein the transmembrane domain is a CD28 or a CD8 transmembrane domain.

8. The chimeric antigen receptor according to claim 7, wherein the transmembrane domain is a CD28 transmembrane domain that comprises SEQ ID NO: 6.

9. The chimeric antigen receptor according to claim 1, wherein the chimeric antigen receptor comprises (a) an extracellular and transmembrane domain of CD28 as set forth in SEQ ID NO: 2 or (b) an extracellular and transmembrane domain of CD8 as set forth in SEQ ID NO: 14.

10. The chimeric antigen receptor according to claim 1, wherein the linker of the scFv comprises at least one of SEQ ID NO: 130 or SEQ ID NO: 132.

11. The chimeric antigen receptor of claim 1, wherein the scFv comprises:

(a) a VH region comprising the amino acid sequence of SEQ ID NO: 16 and a VL region comprising the amino acid sequence of SEQ ID NO: 21;

(b) a VH region comprising the amino acid sequence of SEQ ID NO: 50 and a VL region comprising the amino acid sequence of SEQ ID NO: 55;

(c) a VH region comprising the amino acid sequence of SEQ ID NO: 72 and a VL region comprising the amino acid sequence of SEQ ID NO: 77; or

(d) a VH region comprising the amino acid sequence of SEQ ID NO: 94 and a VL region comprising the amino acid sequence of SEQ ID NO: 99.

12. A chimeric antigen receptor that binds to C-type lectin-like-1 ("CLL-1"), wherein the chimeric antigen receptor is a polypeptide comprising a single chain Fv ("scFv") that binds CLL-1, a transmembrane domain, and an intracellular activating domain that is a signaling domain of CD3 zeta, and wherein the scFv comprises a heavy chain variable region (VH) and light chain variable region (VL) pair that is selected from the group consisting of:

(a) a VH region comprising the amino acid sequence of SEQ ID NO: 16 and a VL region comprising the amino acid sequence of SEQ ID NO: 21;

(b) a VH region comprising the amino acid sequence of SEQ ID NO: 50 and a VL region comprising the amino acid sequence of SEQ ID NO: 55;

(c) a VH region comprising the amino acid sequence of SEQ ID NO: 72 and a VL region comprising the amino acid sequence of SEQ ID NO: 77; and

(d) a VH region comprising the amino acid sequence of SEQ ID NO: 94 and a VL region comprising the amino acid sequence of SEQ ID NO: 99.

13. An isolated polynucleotide encoding a chimeric antigen receptor of claim 1 or 12.

14. A vector comprising a polynucleotide of claim 13.

15. The vector according to claim 14 which is a retroviral vector, a DNA vector, a plasmid, a RNA vector, an adenoviral vector, an adenovirus associated vector, or a lentiviral vector.

16. An immune cell comprising the vector of claim 14.

17. The immune cell according to claim 16, wherein the immune cell is a T cell, tumor infiltrating lymphocyte (TIL), NK cell, or NK-T cell.

18. The immune cell according to claim 17, wherein the cell is an autologous T cell.

19. The immune cell according to claim 17, wherein the cell is an allogeneic T cell.

20. A pharmaceutical composition comprising the T cell of claim 18 and a pharmaceutically acceptable carrier.

21. A chimeric antigen receptor polypeptide comprising an amino acid sequence set forth in:

SEQ ID NO: 28; SEQ ID NO: 32; SEQ ID NO: 36; SEQ ID NO: 40; SEQ ID NO: 44; SEQ ID NO: 48; SEQ ID NO: 62; SEQ ID NO: 66; SEQ ID NO: 70; SEQ ID NO: 84; SEQ ID NO: 88; SEQ ID NO: 92; SEQ ID NO: 106; SEQ ID NO: 110; SEQ ID NO: 114; SEQ ID NO: 118; SEQ ID NO: 122; and SEQ ID NO: 126.

22. An isolated polynucleotide comprising a nucleic acid sequence as set forth in:

SEQ ID NO: 27; SEQ ID NO: 31; SEQ ID NO: 35; SEQ ID NO: 39; SEQ ID NO: 43; SEQ ID NO: 47; SEQ ID NO: 61; SEQ ID NO: 65; SEQ ID NO: 69; SEQ ID NO: 83; SEQ ID NO: 87; SEQ ID NO: 91; SEQ ID NO: 105; SEQ ID NO: 109 SEQ ID NO: 113; SEQ ID NO: 117; SEQ ID NO: 121; or SEQ ID NO: 125.

23. A vector comprising a polynucleotide of claim 22.

24. The vector according to claim 23 which is a retroviral vector, a DNA vector, a plasmid, a RNA vector, an adenoviral vector, an adenovirus associated vector, or a lentiviral vector.

25. An immune cell comprising the vector of claim 23.

26. The immune cell according to claim 25, wherein the immune cell is a T cell, a tumor infiltrating lymphocyte (TIL), an NK cell, or an NK-T cell.

27. The immune cell according to claim 26, wherein the cell is an autologous T cell.

28. The immune cell according to claim 26, wherein the cell is an allogeneic T cell.

29. A pharmaceutical composition comprising T cells according to claim 27 or 28 and a pharmaceutically acceptable carrier.

30. An antigen-binding molecule that comprises a heavy chain variable region (VH) and a light chain variable region (VL) pair that binds C-type lectin-like-1 ("CLL-1"), wherein the VH and VL pair is selected from the group consisting of:

(a) a VH region comprising complementarity determining regions ("CDRs") 1, 2, and 3 with amino acid sequences SEQ ID NO: 17, SEQ ID NO: 18, and SEQ ID NO: 19, respectively, and a VL region comprising CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO: 22, SEQ ID NO: 23, and SEQ ID NO: 24, respectively;

(b) a VH region comprising CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO: 51, SEQ ID NO: 52, and SEQ ID NO: 53, respectively, and a VL region comprising CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO: 56, SEQ ID NO: 57, and SEQ ID NO: 58, respectively;

(c) a VH region comprising CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO: 73, SEQ ID NO: 74, and SEQ ID NO: 75, respectively, and a VL region comprising CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO: 78, SEQ ID NO: 79, and SEQ ID NO: 80, respectively; and

(d) a VH region comprising CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO: 95, SEQ ID NO: 96, and SEQ ID NO: 97, respectively, and a VL region comprising

CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO: 100, SEQ ID NO: 101, and SEQ ID NO: 102, respectively.

31. The antigen-binding molecule according to claim 30, wherein the VH and VL pair is selected from the group consisting of:

(a) a VH region comprising the amino acid sequence of SEQ ID NO: 16 and a VL region comprising the amino acid sequence of SEQ ID NO: 21;

(b) a VH region comprising the amino acid sequence of SEQ ID NO: 50 and a VL region comprising the amino acid sequence of SEQ ID NO: 55;

(c) a VH region comprising the amino acid sequence of SEQ ID NO: 72 and a VL region comprising the amino acid sequence of SEQ ID NO: 77; and

(d) a VH region comprising the amino acid sequence of SEQ ID NO: 94 and a VL region comprising the amino acid sequence of SEQ ID NO: 99.

32. The antigen binding molecule according to claim 30, wherein the VH and VL pair comprises a VH region comprising complementarity determining regions ("CDRs") 1, 2, and 3 with amino acid sequences SEQ ID NO: 17, SEQ ID NO: 18, and SEQ ID NO: 19, respectively, and a VL region comprising CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO: 22, SEQ ID NO: 23, and SEQ ID NO: 24, respectively.

33. The antigen binding molecule according to claim 30, wherein the VH and VL pair comprises a VH region comprising CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO: 51, SEQ ID NO: 52, and SEQ ID NO: 53, respectively, and a VL region comprising CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO: 56, SEQ ID NO: 57, and SEQ ID NO: 58, respectively.

34. The antigen binding molecule according to claim 30, wherein the VH and VL pair comprises a VH region comprising CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO: 73, SEQ ID NO: 74, and SEQ ID NO: 75, respectively, and a VL region comprising CDRs 1,

2, and 3 with amino acid sequences SEQ ID NO: 78, SEQ ID NO: 79, and SEQ ID NO: 80, respectively.

35. The antigen binding molecule according to claim 30, wherein the VH and VL pair comprises a VH region comprising CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO: 95, SEQ ID NO: 96, and SEQ ID NO: 97, respectively, and a VL region comprising CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO: 100, SEQ ID NO: 101, and SEQ ID NO: 102, respectively.

36. The antigen binding molecule according to claim 30, wherein the antigen binding molecule is an antibody, or an immunologically functional fragment thereof.

37. The antigen binding molecule according to claim 36, wherein the antigen binding molecule is a scFv fragment, a peptibody, an Fab fragment, a monoclonal antibody, a bispecific antibody, a minibody, a domain antibody, a synthetic antibody, a chimeric antibody, a humanized antibody, a human antibody, or an antibody fusion protein.

38. An isolated polynucleotide encoding an antigen binding molecule, or an immunologically functional fragment thereof, according to claim 30.

39. A vector comprising a polynucleotide of claim 38.

40. The vector according to claim 39 which is a retroviral vector, a DNA vector, a plasmid, a RNA vector, an adenoviral vector, an adenovirus associated vector, or a lentiviral vector.

41. A cell comprising the vector of claim 39.

42. The cell according to claim 41, wherein the cell is a T cell, a malignancy infiltrating lymphocyte (TIL), an NK cell, or an NK-T cell.

43. A pharmaceutical composition comprising an antigen binding molecule, or an immunologically functional fragment thereof, of claim 30, or the cell of claim 41, and a pharmaceutically acceptable carrier.

44. A pharmaceutical composition comprising the T cell of claim 19 and a pharmaceutically acceptable carrier.