

[0009a] In one aspect, the present disclosure refers to a chimeric antigen receptor comprising an antigen binding molecule that specifically binds to DLL3, a costimulatory domain, and an activating domain that is a signaling domain of CD3 zeta, wherein the antigen binding molecule comprises: (i) a) a variable heavy chain CDR1 comprising an amino acid sequence differing by not more than 3, 2, 1, or 0 amino acid residues from that of SEQ ID NO:42; a variable heavy chain CDR2 comprising an amino acid sequence differing by not more than 3, 2, 1, or 0 amino acid residues from that of SEQ ID NO:43; a variable heavy chain CDR3 comprising an amino acid sequence differing by not more than 3, 2, 1, or 0 amino acid residues from that of SEQ ID NO:44; a variable light chain CDR1 comprising an amino acid sequence differing by not more than 3, 2, 1, or 0 amino acid residues from that of SEQ ID NO:47; a variable light chain CDR2 comprising an amino acid sequence differing by not more than 3, 2, 1, or 0 amino acid residues from that of SEQ ID NO:48; a variable light chain CDR3 comprising an amino acid sequence differing by not more than 3, 2, 1, or 0 amino acid residues from that of SEQ ID:49; or b) a variable heavy chain CDR1 comprising an amino acid sequence of a variable heavy chain CDR1 sequence of clone 1H2.1; a variable heavy chain CDR2 comprising an amino acid sequence of a variable heavy chain CDR2 sequence of clone 1H2.1; a variable heavy chain CDR3 comprising an amino acid sequence of a variable heavy chain CDR3 sequence of clone 1H2.1; a variable light chain CDR1 comprising an amino acid sequence of a variable light chain CDR1 sequence of clone 1H2.1; a variable light chain CDR2 comprising an amino acid sequence of a variable light chain CDR2 sequence of clone 1H2.1; a variable light chain CDR3 comprising an amino acid sequence of a variable light chain CDR3 sequence of clone 1H2.1; or c) a variable heavy chain sequence differing by not more than 10, 9, 8, 7, 6, 5, 4, 3, 2, 1, or 0 residues from the variable heavy chain sequence of clone 1H2.1; and a variable light chain sequence differing by not more than 10, 9, 8, 7, 6, 5, 4, 3, 2, 1, or 0 residues from the variable light chain sequence of clone 1H2.1; and (ii) the costimulatory domain is a CD28 costimulatory domain comprising a sequence that differs at no more than 10, 9, 8, 7, 6, 5, 4, 3, 2, 1, or 0 amino acid residues from the sequence of SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 4 in combination with SEQ ID NO: 6 or SEQ ID NO: 8.

[0009b] In another aspect, the present disclosure refers to a polynucleotide encoding the chimeric antigen receptor as described herein. In another aspect, the present disclosure refers to a vector comprising the polynucleotide as described herein. In yet another aspect, the present disclosure refers to an immune cell comprising the vector as described herein. In another aspect, the present disclosure refers to a pharmaceutical composition comprising an

immune cell as described herein.

[0009c] In a further aspect, the present disclosure refers to an isolated polypeptide comprising the amino acid sequence of SEQ ID NO: 18 or 20. In a further aspect, the present disclosure refers to a vector encoding the polypeptide as described herein. In a further aspect, the present disclosure refers to an immune cell comprising the polypeptide as described herein. In a further aspect, the present disclosure refers to an isolated polynucleotide encoding a chimeric antigen receptor (CAR) or T cell receptor (TCR) comprising an antigen binding molecule that specifically binds to DLL3, wherein the antigen binding molecule has a sequence comprising SEQ ID NO: 17 or 19.

[0009d] In a further aspect, the present disclosure refers to the polynucleotide, the polypeptide, the chimeric antigen receptor, the cell, or the pharmaceutical composition as disclosed herein for use in treating a disease or a disorder.

[0009e] In a still further aspect, the present disclosure refers to the use of the polynucleotide as described herein, the polypeptide as described herein, the chimeric antigen receptor as described herein, the cell as described herein, or the pharmaceutical composition as described herein in the manufacture of a medicament for treating a disease or disorder in a subject in need thereof, wherein the disease or disorder is cancer.

[0010] In some examples, the disclosure relates to a chimeric antigen receptor comprising an antigen binding molecule that specifically binds to DLL3, wherein the antigen binding molecule comprises at least one of: (a) a variable heavy chain CDR1 comprising an amino acid sequence differing from that of SEQ ID NO:42 or SEQ ID NO:52 or SEQ ID NO:62 by not more than 3, 2, 1, or 0 amino acid residues; (b) a variable heavy chain CDR2 comprising an amino acid sequence differing from that of SEQ ID NO:43 or SEQ ID NO:53 or SEQ ID NO:63 by not more than 3, 2, 1, or 0 amino acid residues; (c) a variable heavy chain CDR3 comprising an amino acid sequence differing from that of 44 or SEQ ID NO:54 or SEQ ID NO:64 by not more than 3, 2, 1, or 0 amino acid residues; (d) a variable light chain CDR1 comprising an amino acid sequence differing from that of SEQ ID NO:47 or SEQ ID NO:57 or SEQ ID NO:67 by not more than 3, 2, 1, or 0 amino acid residues; (e) a variable light chain CDR2 comprising an amino acid sequence differing from that of SEQ ID NO:48 or

What is Claimed

1. A chimeric antigen receptor comprising an antigen binding molecule that specifically binds to DLL3, a costimulatory domain, and an activating domain that is a signaling domain of CD3 zeta, wherein the antigen binding molecule comprises:
 - (i)
 - a) a variable heavy chain CDR1 comprising an amino acid sequence differing by not more than 3, 2, 1, or 0 amino acid residues from that of SEQ ID NO:42; a variable heavy chain CDR2 comprising an amino acid sequence differing by not more than 3, 2, 1, or 0 amino acid residues from that of SEQ ID NO:43; a variable heavy chain CDR3 comprising an amino acid sequence differing by not more than 3, 2, 1, or 0 amino acid residues from that of SEQ ID NO:44; a variable light chain CDR1 comprising an amino acid sequence differing by not more than 3, 2, 1, or 0 amino acid residues from that of SEQ ID NO:47; a variable light chain CDR2 comprising an amino acid sequence differing by not more than 3, 2, 1, or 0 amino acid residues from that of SEQ ID NO:48; and a variable light chain CDR3 comprising an amino acid sequence differing by not more than 3, 2, 1, or 0 amino acid residues from that of SEQ ID:49; or
 - b) a variable heavy chain CDR1 comprising an amino acid sequence of a variable heavy chain CDR1 sequence of clone 1H2.1; a variable heavy chain CDR2 comprising an amino acid sequence of a variable heavy chain CDR2 sequence of clone 1H2.1; a variable heavy chain CDR3 comprising an amino acid sequence of a variable heavy chain CDR3 sequence of clone 1H2.1; a variable light chain CDR1 comprising an amino acid sequence of a variable light chain CDR1 sequence of clone 1H2.1; a variable light chain CDR2 comprising an amino acid sequence of a variable light chain CDR2 sequence of clone 1H2.1; and a variable light chain CDR3 comprising an amino acid sequence of a variable light chain CDR3 sequence of clone 1H2.1; or
 - c) a variable heavy chain sequence differing by not more than 10, 9, 8, 7, 6, 5, 4, 3, 2, 1, or 0 residues from the variable heavy chain sequence of clone 1H2.1; and

- a variable light chain sequence differing by not more than 10, 9, 8, 7, 6, 5, 4, 3, 2, 1, or 0 residues from the variable light chain sequence of clone 1H2.1; and
- (ii) the costimulatory domain is a CD28 costimulatory domain comprising a sequence that differs at no more than 10, 9, 8, 7, 6, 5, 4, 3, 2, 1, or 0 amino acid residues from the sequence of SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 4 in combination with SEQ ID NO: 6 or SEQ ID NO: 8.
2. The chimeric antigen receptor according to claim 1 wherein the costimulatory domain further comprises 4-1BB.
 3. The chimeric antigen receptor according to claim 1 wherein the CD3 zeta comprises a sequence that differs at no more than 10, 9, 8, 7, 6, 5, 4, 3, 2, 1, or 0 amino acid residues from the sequence of SEQ ID NO:10.
 4. A polynucleotide encoding the chimeric antigen receptor of claim 1.
 5. A vector comprising the polynucleotide of claim 4.
 6. The vector according to claim 5 which is a retroviral vector, a DNA vector, a plasmid, a RNA vector, an adenoviral vector, an adenovirus associated vector, a lentiviral vector, or any combination thereof.
 7. An immune cell comprising the vector of claim 5.
 8. The immune cell according to claim 7, wherein the immune cell is a T cell, tumor infiltrating lymphocyte (TIL), NK cell, TCR-expressing cell, dendritic cell, or NK-T cell.
 9. The immune cell according to claim 8, wherein the cell is an autologous T cell.
 10. The immune cell according to claim 8, wherein the cell is an allogeneic T cell.
 11. The immune cell of claim 7, wherein the vector is to be isolated from a patient's body or is grown from a sample taken from a patient's body.
 12. The immune cell of claim 7, wherein the vector is to be isolated from a donor's body or is grown from a sample taken from a patient's body.
 13. A pharmaceutical composition comprising an immune cell of claim 7.
 14. An isolated polypeptide comprising the amino acid sequence of SEQ ID NO:18 or 20.
 15. A vector encoding the polypeptide of claim 14.

16. An immune cell comprising the polypeptide 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, TCR-expressing cell, dendritic cell, or NK-T cell.
18. The T cell of claim 17 that is an autologous T cell.
19. The T cell of claim 17 that is an allogeneic T cell.
20. An isolated polynucleotide encoding a chimeric antigen receptor (CAR) or T cell receptor (TCR) comprising an antigen binding molecule that specifically binds to DLL3, wherein the antigen binding molecule has a sequence comprising SEQ ID NO:17 or 19.
21. The polynucleotide according to claim 4 or 20, the polypeptide according to claim 14, the chimeric antigen receptor according to claim 1, the cell according to claim 7 or 16, or the pharmaceutical composition according to claim 13 for use in treating a disease or a disorder.
22. Use of the polynucleotide according to claim 4 or 20, the polypeptide according to claim 14, the chimeric antigen receptor according to claim 1, the cell according to claim 7 or 16, or the pharmaceutical composition according to claim 13 in the manufacture of a medicament for treating a disease or disorder in a subject in need thereof,
23. wherein the disease or disorder is cancer. The use according to claim 22 wherein the cancer is adrenal, liver, kidney, bladder, breast, gastric, ovarian, cervical, uterine, esophageal, colorectal, prostate (e.g., prostate adenocarcinoma), pancreatic, lung (both small cell and non- small cell), thyroid, carcinomas, sarcomas, glioblastomas, head and neck tumors, large cell neuroendocrine carcinoma (LCNEC), medullary thyroid cancer, glioblastoma, neuroendocrine prostate cancer, (NEPC), high-grade gastroenteropancreatic cancer (GEP) and malignant melanoma.
24. The use according to claim 23, wherein the cancer is small cell lung cancer.
25. The lentiviral vector according to claim 6, wherein the lentiviral vector is a pGAR vector.