

What is Claimed

1. A chimeric antigen receptor comprising an antigen binding molecule that specifically binds to DLL3, wherein the antigen binding molecule comprises:
 - 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 or SEQ ID NO:52 or SEQ ID NO:62; or
 - b) 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 or SEQ ID NO:53 or SEQ ID NO:63; or
 - c) 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 or SEQ ID NO:54 or SEQ ID NO:64; or
 - d) 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 or SEQ ID NO:57 or SEQ ID NO:67; or
 - e) 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 or SEQ ID NO:58 or SEQ ID NO:68; or
 - f) 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 NO:49 or SEQ ID NO:59 or SEQ ID NO:69; or
 - g) a variable heavy chain CDR1 comprising an amino acid sequence of a variable heavy chain CDR1 sequence of clone 1H2.1, clone 8D2, or clone 6B2; or
 - h) a variable heavy chain CDR2 comprising an amino acid sequence of a variable heavy chain CDR2 sequence of clone 1H2.1, clone 8D2, or clone 6B2; or
 - i) a variable heavy chain CDR3 comprising an amino acid sequence of a variable heavy chain CDR3 sequence of clone 1H2.1, clone 8D2, or clone 6B2; or
 - j) a variable light chain CDR1 comprising an amino acid sequence of a variable light chain CDR1 sequence of clone 1H2.1, clone 8D2, or clone 6B2; or

- k) a variable light chain CDR2 comprising an amino acid sequence of a variable light chain CDR2 sequence of clone 1H2.1, clone 8D2, or clone 6B2; or
 - l) a variable light chain CDR3 comprising an amino acid sequence of a variable light chain CDR3 sequence of clone 1H2.1, clone 8D2, or clone 6B2; or
 - m) 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, clone 8D2, or clone 6B2; or
 - n) 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, clone 8D2, or clone 6B2.
2. The chimeric antigen receptor according to claim 1 further comprising at least one costimulatory domain.
 3. The chimeric antigen receptor according to claim 1 further comprising at least one activating domain.
 4. The chimeric antigen receptor according to claim 2 wherein the costimulatory domain is a signaling region of CD28, CD8, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, programmed death-1 (PD-1), inducible T cell costimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1 (CD11a/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class I molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CD28, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG

(CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, or any combination thereof.

5. The chimeric antigen receptor according to claim 4 wherein the costimulatory domain comprises CD28.
6. The chimeric antigen receptor according to claim 5 wherein the CD28 costimulatory domain 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:2, SEQ ID NO:4, SEQ ID NO:6, or SEQ ID NO:8.
7. The chimeric antigen receptor according to claim 4 wherein the costimulatory domain comprises CD8.
8. The chimeric antigen receptor according to claim 7 wherein the CD8 costimulatory domain 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:14.
9. The chimeric antigen receptor according to claim 4 wherein the costimulatory domain comprises 4-1BB.
10. The chimeric antigen receptor according to claim 9 wherein the CD8 costimulatory domain 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:16.
11. The chimeric antigen receptor according to claim 3 wherein the activating domain comprises CD3.
12. The chimeric antigen receptor according to claim 7 wherein the CD3 comprises CD3 zeta.
13. The chimeric antigen receptor according to claim 8 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.
14. The chimeric antigen receptor according to claim 1 wherein the costimulatory domain 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:2 and the activating domain 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.
15. A polynucleotide encoding the chimeric antigen receptor of claim 1.

16. A vector comprising the polynucleotide of claim 15.
17. The vector according to claim 16 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.
18. An immune cell comprising the vector of claim 16.
19. The immune cell according to claim 18, wherein the immune cell is a T cell, tumor infiltrating lymphocyte (TIL), NK cell, TCR-expressing cell, dendritic cell, or NK-T cell.
20. The immune cell according to claim 19, wherein the cell is an autologous T cell.
21. The immune cell according to claim 19, wherein the cell is an allogeneic T cell.
22. The immune cell of claim 18, wherein the vector is introduced into a cell that is isolated from a patient's body or that is grown from a sample taken from a patient's body.
23. The immune cell of claim 18, wherein the vector is introduced into a cell that is isolated from a donor's body or that is grown from a sample taken from a patient's body.
24. A pharmaceutical composition comprising an immune cell of claim 18.
25. A chimeric antigen receptor comprising:
 - (a) a VH region of clone 1H2.1 and a VL region of clone 1H2.1;
 - (b) a VH region of clone 8D2 and a VL region of clone 8D2; or
 - (c) a VH region of clone 6B2 and a VL region of clone 6B2;wherein the VH and VL region is linked by at least one linker.
26. The chimeric antigen receptor according to claim 25, wherein the linker comprises the scFv G4S linker or the scFv Whitlow linker.
27. The chimeric antigen receptor according to claim 25, further comprising a costimulatory domain.
28. The chimeric antigen receptor according to claim 25, further comprising an activating domain.
29. The chimeric antigen receptor according to claim 27 wherein the costimulatory domain is a signaling region of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, programmed

death-1 (PD-1), inducible T cell costimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1 (CD11a/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class I molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CD28, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, or any combination thereof.

30. An immune cell comprising the chimeric antigen receptor of claim 25.
31. The immune cell according to claim 30, wherein the immune cell is a T cell, tumor infiltrating lymphocyte (TIL), NK cell, TCR-expressing cell, dendritic cell, or NK-T cell.
32. The T cell of claim 31 that is an autologous T cell.
33. The T cell of claim 32 that is an allogeneic T cell.
34. A pharmaceutical composition comprising the cell of claim 30.
35. An isolated polynucleotide comprising a sequence encoding the chimeric antigen receptor of claim 25.
36. A vector comprising the polynucleotide according to claim 35.
37. An immune cell comprising the vector of claim 36.
38. The immune cell according to claim 37, wherein the immune cell is a T cell, tumor infiltrating lymphocyte (TIL), NK cell, TCR-expressing cell, dendritic cell, or NK-T cell.

39. The T cell of claim 38 that is an autologous T cell.
40. The T cell of claim 38 that is an allogeneic T cell.
41. An isolated polypeptide comprising the amino acid sequence of construct 1H2.1 CD28T, construct 1H2.1 4-1BB, construct 8D2 CD28T, construct 8D2 4-1BB, construct 6B2 CD28T, or construct 6B2 4-1BB.
42. A vector encoding the polypeptide of claim 41.
43. An immune cell comprising the polypeptide of claim 41.
44. The immune cell according to claim 43, wherein the immune cell is a T cell, tumor infiltrating lymphocyte (TIL), NK cell, TCR-expressing cell, dendritic cell, or NK-T cell.
45. The T cell of claim 44 that is an autologous T cell.
46. The T cell of claim 44 that is an allogeneic T cell.
47. 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 comprises a variable heavy chain CDR3 comprising the amino acid sequence of a variable heavy chain CDR3 of clone 1H2.1, clone 8D2, or clone 6B2.
48. The polynucleotide according to claim 47 further comprising an activating domain.
49. The polynucleotide according to claim 48 wherein the activating domain is CD3.
50. The polynucleotide according to claim 49 wherein the CD3 is CD3 zeta.
51. The polynucleotide according to claim 50 wherein the CD3 zeta comprises the amino acid sequence set forth in SEQ ID NO:9.
52. The polynucleotide according to claim 47 further comprising a costimulatory domain.
53. The polynucleotide according to claim 52 wherein the costimulatory domain is a signaling region of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, programmed death-1 (PD-1), inducible T cell costimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1 (CD11a/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class I molecule, TNF receptor

proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, or any combination thereof.

54. The polynucleotide according to claim 53 wherein the CD28 costimulatory domain encodes the amino acid sequence set forth in SEQ ID NO 2.
55. A vector comprising the polynucleotide of claim 47.
56. An immune cell comprising the vector of claim 55.
57. The immune cell of claim 56, wherein the immune cell is a T cell, tumor infiltrating lymphocyte (TIL), NK cell, TCR-expressing cell, dendritic cell, or NK-T cell.
58. The T cell of claim 57 that is an autologous T cell.
59. The T cell of claim 57 that is an allogeneic T cell.
60. An isolated polynucleotide encoding a chimeric antigen receptor (CAR) or T cell receptor (TCR), said CAR or TCR comprising an antigen binding molecule that specifically binds to DLL3, wherein the antigen binding molecule comprises:
 - a. 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, clone 8D2, or clone 6B2; and/or
 - b. 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, clone 8D2, or clone 6B2.

61. The polynucleotide according to claim 60 further comprising an activating domain.
62. The polynucleotide according to claim 61 wherein the activating domain is CD3.
63. The polynucleotide according to claim 62 wherein the CD3 is CD3 zeta.
64. The polynucleotide according to claim 63 wherein the CD3 zeta comprises the amino acid sequence set forth in SEQ ID NO:9.
65. The polynucleotide according to claim 60 further comprising a costimulatory domain.
66. The polynucleotide according to claim 65 wherein the costimulatory domain is a signaling region of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, programmed death-1 (PD-1), inducible T cell costimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1 (CD11a/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class I molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, or any combination thereof.
67. The polynucleotide according to claim 66 wherein the CD28 costimulatory domain comprises the nucleotide sequence set forth in SEQ ID NO:3.
68. The polynucleotide according to claim 67 wherein the CD28 costimulatory domain comprises the nucleotide sequence set forth in SEQ ID NO:1.
69. 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 heavy chain comprises CDR1 (SEQ ID NO:42), CDR2 (SEQ ID NO:43), and CDR3 (SEQ ID NO:44) and the antigen binding molecule light chain comprises CDR1 (SEQ ID NO:47), CDR2 (SEQ ID NO:48), and CDR3 (SEQ ID NO:49).

70. 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 heavy chain comprises CDR1 (SEQ ID NO:52), CDR2 (SEQ ID NO:53), and CDR3 (SEQ ID NO:54) and the antigen binding molecule light chain comprises CDR1 (SEQ ID NO:57), CDR2 (SEQ ID NO:58), and CDR3 (SEQ ID NO:59).
71. 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 heavy chain comprises CDR1 (SEQ ID NO:62), CDR2 (SEQ ID NO:63), and CDR3 (SEQ ID NO:64) and the antigen binding molecule light chain comprises CDR1 (SEQ ID NO:67), CDR2 (SEQ ID NO:68), and CDR3 (SEQ ID NO:69).
72. A method of treating a disease or disorder in a subject in need thereof comprising administering to the subject the polynucleotide according to claim 15, 47, 60, 69, 70 or 71.
73. A method of treating a disease or disorder in a subject in need thereof comprising administering to the subject the polypeptide according to claim 41.
74. A method of treating a disease or disorder in a subject in need thereof comprising administering to the subject the chimeric antigen receptor according to claim 1 or 25.
75. A method of treating a disease or disorder in a subject in need thereof comprising administering to the subject the cell according to claim 18, 30, 37, 43, or 56.
76. A method of treating a disease or disorder in a subject in need thereof comprising administering to the subject the pharmaceutical composition according to claim 24 or 34.
77. The method according to any of claims 72, 73, 74, 75, or 76 wherein the disease or disorder is cancer.
78. The method according to claim 77 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.

79. The method according to claim 77, wherein the cancer is small cell lung cancer.

80. The lentiviral vector according to claim 17, wherein the lentiviral vector is a pGAR vector.