

What is Claimed

1. A chimeric antigen receptor comprising an antigen binding molecule that specifically binds to FLT3, 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: 17; 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:18 or SEQ ID NO:26; 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 NOs SEQ ID NO: 19 or SEQ ID NO:27; 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:22 or SEQ ID NO:30; 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:23 or 31; 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:24 or SEQ ID NO:32; or
 - g) a variable heavy chain CDR1 comprising an amino acid sequence of a variable heavy chain CDR1 sequence of clone 10E3, clone 2E7, clone 8B5, clone 4E9, or clone 11F11; or
 - h) a variable heavy chain CDR2 comprising an amino acid sequence of a variable heavy chain CDR2 sequence of clone 10E3, clone 2E7, clone 8B5, clone 4E9, or clone 11F11; or
 - i) a variable heavy chain CDR3 comprising an amino acid sequence of a variable heavy chain CDR3 sequence of clone 10E3, clone 2E7, clone 8B5, clone 4E9, or clone 11F11; or
 - j) a variable light chain CDR1 comprising an amino acid sequence of a variable light chain CDR1 sequence of clone 10E3, clone 2E7, clone 8B5, clone 4E9, or clone 11F11; or

- k) a variable light chain CDR2 comprising an amino acid sequence of a variable light chain CDR2 sequence of clone 10E3, clone 2E7, clone 8B5, clone 4E9, or clone 11F11;
or
 - l) a variable light chain CDR3 comprising an amino acid sequence of a variable light chain CDR3 sequence of clone 10E3, clone 2E7, clone 8B5, clone 4E9, or clone 11F11;
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 10E3, clone 2E7, clone 8B5, clone 4E9, or clone 11F11; 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 10E3, clone 2E7, clone 8B5, clone 4E9, or clone 11F11.
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, 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, 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.

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 3 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.
8. The chimeric antigen receptor according to claim 3 wherein the activating domain comprises CD3.
9. The chimeric antigen receptor according to claim 7 wherein the CD3 comprises CD3 zeta.
10. 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.
11. 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.
12. A polynucleotide encoding the chimeric antigen receptor of claim 1.
13. A vector comprising the polynucleotide of claim 12.
14. The vector according to claim 13 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.
15. An immune cell comprising the vector of claim 13.

16. The immune cell according to claim 15, wherein the immune cell is a T cell, tumor infiltrating lymphocyte (TIL), NK cell, TCR-expressing cell, dendritic cell, or NK-T cell.
17. The immune cell according to claim 16, wherein the cell is an autologous T cell.
18. The immune cell according to claim 16, wherein the cell is an allogeneic T cell.
19. The immune cell of claim 15, 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.
20. The immune cell of claim 15, 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.
21. A pharmaceutical composition comprising an immune cell of claim 15.
22. A chimeric antigen receptor comprising:
 - (a) a VH region of clone 10E3 and a VL region of clone 10E3;
 - (b) a VH region of clone 2E7 and a VL region of clone 2E7;
 - (c) a VH region of clone 8B5 and a VL region of clone 8B5;
 - (d) a VH region of clone 4E9 and a VL region of clone 4E9; or
 - (e) a VH region of clone 11F11 and a VL region of clone 11F11,wherein the VH and VL region is linked by at least one linker.
23. The chimeric antigen receptor according to claim 22, wherein the linker comprises the scFv G4S linker or the scFv Whitlow linker.
24. The chimeric antigen receptor according to claim 22, further comprising a costimulatory domain.
25. The chimeric antigen receptor according to claim 22, further comprising an activating domain.
26. The chimeric antigen receptor according to claim 24 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.

27. An immune cell comprising the chimeric antigen receptor of claim 22.
28. The immune cell according to claim 27, wherein the immune cell is a T cell, tumor infiltrating lymphocyte (TIL), NK cell, TCR-expressing cell, dendritic cell, or NK-T cell.
29. The T cell of claim 28 that is an autologous T cell.
30. The T cell of claim 29 that is an allogeneic T cell.
31. A pharmaceutical composition comprising the cell of claim 27.
32. An isolated polynucleotide comprising a sequence encoding the chimeric antigen receptor of claim 22.
33. A vector comprising the polynucleotide according to claim 32.
34. An immune cell comprising the vector of claim 33.
35. The immune cell according to claim 34, wherein the immune cell is a T cell, tumor infiltrating lymphocyte (TIL), NK cell, TCR-expressing cell, dendritic cell, or NK-T cell.
36. The T cell of claim 35 that is an autologous T cell.
37. The T cell of claim 35 that is an allogeneic T cell.
38. An isolated polypeptide comprising the amino acid sequence of construct 10E3 CD28, construct 10E3 CD28T, construct 10E3 CD8, construct 2E7 CD28, construct 2E7 CD28T, construct 2E7 CD8, construct 8B5 CD28, construct 8B5 CD28T, construct 8B5 CD8, construct 4E9 CD28, construct 4E9 CD28T, construct 4E9 CD8, construct 11F11 CD28, construct 11F11 CD28T, or construct 11F11 CD8.

39. A vector encoding the polypeptide of claim 38.
40. An immune cell comprising the polypeptide of claim 38.
41. The immune cell according to claim 40, wherein the immune cell is a T cell, tumor infiltrating lymphocyte (TIL), NK cell, TCR-expressing cell, dendritic cell, or NK-T cell.
42. The T cell of claim 41 that is an autologous T cell.
43. The T cell of claim 41 that is an allogeneic T cell.
44. An isolated polynucleotide encoding a chimeric antigen receptor (CAR) or T cell receptor (TCR) comprising an antigen binding molecule that specifically binds to FLT3, wherein the antigen binding molecule comprises a variable heavy chain CDR3 comprising the amino acid sequence of a variable heavy chain CDR3 of clone 10E3, clone 2E7, clone 8B5.
45. The polynucleotide according to claim 44 further comprising an activating domain.
46. The polynucleotide according to claim 45 wherein the activating domain is CD3.
47. The polynucleotide according to claim 46 wherein the CD3 is CD3 zeta.
48. The polynucleotide according to claim 47 wherein the CD3 zeta comprises the amino acid sequence set forth in SEQ ID NO: 9.
49. The polynucleotide according to claim 44 further comprising a costimulatory domain.
50. The polynucleotide according to claim 49 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, 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.

51. The polynucleotide according to claim 50 wherein the CD28 costimulatory domain encodes the amino acid sequence set forth in SEQ ID NO 2.
52. A vector comprising the polynucleotide of claim 41.
53. An immune cell comprising the vector of claim 49.
54. The immune cell of claim 50, wherein the immune cell is a T cell, tumor infiltrating lymphocyte (TIL), NK cell, TCR-expressing cell, dendritic cell, or NK-T cell.
55. The T cell of claim 51 that is an autologous T cell.
56. The T cell of claim 51 that is an allogeneic T cell.
57. 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 FLT3, 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 10E3, clone 2E7, clone 8B5, clone 4E9, or clone 11F11; 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 10E3, clone 2E7, clone 8B5, clone 4E9, or clone 11F11.
58. The polynucleotide according to claim 54 further comprising an activating domain.
59. The polynucleotide according to claim 55 wherein the activating domain is CD3.
60. The polynucleotide according to claim 56 wherein the CD3 is CD3 zeta.
61. The polynucleotide according to claim 60 wherein the CD3 zeta comprises the amino acid sequence set forth in SEQ ID NO: 9.
62. The polynucleotide according to claim 57 further comprising a costimulatory domain.

63. The polynucleotide according to claim 62 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.
64. The polynucleotide according to claim 63 wherein the CD28 costimulatory domain comprises the nucleotide sequence set forth in SEQ ID NO 3.
65. The polynucleotide according to claim 64 wherein the CD28 costimulatory domain comprises the nucleotide sequence set forth in SEQ ID NO 1.
66. An isolated polynucleotide encoding a chimeric antigen receptor (CAR) or T cell receptor (TCR) comprising an antigen binding molecule that specifically binds to FLT3, wherein the antigen binding molecule heavy chain comprises CDR1 (SEQ ID NO: 17), CDR2 (SEQ ID NO: 18), and CDR3 (SEQ ID NO: 19) and the antigen binding molecule light chain comprises CDR1 (SEQ ID NO: 22), CDR2 (SEQ ID NO: 23), and CDR3 (SEQ ID NO: 24).
67. An isolated polynucleotide encoding a chimeric antigen receptor (CAR) or T cell receptor (TCR) comprising an antigen binding molecule that specifically binds to FLT3, wherein the antigen binding molecule heavy chain comprises CDR1 (SEQ ID NO:17), CDR2 (SEQ ID NO:26), and CDR3 (SEQ ID NO:27) and the antigen binding molecule light chain comprises CDR1 (SEQ ID NO:30), CDR2 (SEQ ID NO:31), and CDR3 (SEQ ID NO:32).

68. A method of treating a disease or disorder in a subject in need thereof comprising administering to the subject the polynucleotide according to claim 12, 44, 57, 66, or 67.
69. A method of treating a disease or disorder in a subject in need thereof comprising administering to the subject the polypeptide according to claim 38.
70. 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 22.
71. A method of treating a disease or disorder in a subject in need thereof comprising administering to the subject the cell according to claim 15, 27, 34, 40, or 53.
72. 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 21 or 31.
73. The method according to any of claims 68, 69, 70, 71, or 72 wherein the disease or disorder is cancer.
74. The method according to claim 73 wherein the cancer is leukemia, lymphoma, or myeloma.
75. The method according to claim 73, wherein the cancer is AML.
76. The method according to any of claims 68, 69, 70, 71, or 72 wherein the disease or disorder is at least one of acute myeloid leukemia (AML), chronic myelogenous leukemia (CML), chronic myelomonocytic leukemia (CMML), juvenile myelomonocytic leukemia, atypical chronic myeloid leukemia, acute promyelocytic leukemia (APL), acute monoblastic leukemia, acute erythroid leukemia, acute megakaryoblastic leukemia, myelodysplastic syndrome (MDS), myeloproliferative disorder, myeloid neoplasm, myeloid sarcoma), and inflammatory/autoimmune disease.
77. The method according to claim 76 wherein the inflammatory/autoimmune disease is at least one of rheumatoid arthritis, psoriasis, allergies, asthma, Crohn's disease, IBD, IBS, fibromyalgia, mastocytosis, and Celiac disease.
78. The lentiviral vector according to claim 14, wherein the lentiviral vector is a pGAR vector.