

hypervariable or complementarity determining regions (CDRs). When the TCR engages with antigenic peptide and MHC (peptide/MHC), the T cell becomes activated, enabling it to attack and destroy the target cell.

[0017] However, current therapies have shown varying levels of effectiveness with undesired side effects. Therefore, a need exists to identify novel and improved therapies for treating FLT3 related diseases and disorders.

SUMMARY

[00017a] In one aspect, the disclosure relates to a chimeric antigen receptor comprising an antigen binding molecule that specifically binds to FLT3, a costimulatory domain, and an activating domain that is a signaling domain of CD3 zeta, wherein the antigen binding molecule comprises: a) a variable heavy chain region comprising complementary determining regions (“CDRs”) 1, 2, and 3 with amino acid sequences SEQ ID NO:43, SEQ ID NO:44, and SEQ ID NO:45, respectively, and a variable light chain region comprising CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO:48, SEQ ID NO:49, and SEQ ID NO:50, respectively; or b) a variable heavy chain region comprising complementary determining regions (“CDRs”) 1, 2, and 3 with amino acid sequences SEQ ID NO:53, SEQ ID NO:54, and SEQ ID NO:55, respectively, and a variable light chain region comprising CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO:58, SEQ ID NO:59, and SEQ ID NO:60, respectively; and the costimulatory domain is a CD28 costimulatory domain consisting of a sequence of SEQ ID NO: 2.

[00017b] In another aspect, the disclosure relates to a polynucleotide encoding the chimeric antigen receptor according to the disclosure.

[00017c] In another aspect, the disclosure relates to a vector comprising the polynucleotide according to the disclosure.

[00017d] In another aspect, the disclosure relates to an immune cell comprising the vector according to the disclosure.

[00017e] In another aspect, the disclosure relates to a pharmaceutical composition comprising an immune cell according to the disclosure.

[00017f] In another aspect, the disclosure relates to an isolated polypeptide comprising the amino acid sequence of SEQ ID NO:76 or SEQ ID NO:82.

[00017g] In another aspect, the disclosure relates to a vector encoding the polypeptide according to the disclosure.

[00017h] In another aspect, the disclosure relates to an immune cell comprising the polypeptide according to the disclosure.

[00017i] In another aspect, the disclosure relates to an isolated polynucleotide encoding a chimeric antigen receptor (CAR), said CAR comprising an antigen binding molecule that specifically binds to FLT3, wherein the antigen binding molecule comprises the polynucleotide sequence SEQ ID NO:75 or SEQ ID NO:81.

[00017j] In another aspect, the disclosure relates to a polynucleotide according to the disclosure, the polypeptide according to the disclosure, the chimeric antigen receptor according to the disclosure, the cell according to the disclosure, or the pharmaceutical composition according to the disclosure for use in treating a disease or a disorder.

[00017k] In another aspect, the disclosure relates to a use of the polynucleotide according to the disclosure, in the manufacture of a medicament for treating cancer wherein the cancer is selected from the group consisting of leukemia, lymphoma, myeloma, 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; wherein the inflammatory/autoimmune disease is selected from the group consisting of rheumatoid arthritis, psoriasis, allergies, asthma, Crohn's disease, irritable bowel disease (IBD), irritable bowel syndrome (IBS), fibromyalgia, mastocytosis, and Celiac disease.

[00017l] In another aspect, the disclosure relates to a use of the chimeric antigen receptor according to the disclosure in the manufacture of a medicament for treating cancer wherein the cancer is selected from the group consisting of leukemia, lymphoma, myeloma, 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; wherein the

inflammatory/autoimmune disease is selected from the group consisting of rheumatoid arthritis, psoriasis, allergies, asthma Crohn's disease, IBD, IBS, fibromyalgia, mastocytosis, and Celiac disease.

[00017m] In another aspect, the disclosure relates to a use of the cell according to the disclosure, in the manufacture of a medicament for treating cancer wherein the cancer is selected from the group consisting of leukemia, lymphoma, myeloma, 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; wherein the inflammatory/autoimmune disease is selected from the group consisting of rheumatoid arthritis, psoriasis, allergies, asthma, Crohn's disease, IBD, IBS, fibromyalgia, mastocytosis, and Celiac disease.

[00017n] In another aspect, the disclosure relates to a use of the pharmaceutical composition according to the disclosure in the manufacture of a medicament for treating cancer wherein the cancer is selected from the group consisting 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; wherein the inflammatory/autoimmune disease is selected from the group consisting of rheumatoid arthritis, psoriasis, allergies, asthma, Crohn's disease, IBD, IBS, fibromyalgia, mastocytosis, and Celiac disease.

[0018] The disclosure relates to engineered immune cells (such as CARs or TCRs), antigen binding molecules (including but not limited to, antibodies, scFvs, heavy and/or light chains, and CDRs of these antigen binding molecules) with specificity to FLT3.

[0019] The disclosure further relates to a novel CD28 sequence useful as costimulatory domains in these cells.

[0020] Chimeric antigen receptors of the disclosure typically comprise: (i) a FLT3 specific antigen binding molecule, (ii) one or more costimulatory domain, and (iii) one or more

activating domain. It will be appreciated that each domain may be heterogeneous, thus comprised of sequences derived from different protein chains.

[0021] In some examples, the disclosure relates to a chimeric antigen receptor comprising an antigen binding molecule that specifically binds to FLT3, 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: 17 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:18 or SEQ ID NO:26 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 SEQ ID NOs SEQ ID NO: 19 or SEQ ID NO:27 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:22 or SEQ ID NO:30 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:23 or 31 by not more than 3, 2, 1, or 0 amino acid residues; (f) a variable light chain CDR3 comprising an amino acid sequence differing from that of SEQ ID:24 or SEQ ID NO:32 by not more than 3, 2, 1, or 0 amino acid residues.

[0022] In other examples, the chimeric antigen receptor further comprises at least one costimulatory domain. In further examples, the chimeric antigen receptor further comprises at least one activating domain.

[0023] In certain examples the costimulatory domain is a signaling region of CD28, CD28T, 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 1 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, BAFTR, 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.

[0024] In some examples, the costimulatory domain is derived from 4-1BB. In other examples, the costimulatory domain is derived from OX40. See also Hombach *et al.*, *Oncoimmunology*. 2012 Jul. 1; 1(4): 458–466. In still other examples, the costimulatory domain comprises ICOS as described in Guedan *et al.*, August 14, 2014; *Blood*: 124 (7) and Shen *et al.*, *Journal of Hematology & Oncology* (2013) 6:33. In still other examples, the costimulatory domain comprises CD27 as described in Song *et al.*, *Oncoimmunology*. 2012 Jul. 1; 1(4): 547–549.

[0025] In certain examples, the CD28 costimulatory domain comprises SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 8. In additional examples, the CD8 costimulatory domain comprises SEQ ID NO: 14. In further examples, the activating domain comprises CD3, CD3 zeta, or CD3 zeta having the sequence set forth in SEQ ID NO: 10.

[0026] In other examples, the disclosure relates to a chimeric antigen receptor wherein the costimulatory domain comprises SEQ ID NO: 2 and the activating domain comprises SEQ ID NO: 10.

[0027] The disclosure further relates to polynucleotides encoding the chimeric antigen receptors, and vectors comprising the polynucleotides. The vector can be, for example, 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. The disclosure further relates to immune cells comprising the vectors. In some examples, the lentiviral vector is a pGAR vector.

[0028] Exemplary immune cells include, but are not limited to T cells, tumor infiltrating lymphocytes (TILs), NK cells, TCR-expressing cells, dendritic cells, or NK-T cells. The T cells can be autologous, allogeneic, or heterologous. In other examples, the disclosure relates to pharmaceutical compositions comprising the immune cells of described herein.

[0029] In certain examples, the disclosure relates to antigen binding molecules (and chimeric antigen receptors comprising these molecules) comprising at least one of:

- (a) a VH region differing from the amino acid sequence of the VH region of 10E3 by no more than 10, 9, 8, 7, 6, 5, 4, 3, 2, 1, or 0 amino acid residues and a VL region differing from the amino acid sequence of the VL region of 10E3 by no more than 10, 9, 8, 7, 6, 5, 4, 3, 2, 1, or 0 amino acid residues;
- (b) a VH region differing from the amino acid sequence of the VH region of 2E7 by no more than 10, 9, 8, 7, 6, 5, 4, 3, 2, 1, or 0 amino acid residues and a VL region differing from the amino acid sequence of the VL region of 2E7 by no more than 10, 9, 8, 7, 6, 5, 4, 3, 2, 1, or 0 amino acid residues;
- (c) a VH region differing from the amino acid sequence of the VH region of 8B5 by no more than 10, 9, 8, 7, 6, 5, 4, 3, 2, 1, or 0 amino acid residues and a VL region differing from the amino acid sequence of the VL region of 8B5 by no more than 10, 9, 8, 7, 6, 5, 4, 3, 2, 1, or 0 amino acid residues;
- (d) a VH region differing from the amino acid sequence of the VH region of 4E9 by no more than 10, 9, 8, 7, 6, 5, 4, 3, 2, 1, or 0 amino acid residues and a VL region differing

from the amino acid sequence of the VL region of 4E9 by no more than 10, 9, 8, 7, 6, 5, 4, 3, 2, 1, or 0 amino acid residues; and

(e) a VH region differing from the amino acid sequence of the VH region of 11F11 by no more than 10, 9, 8, 7, 6, 5, 4, 3, 2, 1, or 0 amino acid residues and a VL region differing from the amino acid sequence of the VL region of 10E3 by no more than 10, 9, 8, 7, 6, 5, 4, 3, 2, 1, or 0 amino acid residues;

and wherein the VH and VL region or regions are linked by at least one linker.

[0030] In other examples, the disclosure relates to antigen binding molecules (and chimeric antigen receptors comprising these molecules) wherein the linker comprises at least one of the scFv G4S linker and the scFv Whitlow linker.

[0031] In other examples, the disclosure relates to vectors encoding the polypeptides of the disclosure and to immune cells comprising these polypeptides. Preferred immune cells include T cells, tumor infiltrating lymphocytes (TILs), NK cells, TCR-expressing cells, dendritic cells, or NK-T cells. The T cells may be autologous, allogeneic, or heterologous.

[0032] In other examples, the disclosure relates to isolated polynucleotides 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 (V_H) chain CDR3 comprising an amino acid sequence of SEQ ID NO: 19 or SEQ ID NO:27. The polynucleotides may further comprise an activating domain. In preferred examples, the activating domain is CD3, more preferably CD3 zeta, more preferably the amino acid sequence set forth in SEQ ID NO: 9.

[0033] In other examples, the disclosure includes a costimulatory domain, such as CD28, CD28T, OX40, 4-1BB/CD137, CD2, CD3 (alpha, beta, delta, epsilon, gamma, zeta), CD4, CD5, CD7, CD9, CD16, CD22, CD27, CD30, CD 33, CD37, CD40, CD 45, CD64, CD80, CD86, CD134, CD137, CD154, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1 (CD11a/CD18), CD247, CD276 (B7-H3), LIGHT (tumor necrosis factor superfamily member 14; TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class I molecule, TNF, TNFr, integrin, signaling lymphocytic activation molecule, BTLA, Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRP1), 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, CD83 ligand, or fragments or combinations thereof. Preferred costimulatory domains are recited hereinbelow.

[0034] In further examples, the disclosure relates to isolated polynucleotides encoding a chimeric antigen receptor (CAR) or T cell receptor (TCR), wherein said CAR or TCR comprises an antigen binding molecule that specifically binds to FLT3, and wherein the antigen binding molecule comprises a variable light (V_L) chain CDR3 comprising an amino acid sequence selected from SEQ ID NO:24 and SEQ ID NO:32. The polynucleotide can further comprise an activating domain. The polynucleotide can further comprise a costimulatory domain.

[0035] In other examples, the disclosure relates to isolated polynucleotides 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).

[0036] In other examples, the disclosure relates to isolated polynucleotides 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).

[0037] The disclosure further relates to antigen binding molecules to FLT3 comprising at least one variable heavy chain CDR3 or variable light chain CDR3 sequence as set forth herein. The disclosure further relates to antigen binding molecules to FLT3 comprising at least one variable heavy chain CDR1, CDR2, and CDR3 sequences as described herein. The disclosure further relates to antigen binding molecules to FLT3 comprising at least one variable light chain

CDR1, CDR2, and CDR3 sequences as described herein. The disclosure further relates to antigen binding molecules to FLT3 comprising both variable heavy chain CDR1, CDR2, CDR3, and variable light chain CDR1, CDR2, and CDR3 sequences as described herein.

[0038] Additional heavy and light chain variable domains and CDR polynucleotide and amino acid sequences suitable for use in FLT3-binding molecules according to the present disclosure are found in U.S. Provisional Application Number 62/199,944, filed on July 31, 2015.

[0039] The disclosure further relates to methods of treating a disease or disorder in a subject in need thereof comprising administering to the subject the antigen binding molecules, the CARs, TCRs, polynucleotides, vectors, cells, or compositions according to the disclosure. Suitable diseases for treatment include, but are not limited to, 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), or combinations thereof. Additional diseases include inflammatory and/or autoimmune diseases such as rheumatoid arthritis, psoriasis, allergies, asthma, Crohn's disease, IBD, IBS, fibromyalgia, mastocytosis, and Celiac disease.

BRIEF DESCRIPTION OF THE FIGURES

[0040] FIG. 1, depicts flow cytometric analysis of FLT3 cell surface expression on human cell lines.

[0041] FIG. 2, depicts CAR expression in primary human T cells electroporated with mRNA encoding for various CARs.

[0042] FIG. 3, depicts cytolytic activity of electroporated CAR T cells against multiple cell lines following 16 hours of coculture.

[0043] FIG. 4, comprising of FIGS. 3A, and 3B, depicts IFN γ , IL-2, and TNF α production by electroporated CAR T cells following 16 hours of coculture with the indicated target cell lines.

[0044] FIG. 5, depicts CAR expression in lentivirus transduced primary human T cells from two healthy donors.

What is claimed:

1. A chimeric antigen receptor comprising an antigen binding molecule that specifically binds to FLT3, a costimulatory domain, and an activating domain that is a signaling domain of CD3 zeta, wherein the antigen binding molecule comprises:
 - a) a variable heavy chain region comprising complementary determining regions (“CDRs”) 1, 2, and 3 with amino acid sequences SEQ ID NO:43, SEQ ID NO:44, and SEQ ID NO:45, respectively, and a variable light chain region comprising CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO:48, SEQ ID NO:49, and SEQ ID NO:50, respectively; or
 - b) a variable heavy chain region comprising complementary determining regions (“CDRs”) 1, 2, and 3 with amino acid sequences SEQ ID NO:53, SEQ ID NO:54, and SEQ ID NO:55, respectively, and a variable light chain region comprising CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO:58, SEQ ID NO:59, and SEQ ID NO:60, respectively;
and the costimulatory domain is a CD28 costimulatory domain consisting of a sequence of SEQ ID NO: 2.
2. The chimeric antigen receptor according to claim 1 wherein the CD3 zeta comprises a sequence of SEQ ID NO: 10.
3. A polynucleotide encoding the chimeric antigen receptor of claim 1.
4. A vector comprising the polynucleotide of claim 3.
5. The vector according to claim 4 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.
6. An immune cell comprising the vector of claim 4.
7. The immune cell according to claim 6, wherein the immune cell is a T cell, tumor infiltrating lymphocyte (TIL), NK cell, TCR-expressing cell, dendritic cell, or NK-T cell.
8. The immune cell according to claim 7, wherein the cell is an autologous T cell.
9. The immune cell according to claim 7, wherein the cell is an allogeneic T cell.

10. The immune cell of claim 6, 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.
11. The immune cell of claim 6, 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.
12. A pharmaceutical composition comprising an immune cell of claim 6.
13. An isolated polypeptide comprising the amino acid sequence of SEQ ID NO:76 or SEQ ID NO:82.
14. A vector encoding the polypeptide of claim 13.
15. An immune cell comprising the polypeptide 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 T cell of claim 16 that is an autologous T cell.
18. The T cell of claim 16 that is an allogeneic T cell.
19. An isolated polynucleotide encoding a chimeric antigen receptor (CAR), said CAR comprising an antigen binding molecule that specifically binds to FLT3, wherein the antigen binding molecule comprises the polynucleotide sequence SEQ ID NO:75 or SEQ ID NO:81.
20. The polynucleotide according to claim 3 or 19, the polypeptide according to claim 13, the chimeric antigen receptor according to claim 1, the cell according to claim 6 or 15, or the pharmaceutical composition according to claim 12 for use in treating a disease or a disorder.
21. Use of the polynucleotide according to claim 3 or 19, in the manufacture of a medicament for treating cancer wherein the cancer is selected from the group consisting of leukemia, lymphoma, myeloma, 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; wherein the inflammatory/autoimmune disease is selected from the group consisting of rheumatoid arthritis, psoriasis, allergies, asthma, Crohn's disease,

irritable bowel disease (IBD), irritable bowel syndrome (IBS), fibromyalgia, mastocytosis, and Celiac disease.

22. Use of the chimeric antigen receptor according to claim 1 in the manufacture of a medicament for treating cancer wherein the cancer is selected from the group consisting of leukemia, lymphoma, myeloma, 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; wherein the inflammatory/autoimmune disease is selected from the group consisting of rheumatoid arthritis, psoriasis, allergies, asthma, Crohn's disease, IBD, IBS, fibromyalgia, mastocytosis, and Celiac disease.
23. Use of the cell according to claim 6 or 15, in the manufacture of a medicament for treating cancer wherein the cancer is selected from the group consisting of leukemia, lymphoma, myeloma, 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; wherein the inflammatory/autoimmune disease is selected from the group consisting of rheumatoid arthritis, psoriasis, allergies, asthma, Crohn's disease, IBD, IBS, fibromyalgia, mastocytosis, and Celiac disease.
24. Use of the pharmaceutical composition according to claim 12 in the manufacture of a medicament for treating cancer wherein the cancer is selected from the group consisting 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; wherein the inflammatory/autoimmune disease is selected from the group consisting of rheumatoid arthritis, psoriasis, allergies, asthma, Crohn's disease, IBD, IBS, fibromyalgia, mastocytosis, and Celiac disease.

25. The use according to any of claims 21, 22 or 23, wherein the cancer is AML.
26. The lentiviral vector according to claim 5, wherein the lentiviral vector is a pGAR vector.