

[0005] A need exists to identify novel and improved therapies for treating STEAP1 related diseases and disorders.

SUMMARY

[0006] 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 STEAP1.

[0007] Chimeric antigen receptors of the disclosure typically comprise: (i) a STEAP1 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.

[0007a] In one aspect, the present disclosure refers to chimeric antigen receptor comprising an antigen binding molecule that specifically binds to STEAP1, 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:89, SEQ ID NO:90, and SEQ ID NO:91, respectively, and a variable light chain region comprising CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO:94, SEQ ID NO:95, and SEQ ID NO:96, respectively; or b) a variable heavy chain region comprising complementary determining regions (“CDRs”) 1, 2, and 3 with amino acid sequences SEQ ID NO:99, SEQ ID NO:100, and SEQ ID NO:101, respectively, and a variable light chain region comprising CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO:104, SEQ ID NO:105, and SEQ ID NO:106, respectively; or

c) a VH region of SEQ ID NO: 88 and a VL region of SEQ ID NO:93, with the proviso that the VH region comprises a variable heavy chain CDR1 of SEQ ID NO: 89, a variable heavy chain CDR2 of SEQ ID NO: 90, and a variable heavy chain CDR3 of SEQ ID NO: 91, and the VL region comprises a variable light chain CDR1 of SEQ ID NO: 94, a variable light chain CDR2 of SEQ ID NO: 95, and a variable light chain CDR3 of SEQ ID NO: 96; or d) a VH region of SEQ ID NO:88 and a VL region of SEQ ID NO:93; or e) a VH region of SEQ ID NO: 98 and a VL region of SEQ ID NO:103, with the proviso that the VH region comprises a variable heavy chain CDR1 of SEQ ID NO: 99, a variable heavy chain CDR2 of SEQ ID NO: 100, and a variable heavy chain CDR3 of SEQ ID NO: 101, and the VL region comprises a variable light chain CDR1 of SEQ ID NO: 104, a variable light chain CDR2 of SEQ ID NO: 105, and a variable light chain CDR3 of SEQ ID NO: 106; or f) a VH region of SEQ ID NO:98 and a VL region of SEQ ID NO:103;

and at least one costimulatory domain, wherein the costimulatory domain is a CD28 costimulatory domain which comprises a sequence of SEQ ID NO: 2.

In another aspect, the present invention refers to polynucleotide encoding the chimeric antigen receptor of the present disclosure.

In yet another aspect, the present invention refers to a vector comprising the polynucleotide of the present disclosure.

In another aspect, the present invention refers to an immune cell comprising the vector of the present disclosure.

In another aspect, the present invention refers to a pharmaceutical composition comprising an immune cell of the present disclosure.

In another aspect, the present invention refers to an isolated polypeptide comprising the amino acid sequence of SEQ ID NO:18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, or 76.

In yet another aspect, the present invention refers to an isolated polynucleotide encoding a chimeric antigen receptor comprising an antigen binding molecule that specifically binds to STEAP1, a costimulatory domain, and an activating domain that is a signaling domain of CD3 zetaa chimeric antigen receptor (CAR) or T cell receptor (TCR) comprising an antigen binding molecule that specifically binds to STEAP1, wherein the antigen binding moleculepolynucleotide comprises the sequence of SEQ ID NO: 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, or 75.

In yet another aspect, the present invention refers to the use of

the cell according to the present disclosure; or the pharmaceutical composition according to the present disclosure in the manufacture of a medicament for treating cancer in a subject in need thereof.

In yet another aspect, the present invention refers to a vector comprising the polynucleotide of the present disclosure, wherein the vector 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.

In yet another aspect, the present invention refers to a vector encoding the polynucleotide of the present disclosure.

In another aspect, the present invention refers to an immune cell comprising the vector of the present disclosure, wherein the immune cell is a T cell, tumor infiltrating lymphocyte (TIL), NK cell, TCR-expressing cell, dendritic cell, NK-T cell, an autologous T cell, or an allogeneic T cell.

In yet another aspect, the present invention refers to the cell according to the present disclosure; or the pharmaceutical composition according to the present disclosure for use in therapy.

What is Claimed

1. A chimeric antigen receptor comprising an antigen binding molecule that specifically binds to STEAP1, 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:89, SEQ ID NO:90, and SEQ ID NO:91, respectively, and a variable light chain region comprising CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO:94, SEQ ID NO:95, and SEQ ID NO:96, respectively; or
 - b) a variable heavy chain region comprising complementary determining regions ("CDRs") 1, 2, and 3 with amino acid sequences SEQ ID NO:99, SEQ ID NO:100, and SEQ ID NO:101, respectively, and a variable light chain region comprising CDRs 1, 2, and 3 with amino acid sequences SEQ ID NO:104, SEQ ID NO:105, and SEQ ID NO:106, respectively; or
 - c) a VH region of SEQ ID NO: 88 and a VL region of SEQ ID NO:93, with the proviso that the VH region comprises a variable heavy chain CDR1 of SEQ ID NO: 89, a variable heavy chain CDR2 of SEQ ID NO: 90, and a variable heavy chain CDR3 of SEQ ID NO: 91, and the VL region comprises a variable light chain CDR1 of SEQ ID NO: 94, a variable light chain CDR2 of SEQ ID NO: 95, and a variable light chain CDR3 of SEQ ID NO: 96; or
 - d) a VH region of SEQ ID NO:88 and a VL region of SEQ ID NO:93; or
 - e) a VH region of SEQ ID NO: 98 and a VL region of SEQ ID NO:103, with the proviso that the VH region comprises a variable heavy chain CDR1 of SEQ ID NO: 99, a variable heavy chain CDR2 of SEQ ID NO: 100, and a variable heavy chain CDR3 of SEQ ID NO: 101, and the VL region comprises a variable light chain CDR1 of SEQ ID NO: 104, a variable light chain CDR2 of SEQ ID NO: 105, and a variable light chain CDR3 of SEQ ID NO: 106; or
 - f) a VH region of SEQ ID NO:98 and a VL region of SEQ ID NO:103;and at least one costimulatory domain, wherein the costimulatory domain is a CD28 costimulatory domain which comprises a sequence of SEQ ID NO: 2.
2. The chimeric antigen receptor according to claim 1 wherein the CD3 zeta comprises the 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, wherein the vector 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.
5. An immune cell comprising the vector of claim 4, wherein the immune cell is a T cell, tumor infiltrating lymphocyte (TIL), NK cell, TCR-expressing cell, dendritic cell, NK-T cell, an autologous T cell, or an allogeneic T cell.
6. The immune cell of claim 5, 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 or 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 donor's body.
7. A pharmaceutical composition comprising an immune cell of claim 5.
8. An isolated polypeptide comprising the amino acid sequence of SEQ ID NO:18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, or 76.
9. A vector encoding the polypeptide of claim 8.
10. An immune cell comprising the vector of claim 9.
11. The immune cell according to claim 10, wherein the immune cell is a T cell, tumor infiltrating lymphocyte (TIL), NK cell, TCR-expressing cell, dendritic cell, or NK-T cell.
12. The immune cell of claim 11 wherein the T cell is an autologous T cell.
13. The immune cell of claim 11 wherein the T cell is an allogeneic T cell.
14. An isolated polynucleotide encoding a chimeric antigen receptor comprising an antigen binding molecule that specifically binds to STEAP1, a costimulatory domain, and an activating domain that is a signaling domain of CD3 zeta, wherein the polynucleotide comprises the sequence of SEQ ID NO: 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, or 75.
15. A vector comprising the polynucleotide of claim 14.
16. An immune cell comprising the vector of claim 15, wherein the immune cell is a T cell, tumor infiltrating lymphocyte (TIL), NK cell, TCR-expressing cell, dendritic cell, NK-T cell, an autologous T cell, or an allogeneic T cell.
17. The cell according to any one of claims 5 to 6, or 10 to 13; or the pharmaceutical composition according to claim 7 for use in therapy.

18. The vector according to claim 4, wherein the lentiviral vector is a pGAR vector having SEQ ID NO:147.
19. Use of the cell according to any one of claims 5 to 6, or 10 to 13; or the pharmaceutical composition according to claim 7 in the manufacture of a medicament for treating cancer in a subject in need thereof.
20. The use according to claim 19 wherein the cancer is prostate cancer.
21. The use according to claim 20, wherein the cancer is metastatic castration resistant prostate cancer.