24, and 28 and (b) the heavy chain variable region CDR sequences of (i) SEQ ID NOS: 7, 10, and 13 or (ii) SEQ ID NOS: 8, 10 and 14.

[0004] The disclosure provides chimeric antigen receptors (CARs) comprising an antigen binding domain specific for thymic stromal lymphopoietin receptor (TSLPR), a transmembrane domain, and an intracellular T cell signaling domain. The CAR may further comprise a 4-1BB intracellular domain, a spacer, or both.

[0004a] In yet another aspect, there is provided a nucleic acid comprising a nucleotide sequence encoding the CAR as described herein.

[0004b] In yet another aspect, there is provided a recombinant expression vector comprising the nucleic acid as described herein.

[0004c] In yet another aspect, there is provided an isolated host cell comprising the recombinant expression vector as described herein.

[0004d] In yet another aspect, there is provided a population of cells comprising at least one host cell as described herein.

[0004e] In yet another aspect, there is provided a pharmaceutical composition comprising the CAR as described herein, the nucleic acid as described herein, the recombinant expression vector as described herein, the host cell as described herein, the population of cells as described herein, or the antibody, or antigen binding portion thereof, as described herein, and a pharmaceutically acceptable carrier.

[0004f] In yet another aspect, the present disclosure provides the CAR as described herein, the nucleic acid as described herein, the recombinant expression vector as described herein, the host cell as described herein, wherein the host cell is a T cell or non-T cell with an immune-effector function, the population of cells as described herein, wherein the population of cells comprises a T cell or non-T cell with an immune-effector function, or the pharmaceutical composition as described herein, wherein the host cell or population of cells of the pharmaceutical composition comprises a T cell or non-T cell with an immune-effector function, for use in the treatment or prevention of cancer in a mammal, wherein the cancer is associated with increased TSLPR expression.

[0004g] In yet another aspect, the present disclosure provides CAR as described herein, the nucleic acid as described herein, the recombinant expression vector as described herein, the host cell as described herein, wherein the host cell is a T cell or non-T cell with an immune-

effector function, the population of cells as described herein, wherein the population of cells comprises a T cell or non-T cell with an immune-effector function, or the pharmaceutical composition as described herein, wherein the host cell or population of cells of the pharmaceutical composition comprises a T cell or non-T cell with an immune-effector function, for use in the treatment or prevention of a proliferative disorder in a mammal, wherein the proliferative disorder is associated with a mutation in the IKZF gene and is associated with increased TSLPR expression.

[0005] Also disclosed are nucleic acids, recombinant expression vectors, host cells, populations of cells, antibodies, or antigen binding portions thereof, and pharmaceutical compositions relating to the CARs of the disclosure.

[0005a] In yet another aspect, there is provided the CAR as described herein, the nucleic acid as described herein, the recombinant expression vector as described herein, the host cell as described herein, the population of cells as described herein, or the pharmaceutical composition as described herein, for use in the treatment or prevention of cancer in a mammal, wherein the cancer is associated with increased TSLPR expression.

[0005b] In yet another aspect, there is provided the CAR as described herein, the nucleic acid as described herein, the recombinant expression vector as described herein, the host cell as described herein, the population of cells as described herein, or the pharmaceutical composition as described herein, for use in the treatment or prevention of a proliferative disorder in a mammal, wherein the proliferative disorder is associated with a mutation in the IKZF gene and is associated with increased TSLPR expression.

[0006] Also disclosed are methods of detecting the presence of a proliferative disorder, e.g., cancer, and methods of treating or preventing a proliferative disorder, e.g., cancer, in a mammal.

CLAIM(S):

1. A chimeric antigen receptor (CAR) comprising an antigen binding domain specific for TSLPR, a transmembrane domain, and an intracellular T cell signaling domain, wherein the antigen binding domain comprises (a) the light chain variable region CDR sequences of (i) SEQ ID NOS: 20, 24, and 27 or (ii) SEQ ID NOS: 21, 24, and 28 and (b) the heavy chain variable region CDR sequences of (i) SEQ ID NOS: 7, 10, and 13 or (ii) SEQ ID NOS: 8, 10, and 14.

2. The CAR according to claim 1, wherein the antigen binding domain comprises the linker sequence of SEQ ID NO: 17.

3. The CAR according to claim 1, wherein the antigen binding domain comprises the sequence of SEQ ID NO: 1.

4. The CAR according to claim 1, wherein the antigen binding domain comprises the sequence of SEQ ID NO: 2.

5. The CAR according to any one of claims 1-4, wherein the transmembrane domain comprises a CD8 amino acid sequence.

6. The CAR according to any one of claims 1-5, wherein the transmembrane domain comprises CD8 amino acid sequence comprising the CD8α hinge sequence of SEQ ID NO: 35 and the transmembrane domain of sequence SEQ ID NO: 36.

7. The CAR according to any one of claims 1-6, wherein the intracellular T cell signaling domain comprises 4-1BB, CD3 zeta, or both.

8. The CAR according to any one of claims 1-7, wherein the intracellular T cell signaling domain comprises the 4-1BB amino acid sequence of SEQ ID NO: 37.

9. The CAR according to any one of claims 1-8, wherein the intracellular T cell signaling domain comprises the CD3 zeta amino acid sequence of SEQ ID NO: 38.

10. The CAR according to any one of claims 1-9, wherein the CAR further comprises the spacer comprising SEQ ID NOS: 30-33.

11. The CAR according to claim 1, wherein the CAR comprises any one of the sequences of SEQ ID NO: 39-46.

12. The CAR according to claim 11, wherein the CAR comprises the sequence of SEQ ID NO: 39.

13. A nucleic acid comprising a nucleotide sequence encoding the CAR according to any one of claims 1-12.

14. The nucleic acid according to claim 13, wherein the nucleotide sequence is codon-optimized.

15. A recombinant expression vector comprising the nucleic acid according to claim 13 or 14.

16. The recombinant expression vector according to claim 15, wherein the recombinant expression vector is a lentiviral vector.

17. An isolated host cell comprising the recombinant expression vector of claim 15 or 16.

18. A population of cells comprising at least one host cell of claim 17.

19. A pharmaceutical composition comprising the CAR of any one of claims 1-12, the nucleic acid of claim 13 or 14, the recombinant expression vector of claim 15 or 16, the host cell of claim 17, or the population of cells of claim 18, and a pharmaceutically acceptable carrier.

20. The CAR of any one of claims 1-12, the nucleic acid of claim 13 or 14, the recombinant expression vector of claim 15 or 16, the host cell of claim 17, wherein the host

cell is a T cell or non-T cell with an immune-effector function, the population of cells of claim 18, wherein the population of cells comprises a T cell or non-T cell with an immune-effector function, or the pharmaceutical composition of claim 19, wherein the host cell or population of cells of the pharmaceutical composition comprises a T cell or non-T cell with an immune-effector function, for use in the treatment or prevention of cancer in a mammal, wherein the cancer is associated with increased TSLPR expression.

21. The CAR, nucleic acid, recombinant expression vector, host cell, population of cells, or pharmaceutical composition for the use according to claim 20, wherein the cancer is ALL.

22. The CAR, nucleic acid, recombinant expression vector, host cell, population of cells, or pharmaceutical composition for the use according to claim 20, wherein the cancer is BCP-ALL.

23. The CAR, nucleic acid, recombinant expression vector, host cell, population of cells, or pharmaceutical composition for the use according to claim 20, wherein the cancer is acute myeloid leukemia.

24. The CAR of any one of claims 1-12, the nucleic acid of claim 13 or 14, the recombinant expression vector of claim 15 or 16, the host cell of claim 17, wherein the host cell is a T cell or non-T cell with an immune-effector function, the population of cells of claim 18, wherein the population of cells comprises a T cell or non-T cell with an immune-effector function, or the pharmaceutical composition of claim 19, wherein the host cell or population of cells of the pharmaceutical composition comprises a T cell or non-T cell with an immune-effector function, for use in the treatment or prevention of a proliferative disorder in a mammal, wherein the proliferative disorder is associated with a mutation in the IKZF gene and is associated with increased TSLPR expression.