

CLAIMS

1. A chimeric antigen receptor protein comprising a target binding moiety, an intracellular signalling region and a domain that promotes synthesis of arginine or an arginine precursor, wherein;

the target binding moiety binds to a target molecule associated with cancer;

the intracellular signalling region comprises a region selected from the group consisting of: a 4-1BB signalling region; an OX-40 signalling region; a CD28 signalling region; an ICOS signalling region; and a CD3 ζ signalling region; and,

the domain that promotes synthesis of arginine or an arginine precursor comprises an enzyme domain selected from the group consisting of: an ASS-1 domain; an OTC domain; an ASL domain; an ODC1 domain; an ArgG domain; an ArgH domain; and an ArgF domain.

2. The chimeric antigen receptor protein according to claim 1, wherein the ASS-1 domain comprises the amino acid sequence of SEQ ID NO. 1; and/or the OTC domain comprises the amino acid sequence of SEQ ID NO. 2.

3. The chimeric antigen receptor protein according to claims 1 or 2, wherein the ASL domain comprises the amino acid sequence encoded by SEQ ID NO. 30; and/or the ODC1 domain comprises the amino acid sequence encoded by SEQ ID NO. 31.

4. The chimeric antigen receptor protein according to any of claims 1 to 3, wherein the ArgG domain comprises the amino acid sequence encoded by SEQ ID NO. 32; and/or the ArgH domain comprises the amino acid sequence encoded by SEQ ID NO. 33.

5. The chimeric antigen receptor protein according to any of claims 1 to 4, wherein the ArgF domain comprises the amino acid sequence encoded by SEQ ID NO. 34.

6. The chimeric antigen receptor protein according to any preceding claim, wherein the target binding moiety is selected from the group consisting of: a GD2 target binding moiety, such as a GD2 target binding moiety comprising the amino acid sequence of SEQ ID NO. 3; a CD33 target binding moiety, such as a CD33 target binding moiety comprising the amino acid sequence of SEQ ID NO. 4; a mesothelin target binding moiety, such as a mesothelin target binding moiety comprising the amino acid sequence of SEQ ID NO. 5; and an EGFRvIII target binding moiety, such as an EGFRvIII target binding moiety comprising the amino acid sequence of SEQ ID NO. 6.

7. The chimeric antigen receptor protein according to any preceding claim, wherein the 4-1BB intracellular signalling region comprises the amino acid sequence of SEQ ID NO. 7.
8. The chimeric antigen receptor fusion target-binding protein according to any preceding claim, wherein the CD3 ζ domain comprises the amino acid sequence of SEQ ID NO: 11 or SEQ ID NO: 40.
9. The chimeric antigen receptor protein according to any preceding claim, comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 12 to 23.
10. The chimeric antigen receptor protein according to any preceding claim, for use as a medicament, optionally for use in the prevention or treatment of cancer.
11. A cell comprising a chimeric antigen receptor protein comprising a target binding moiety, an intracellular signalling region and a domain that promotes synthesis of arginine or an arginine precursor wherein;
the target binding moiety is directed to a target molecule associated with cancer;
the intracellular signalling region comprises a region selected from the group consisting of: a 4-1BB signalling region; an OX-40 signalling region; a CD28 signalling region; an ICOS signalling region; and a CD3 ζ signalling region; and,
the domain that promotes synthesis of arginine or an arginine precursor comprises an enzyme domain selected from the group consisting of: an ASS-1 domain; an OTC domain; an ASL domain; an ArgG domain; an ArgH domain; and an ArgF domain.
12. The cell according to claim 11, wherein the chimeric antigen receptor protein is as defined in any of claims 2 to 5.
13. A cell according to any of claims 11 or 12, for use as a medicament, optionally for use in the prevention or treatment of cancer.
14. A nucleic acid encoding a chimeric antigen receptor protein comprising a target binding moiety, an intracellular signalling region and a domain that promotes synthesis of arginine or an arginine precursor, wherein;
the target binding moiety is directed to a target molecule associated with cancer;
the intracellular signalling region comprises a region selected from the group consisting of: a 4-1BB signalling region; an OX-40 signalling region; a CD28 signalling region; an ICOS signalling region; and a CD3 ζ signalling region; and,

the domain that promotes synthesis of arginine or an arginine precursor comprises an enzyme domain selected from the group consisting of: an ASS-1 domain; an OTC domain; an ASL domain; an ArgG domain; an ArgH domain; and an ArgF domain.

15. A nucleic acid according to claim 14, wherein the chimeric antigen receptor protein is as defined in any of claims 2 to 5.

16. A nucleic acid according to claim 14 or claim 15, comprising the DNA sequence of SEQ ID NO: 38, SEQ ID NO: 39; or SEQ ID NO: 37.

17. A nucleic acid according to any of claims 14 to 16, for use as a medicament, optionally for use in the prevention or treatment of cancer.

18. A pharmaceutical composition comprising a chimeric antigen receptor protein according to any of claims 1 to 10; and/or a cell according to any of claims 11 to 13; and/or a nucleic acid according to any of claims 14 to 17.

19. A pharmaceutical composition according to claim 18, for use as a medicament, optionally for use in the prevention or treatment of cancer.