

CLAIMS

1. A chimeric antigen receptor fusion target-binding protein comprising a target binding moiety, an intracellular signalling region and a domain that promotes synthesis of arginine or an arginine precursor-
2. ~~The fusion target-binding protein according to claim 1, 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,-
3. ~~The fusion target-binding protein according to claim 2, wherein the enzyme domain is selected from the group consisting of: an ASS-1 domain; an OTC domain; an ASL domain; an ODC1-ODC1 domain; an ArgG domain; an ArgH domain; and an ArgF domain.~~
24. The chimeric antigen receptor fusion target-binding protein according to claim 31, wherein the ASS-1 domain comprises the amino acid sequence of SEQ ID NO. 1; and/or-
5. ~~The fusion target-binding protein according to claim 3 or claim 4, wherein the OTC domain comprises the amino acid sequence of SEQ ID NO. 2.~~
63. The chimeric antigen receptor fusion target-binding protein according to any of claims 31 to 32, wherein the ASL domain comprises the amino acid sequence encoded by SEQ ID NO. 30; and/or-
7. ~~The fusion target-binding protein according to any of claims 3 to 6, wherein the ODC1 domain comprises the amino acid sequence encoded by SEQ ID NO. 31.~~
84. The chimeric antigen receptor fusion target-binding protein according to any of claims 31 to 37, wherein the ArgG domain comprises the amino acid sequence encoded by SEQ ID NO. 32; and/or-
9. ~~The fusion target-binding protein according to any of claims 3 to 8, wherein the ArgH domain comprises the amino acid sequence encoded by SEQ ID NO. 33.~~

~~105.~~ The chimeric antigen receptor fusion target-binding protein according to any of claims ~~31~~ to ~~94~~, wherein the ArgF domain comprises the amino acid sequence encoded by SEQ ID NO. 34.

~~11.~~ A fusion target-binding protein comprising a target binding moiety, an intracellular signalling region and a domain that promotes synthesis of tryptophan or a tryptophan precursor.

~~12.~~ The fusion target-binding protein according to claim 11, wherein the domain that promotes synthesis of tryptophan or a tryptophan precursor comprises an enzyme domain.

~~13.~~ The fusion target-binding protein according to claim 11 or claim 12, wherein the enzyme domain is selected from the group consisting of: an TRP5 domain; and an IDO domain;

~~14.~~ The fusion target-binding protein according to claim 13, wherein the TRP5 domain comprises the amino acid sequence encoded by SEQ ID NO. 35.

~~15.~~ The fusion target-binding protein according to claim 13 or claim 14, wherein the IDO domain comprises the amino acid sequence encoded by SEQ ID NO. 36.

~~166.~~ The chimeric antigen receptor fusion target-binding 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.

~~17.~~ The fusion target-binding protein according to claim 16, wherein the GD2 target binding moiety comprises the amino acid sequence of SEQ ID NO. 3.

~~18.~~ The fusion target-binding protein according to claim 16, wherein the CD33 target binding moiety comprises the amino acid sequence of SEQ ID NO. 4.

~~19. The fusion target-binding protein according to claim 16, wherein the mesothelin target binding moiety comprises the amino acid sequence of SEQ ID NO. 5.~~

~~20. The fusion target-binding protein according to claim 16, wherein the EGFRvIII target binding moiety comprises the amino acid sequence of SEQ ID NO. 6~~

~~21. The fusion target-binding protein according to any preceding claim, wherein 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.~~

~~22. The fusion target-binding protein according to claim 21, wherein the intracellular signalling region comprises a 4-1BB signalling region.~~

~~237. The chimeric antigen receptor fusion target-binding protein according to any preceding claim claim 21 or claim 22, wherein the 4-1BB intracellular signalling region comprises the amino acid sequence of SEQ ID NO. 7.~~

~~24. The fusion target-binding protein according to any of claims 24 to 23, wherein the intracellular signalling region comprises a CD3 ζ domain.~~

~~258. The chimeric antigen receptor fusion target-binding protein according to any preceding claim claim 24, wherein the CD3 ζ domain comprises the amino acid sequence of SEQ ID NO: 11 or SEQ ID NO: 40.~~

~~26. The fusion target-binding protein according to any of claims 21 to 25, comprising both a 4-1BB domain and a CD3 ζ domain.~~

~~279. The chimeric antigen receptor fusion target-binding protein according to any preceding claim, comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 12 to 23.~~

~~2810. The chimeric antigen receptor fusion target-binding protein according to any preceding claim, for use as a medicament, optionally.~~

~~29. The fusion target-binding protein for use according to claim 28, for use in the prevention or treatment of cancer.~~

~~3011.~~ A cell comprising a chimeric antigen receptor fusion target-binding 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.

~~3112.~~ The cell according to claim ~~3011~~, wherein the chimeric antigen receptor fusion target-binding protein is as defined in any of claims ~~1-2 to 510~~, or ~~16 to 27~~.

~~32.~~—A cell comprising a fusion target-binding protein comprising a target binding moiety, an intracellular signalling region and a domain that promotes synthesis of tryptophan or a tryptophan precursor.

~~33.~~—The cell according to claim ~~32~~, wherein the fusion target-binding protein is as defined in any of claims ~~11 to 27~~.

~~3413.~~ A cell according to any of claims ~~30-11 to or 1233~~, for use as a medicament, optionally

;

~~35.~~—The cell for use according to claim ~~34~~, for use in the prevention or treatment of cancer.

~~3614.~~ A nucleic acid encoding a chimeric antigen receptor fusion target-binding 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.

~~3715.~~ A nucleic acid according to claim ~~3614~~, wherein the chimeric antigen receptor fusion-target binding protein is as defined in any of claims ~~12~~ to ~~510~~, or ~~16~~ to 27.

~~3816.~~ A nucleic acid according to claim ~~1436~~ or claim ~~3715~~, comprising the DNA sequence of SEQ ID NO: 38, SEQ ID NO: 39; or SEQ ID NO: 37.

~~39.~~ A nucleic acid encoding a fusion target-binding protein comprising a target binding moiety, an intracellular signalling region and a domain that promotes synthesis of tryptophan or a tryptophan precursor.

~~40.~~ A nucleic acid according to claim 39, wherein the fusion target-binding protein is as defined in any of claims 11 to 27.

~~4117.~~ A nucleic acid according to any of claims ~~3614~~ to ~~4016~~, for use as a medicament, optionally.

~~42.~~ The nucleic acid for use according to claim 41, for use in the prevention or treatment of cancer.

~~4318.~~ A pharmaceutical composition comprising a chimeric antigen receptor fusion-target binding protein according to any of claims 1 to ~~3010~~; and/or a cell according to any of claims ~~1130~~ to ~~3513~~; and/or a nucleic acid according to any of claims ~~3614~~ to ~~4217~~.

~~4419.~~ A pharmaceutical composition according to claim ~~4318~~, for use as a medicament, optionally.

~~45.~~ The pharmaceutical composition for use according to claim 44, for use in the prevention or treatment of cancer.

~~46.~~ A method of treating a condition in a subject in need thereof, the method comprising providing the subject with a fusion target-binding protein according to any of claims 1 to 29.

~~47.~~ The method according to claim 45, wherein the fusion target-binding protein is provided by cellular expression of a nucleic acid sequence according to any of claims 37 to 43.

~~48.~~ A method of treating a condition in a subject in need thereof, the method comprising providing the subject with a cell according to any of claims 30 to 35.

49. — ~~A method of treating a condition in a subject in need thereof, the method comprising providing the subject with a nucleic acid according to any of claims 36 to 42.~~

50. — ~~The method according to any of claims 46 to 49, in the treatment of cancer.~~

51. — ~~The method according to any of claims 46 to 50, in the treatment of viral infection.~~