

103, SEQ ID NO: 114, SEQ ID NO: 125, SEQ ID NO: 133, SEQ ID NO: 142; a fragment of any one of the foregoing amino acid sequences, and a homologous sequence of any one of the foregoing amino acid sequences;

(B) an antigen binding region comprising a variable light chain (VL) and variable heavy chain (VH), respectively, with amino acid sequences selected from SEQ ID NOS: 6 and 8; SEQ ID NOS: 17 and 19; SEQ ID NOS: 28 and 30; SEQ ID NOS: 39 and 41; SEQ ID NOS: 49 and 51; SEQ ID NOS: 57 and 59; SEQ ID NOS: 68 and 70; SEQ ID NOS: 79 and 81; SEQ ID NOS: 90 and 92; SEQ ID NOS: 99 and 101; SEQ ID NOS: 110 and 112; SEQ ID NOS: 121 and 123; SEQ ID NOS: 129 and 131; SEQ ID NOS: 138 and 140; fragments of any one of the foregoing amino acid sequences, and homologous sequences of any one of the foregoing amino acid sequences;

(C) an antigen binding region comprising:

(i) a light chain (LC) comprising light chain complementarity determining regions (LCCDR) LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence QSISSY (SEQ ID NO: 1), AAS and QQSYSTPLT (SEQ ID NO: 2) and a heavy chain (HC) comprising heavy chain complementarity determining regions (HCCDR) HCCDR1, HCCDR2 and HCCDR3 respectively, having amino acid sequences GFTSSSYW (SEQ ID NO: 4), IKQDGSEK (SEQ ID NO: 5) and ARGGWSYDM (SEQ ID NO: 6); fragments of any one of the foregoing amino acid sequences, and homologous sequences of any one of the foregoing amino acid sequences;

(ii) a light chain (LC) comprising LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence SSNIGAGYA (SEQ ID NO: 12), TNN and QSYDSSLSGVI (SEQ ID NO: 13) and a heavy chain (HC) comprising HCCDR1, HCCDR2 and HCCDR3

respectively, having amino acid sequences GYTLTELS (SEQ ID NO: 14), FDPEDGET (SEQ ID NO. 15) and ARAYYGFDQ (SEQ ID NO: 16); fragments of any one of the foregoing amino acid sequences, and homologous sequences of any one of the foregoing amino acid sequences;

(iii) a light chain (LC) comprising LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence SSNIGNNA (SEQ ID NO: 23), YND and AAWDDSVNGYV (SEQ ID NO: 24) and a heavy chain (HC) comprising HCCDR1, HCCDR2 and HCCDR3 respectively, having amino acid sequences GYTFTRFG (SEQ ID NO: 25), ISVNNGNT (SEQ ID NO. 26) and ARYMYGRRDS (SEQ ID NO: 27); fragments of any one of the foregoing amino acid sequences, and homologous sequences of any one of the foregoing amino acid sequences;

(iv) a light chain (LC) comprising LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence NIGSKS (SEQ ID NO: 34), YDS and QWWDNHSDV (SEQ ID NO: 35) and a heavy chain (HC) comprising HCCDR1, HCCDR2 and HCCDR3 respectively, having amino acid sequences RNKFSSYA (SEQ ID NO: 36), ISGSGGTT (SEQ ID NO. 37) and ARWYSSYYDV (SEQ ID NO: 38); fragments of any one of the foregoing amino acid sequences, and homologous sequences of any one of the foregoing amino acid sequences;

(v) a light chain (LC) comprising LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence NIGSKS (SEQ ID NO: 34), YDS and QWWDSSSDYV (SEQ ID NO: 45) and a heavy chain (HC) comprising HCCDR1, HCCDR2 and HCCDR3 respectively, having amino acid sequences GFTFSSYA (SEQ ID NO: 46), ISGSGGST (SEQ ID NO. 47) and ARNYISMFDS (SEQ ID NO: 48);

fragments of any one of the foregoing amino acid sequences, and homologous sequences of any one of the foregoing amino acid sequences;

(vi) a light chain (LC) comprising LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence NIGSKS (SEQ ID NO: 34), YDS and QVWDSSSDHV (SEQ ID NO: 55) and a heavy chain (HC) comprising HCCDR1, HCCDR2 and HCCDR3 respectively, having amino acid sequences GFTFSSYA (SEQ ID NO: 46), ISGSGGST (SEQ ID NO: 47) and ARGYSSYYDA (SEQ ID NO: 56); fragments of any one of the foregoing amino acid sequences, and homologous sequences of any one of the foregoing amino acid sequences;

(vii) a light chain (LC) comprising LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence RSNIGENT (SEQ ID NO: 63), SNN and AAWDDRLNGYV (SEQ ID NO: 64) and a heavy chain (HC) comprising HCCDR1, HCCDR2 and HCCDR3 respectively, having amino acid sequences GYTFTNYG (SEQ ID NO: 65), IGAQKGDT (SEQ ID NO: 66) and ARSQGVPFDS (SEQ ID NO: 67); fragments of any one of the foregoing amino acid sequences, and homologous sequences of any one of the foregoing amino acid sequences;

(viii) a light chain (LC) comprising LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence RSNIGSNT (SEQ ID NO: 74), NNN and ATWDDSLNEYV (SEQ ID NO: 75) and a heavy chain (HC) comprising HCCDR1, HCCDR2 and HCCDR3 respectively, having amino acid sequences GYTFTRYG (SEQ ID NO: 76), ISGYNGNT (SEQ ID NO: 77) and ARHGYGYHGD (SEQ ID NO: 78); fragments of any one of the foregoing amino acid sequences, and

homologous sequences of any one of the foregoing amino acid sequences;

(ix) a light chain (LC) comprising LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence SSNIGAGYV (SEQ ID NO: 85), HNN and QSYDSSLGWV (SEQ ID NO: 86) and a heavy chain (HC) comprising HCCDR1, HCCDR2 and HCCDR3 respectively, having amino acid sequences GFTFKDYY (SEQ ID NO: 87), ISTSGNSV (SEQ ID NO. 88) and ARSPGHSDYDS (SEQ ID NO: 89); fragments of any one of the foregoing amino acid sequences, and homologous sequences of any one of the foregoing amino acid sequences;

(x) a light chain (LC) comprising LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence NIGDKS (SEQ ID NO: 96), YDS and QVWASGTDHPYVI (SEQ ID NO: 97) and a heavy chain (HC) comprising HCCDR1, HCCDR2 and HCCDR3 respectively, having amino acid sequences GFTFSSYA (SEQ ID NO: 46), ISGSGGST (SEQ ID NO. 47) and ARMYGSYTDM (SEQ ID NO: 98); fragments of any one of the foregoing amino acid sequences, and homologous sequences of any one of the foregoing amino acid sequences;

(xi) a light chain (LC) comprising LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence SSNIGYNY (SEQ ID NO: 105), RNN and TSWDDSLSGYV (SEQ ID NO: 106) and a heavy chain (HC) comprising HCCDR1, HCCDR2 and HCCDR3 respectively, having amino acid sequences GNAFTNFY (SEQ ID NO: 107), INPSGTDLT (SEQ ID NO. 108) and ARQYAYGYSGFDM (SEQ ID NO: 109); fragments of any one of the foregoing amino acid sequences, and homologous sequences of any one of the foregoing amino acid sequences;

(xii) a light chain (LC) comprising LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence QSVSNW (SEQ ID NO: 116), AAS and QQSYSTPIT (SEQ ID NO: 117) and a heavy chain (HC) comprising HCCDR1, HCCDR2 and HCCDR3 respectively, having amino acid sequences GYTFTSYY (SEQ ID NO: 118), INPNTGGS (SEQ ID NO: 119) and ARGDVITYDE (SEQ ID NO: 120); fragments of any one of the foregoing amino acid sequences, and homologous sequences of any one of the foregoing amino acid sequences;

(xiii) a light chain (LC) comprising LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence NIGSKS (SEQ ID NO: 34), YDD and QVWDINDHYV (SEQ ID NO: 127) and a heavy chain (HC) comprising HCCDR1, HCCDR2 and HCCDR3 respectively, having amino acid sequences GFTFSSYA (SEQ ID NO: 46), ISGSGGST (SEQ ID NO: 47) and ARSQASFMDI (SEQ ID NO: 128); fragments of any one of the foregoing amino acid sequences, and homologous sequences of any one of the foregoing amino acid sequences; or

(xiv) a light chain (LC) comprising LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence NIGSKS (SEQ ID NO: 34), DDS and QVWDSSSDQGV (SEQ ID NO: 135) and a heavy chain (HC) comprising HCCDR1, HCCDR2 and HCCDR3 respectively, having amino acid sequences GFTFSSYA (SEQ ID NO: 46), IGTGGGT (SEQ ID NO: 136) and ARGTYDGDQ (SEQ ID NO: 137); fragments of any one of the foregoing amino acid sequences, and homologous sequences of any one of the foregoing amino acid sequences;

wherein said antigen-binding protein specifically binds to programmed cell death (PD-1).

In another aspect, the present invention refers to a nucleic acid encoding an antigen-binding protein of the present invention.

In yet another aspect, the present invention refers to a vector comprising a nucleic acid of the present invention.

In yet another aspect, the present invention refers to a cell comprising an antigen-binding protein of the present invention, a nucleic acid of the present invention or a vector comprising a nucleic acid of the present invention.

In another aspect, the present invention refers to a pharmaceutical composition comprising an antigen-binding protein of the present invention, a nucleic acid of the present invention, a vector of the present invention, a cell of the present invention.

In yet another aspect, the present invention refers to the use of an antigen-binding protein or an antigen binding fragment thereof of the present invention, a nucleic acid of the present invention, a vector of the present invention, a cell of the present invention, or a pharmaceutical composition the present invention in the manufacture of a medicament for treating cancer.

In another aspect, the present invention refers to a vector comprising a nucleic acid encoding a recombinant anti-PD-1 antigen-binding protein as defined in the present invention and a nucleic acid encoding a chimeric antigen receptor, wherein said recombinant anti-PD-1 antigen-binding protein is not identical to said chimeric antigen receptor.

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

In yet another aspect, the present invention refers to a cell comprising a nucleic acid encoding a recombinant anti-PD-1 antigen-binding protein as defined in the present invention and a nucleic acid encoding a chimeric antigen receptor, wherein said recombinant anti-PD-1 antigen-binding protein is not identical to said chimeric antigen receptor.

In yet another aspect, the present invention refers to a cell comprising a recombinant anti-PD-1 antigen-binding protein as defined in the present invention and a chimeric antigen receptor, wherein said recombinant anti-PD-1 antigen-binding protein is not identical to said chimeric antigen receptor.

In yet another aspect, the present invention refers to a pharmaceutical composition comprising a vector or a cell of the present invention.

In yet another invention, the present invention refers to the use of a vector or cell of the present invention, or a pharmaceutical composition of the present invention, in the manufacture of a medicament for treating cancer, wherein the recombinant anti-PD-1 antigen-binding protein is a PD-1 antagonist. In one other aspect, the present invention refers to the use of a combination of a nucleic acid encoding a recombinant anti-PD-1 antigen-binding protein as defined in the present invention and a nucleic acid encoding a chimeric antigen receptor in the manufacture of a pharmaceutical for treating cancer, wherein the use comprises that at least one T cell of the subject is to be transduced with the medicament, wherein said recombinant anti-PD-1 antigen-binding protein is not identical to said chimeric antigen receptor. In yet another aspect, the present invention refers to the antigen-binding protein or an antigen binding fragment thereof of the present invention, a nucleic acid of the present invention, a vector of the present invention, a cell of the present invention, a pharmaceutical composition of the present invention or a vector or cell of the present invention for use in therapy.

Also disclosed herein is:

[008] In one example, the disclosure relates to recombinant antigen-binding proteins, antibodies and chimeric antigen receptors or antigen-binding portions thereof that bind specifically to PD-1 and prevent binding of its ligand.

[009] In one example, the disclosure relates to a recombinant antigen-binding protein or antigen-binding fragment thereof comprising one of:

CLAIMS

We claim:

1. A recombinant antigen-binding protein or antigen-binding fragment thereof comprising one of:

(A) an antigen binding region comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 10, SEQ ID NO: 21, SEQ ID NO: 32, SEQ ID NO: 43, SEQ ID NO: 53, SEQ ID NO: 61, SEQ ID NO: 72, SEQ ID NO: 83, SEQ ID NO: 94, SEQ ID NO: 103, SEQ ID NO: 114, SEQ ID NO: 125, SEQ ID NO: 133, SEQ ID NO: 142, a fragment of any one of the foregoing amino acid sequences, and a homologous sequence to any one of the foregoing amino acid sequences;

(B) an antigen binding region comprising a variable light chain (VL) and variable heavy chain (VH), respectively, with amino acid sequences selected from SEQ ID NOS: 6 and 8; SEQ ID NOS: 17 and 19; SEQ ID NOS: 28 and 30; SEQ ID NOS: 39 and 41; SEQ ID NOS: 49 and 51; SEQ ID NOS: 57 and 59; SEQ ID NOS: 68 and 70; SEQ ID NOS: 79 and 81; SEQ ID NOS: 90 and 92; SEQ ID NOS: 99 and 101; SEQ ID NOS: 110 and 112; SEQ ID NOS: 121 and 123; SEQ ID NOS: 129 and 131; SEQ ID NOS: 138 and 140, fragments of the foregoing of amino acid sequences, and homologous sequences to the foregoing amino acid sequences;

(C) an antigen binding region comprising:

(i) a light chain (LC) comprising light chain complementarity determining regions (LCCDR) LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence QSISSY (SEQ ID NO: 1), AAS and QQSYSTPLT (SEQ ID NO: 2) and a heavy chain (HC) comprising heavy chain complementarity determining regions (HCCDR) HCCDR1, HCCDR2 and HCCDR3 respectively, having amino acid sequences GFTSSSYW (SEQ ID NO: 4), IKQDGSEK (SEQ ID NO. 5) and ARGGWSYDM (SEQ ID NO: 6), fragments of the foregoing amino acid sequences, and homologous sequences to the foregoing amino acid sequences;

(ii) a light chain (LC) comprising LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence SSNIGAGYA (SEQ ID NO: 12), TNN and QSYDSSLGVI (SEQ ID NO: 13) and a heavy chain (HC) comprising HCCDR1, HCCDR2 and HCCDR3 respectively, having amino acid sequences GYTLTELS (SEQ ID NO: 14), FDPEDGET (SEQ ID NO. 15) and ARAYYGFDQ (SEQ ID NO: 16), fragments of the foregoing amino acid sequences, and homologous sequences to the foregoing amino acid sequences;

(iii) a light chain (LC) comprising LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence SSNIGNNA (SEQ ID NO: 23), YND and AAWDDSVNGYV (SEQ ID NO: 24) and a heavy chain (HC) comprising HCCDR1, HCCDR2 and HCCDR3 respectively, having amino acid sequences GYTFTRFG (SEQ ID NO: 25), ISVNNGNT (SEQ ID NO. 26) and ARYMYGRRDS (SEQ ID NO: 27), fragments of the foregoing amino acid sequences, and homologous sequences to the foregoing amino acid sequences;

(iv) a light chain (LC) comprising LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence NIGSKS (SEQ ID NO: 34), YDS and QVWDNHSDVV (SEQ ID NO: 35) and a heavy chain (HC) comprising HCCDR1, HCCDR2 and HCCDR3 respectively, having amino acid sequences RNKFSSYA (SEQ ID NO: 36), ISGSGGTT (SEQ ID NO. 37) and ARWYSSYYDV (SEQ ID NO: 38); fragments of the foregoing amino acid sequences; and homologous sequences to the foregoing amino acid sequences;

(v) a light chain (LC) comprising LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence NIGSKS (SEQ ID NO: 34), YDS and QVWDSSSDYV (SEQ ID NO: 45) and a heavy chain (HC) comprising HCCDR1, HCCDR2 and HCCDR3 respectively, having amino acid sequences GFTFSSYA (SEQ ID NO: 46), ISGSGGST (SEQ ID NO. 47) and ARNYISMFDS (SEQ ID NO: 48), fragments of the foregoing amino acid sequences, and homologous sequences to the foregoing amino acid sequences;

(vi) a light chain (LC) comprising LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence NIGSKS (SEQ ID NO: 34), YDS and QVWDSSSDHV (SEQ ID NO: 55) and a heavy chain (HC) comprising HCCDR1, HCCDR2 and HCCDR3 respectively, having amino acid sequences GFTFSSYA (SEQ ID NO: 46), ISGSGGST (SEQ ID NO. 47) and ARGYSSYYDA (SEQ ID NO: 56), fragments of the foregoing amino acid sequences, and homologous sequences to the foregoing amino acid sequences;

(vii) a light chain (LC) comprising LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence RSNIGENT (SEQ ID NO: 63), SNN and AAWDDRLNGYV (SEQ ID NO: 64) and a heavy chain (HC) comprising HCCDR1, HCCDR2 and HCCDR3 respectively, having amino acid sequences GYTFTNYG (SEQ ID NO: 65), IGAQKGDT (SEQ ID NO. 66) and ARSQGVPFDS (SEQ ID NO: 67), fragments of the foregoing amino acid sequences, and homologous sequences to the foregoing amino acid sequences;

(viii) a light chain (LC) comprising LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence RSNIGSNT (SEQ ID NO: 74), NNN and ATWDDSLNEYV (SEQ ID NO: 75) and a heavy chain (HC) comprising HCCDR1, HCCDR2 and HCCDR3 respectively, having amino acid sequences GYTFTRYG (SEQ ID NO: 76), ISGYNGNT (SEQ ID NO. 77) and ARHGYGYHGD (SEQ ID NO: 78), fragments of the foregoing amino acid sequences, and homologous sequences to the foregoing amino acid sequences;

(ix) a light chain (LC) comprising LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence SSNIGAGYV (SEQ ID NO: 85), HNN and QSYDSSLGWW (SEQ ID NO: 86) and a heavy chain (HC) comprising HCCDR1, HCCDR2 and HCCDR3 respectively, having amino acid sequences GFTFKDYY (SEQ ID NO: 87), ISTSGNSV (SEQ ID NO. 88) and ARSPGHSDYDS (SEQ ID NO: 89), fragments of the foregoing amino acid sequences, and homologous sequences to the foregoing amino acid sequences;

(x) a light chain (LC) comprising LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence NIGDKS (SEQ ID NO: 96), YDS and QVWASGTDHPYVI (SEQ ID NO: 97) and a heavy chain (HC) comprising HCCDR1, HCCDR2 and HCCDR3 respectively, having amino acid sequences GFTFSSYA (SEQ ID NO: 46), ISGSGGST (SEQ ID NO. 47) and ARMYGSYTDM (SEQ ID NO: 98), fragments of the foregoing amino acid sequences, and homologous sequences to the foregoing amino acid sequences;

(xi) a light chain (LC) comprising LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence SSNIGYNY (SEQ ID NO: 105), RNN and TSWDDSLSGYV (SEQ ID NO: 106) and a heavy chain (HC) comprising HCCDR1, HCCDR2 and HCCDR3 respectively, having amino acid sequences GNAFTNFY (SEQ ID NO: 107), INPSGTDLT (SEQ ID NO. 108) and ARQYAYGYSGFDM (SEQ ID NO: 109), fragments of the foregoing amino acid sequences, and homologous sequences to the foregoing amino acid sequences;

(xii) a light chain (LC) comprising LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence QSVSNW (SEQ ID NO: 116), AAS and QQSYSTPIT (SEQ ID NO: 117) and a heavy chain (HC) comprising HCCDR1, HCCDR2 and HCCDR3 respectively, having amino acid sequences GYTFTSYY (SEQ ID NO: 118), INPNTGGS (SEQ ID NO. 119) and ARGDVTYDE (SEQ ID NO: 120), fragments of the foregoing amino acid sequences, and homologous sequences to the foregoing amino acid sequences;

(xiii) a light chain (LC) comprising LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence NIGSKS (SEQ ID NO: 34), YDD and QVWDINDHYV (SEQ ID NO: 127) and a heavy chain (HC) comprising HCCDR1, HCCDR2 and HCCDR3 respectively, having amino acid sequences GFTFSSYA (SEQ ID NO: 46), ISGSGGST (SEQ ID NO. 47) and ARSQASFMDI (SEQ ID NO: 128), fragments of the foregoing amino acid sequences, and homologous sequences to the foregoing amino acid sequences; or

(xiv) a light chain (LC) comprising LCCDR1, LCCDR2 and LCCDR3 respectively, having the amino acid sequence NIGSKS (SEQ ID NO: 34), DDS and QVWDSSSDQGV (SEQ ID NO: 135) and a heavy chain (HC) comprising HCCDR1, HCCDR2 and HCCDR3 respectively, having amino acid sequences GFTFSSYA (SEQ ID NO: 46), IGTGGGT (SEQ ID NO. 136) and ARGTYDGDQ (SEQ ID NO: 137), fragments of the foregoing amino acid sequences, and homologous sequences to the foregoing amino acid sequences;

wherein said antigen-binding protein specifically binds to programmed cell death (PD-1).

2. The recombinant antigen-binding protein of claim 1, wherein said protein is an antibody.

3. The recombinant antigen-binding protein of claim 2, wherein the antibody is a human antibody.

4. The recombinant antigen-binding protein of claim 2, wherein said antibody or antigen-binding fragment thereof is intact Ig, Fab, F(ab')₂, Fv, or scFv.

5. The antigen-binding protein of claim 1, wherein said antigen-binding protein is a PD-1 agonist.

6. The antigen-binding protein of claim 1, wherein said antigen-binding protein is a PD-1 antagonist.

7. The antigen-binding protein of claim 1, wherein said antigen-binding protein is a chimeric antigen receptor (CAR).

8. A nucleic acid encoding an antigen-binding protein of any one of claims 1-7.

9. A vector comprising a nucleic acid of claim 8.

10. A cell comprising an antigen-binding protein of any one of claims 1-7, a nucleic acid of claim 8 or a vector of claim 9.

11. A pharmaceutical composition comprising an antigen-binding protein of any one of claims 1-7, a nucleic acid of claim 8, a vector of claim 9, a cell of claim 10.

12. Use of an antigen-binding protein or an antigen binding fragment thereof of any one of claims 1-7, a nucleic acid of claim 8, a vector of claim 9, a cell of claim 10, or a pharmaceutical composition of claim 11 in the manufacture of a medicament for treating cancer.

13. The use of claim 12, wherein the antigen-binding protein or antigen binding fragment thereof inhibits, reduces, modulates or abolishes signal transduction mediated by PD-1.

14. A vector comprising a nucleic acid encoding a recombinant anti-PD-1 antigen-binding protein as defined in any one of claims 1 to 7 and a nucleic acid encoding a chimeric antigen receptor, wherein said recombinant anti-PD-1 antigen-binding protein is not identical to said chimeric antigen receptor.

15. A cell comprising the vector of claim 14.

16. A cell comprising a nucleic acid encoding a recombinant anti-PD-1 antigen-binding protein as defined in any one of claims 1 to 7 and a nucleic acid encoding a chimeric antigen receptor, wherein said recombinant anti-PD-1 antigen-binding protein is not identical to said chimeric antigen receptor.

17. A cell comprising a recombinant anti-PD-1 antigen-binding protein as defined in any one of claims 1 to 7 and a chimeric antigen receptor, wherein said recombinant anti-PD-1 antigen-binding protein is not identical to said chimeric antigen receptor.

18. The vector or the cell of any one of claims 14-17, wherein the chimeric antigen receptor does not specifically bind to PD-1.

19. The vector or the cell of any one of claims 14-18, wherein the recombinant anti-PD-1 antigen-binding protein is an antibody.

20. The vector or the cell of any one of claims 14-19, wherein the recombinant anti-PD-1 antigen-binding protein is a human antibody.

21. The vector or the cell of any one of claims 14-20, wherein the recombinant anti-PD-1 antigen-binding protein is an intact Ig, Fab, F(ab')₂, Fv, or scFv.

22. The vector or the cell of any one of claims 14-21, wherein the recombinant anti-PD-1 antigen-binding protein is a PD-1 agonist.

23. The vector or the cell of any one of claims 14-21, wherein the recombinant anti-PD-1 antigen-binding protein is a PD-1 antagonist.

24. The vector or the cell of any one of claims 14-23, wherein the recombinant anti-PD-1 antigen-binding protein is a secretable protein.

25. The vector or the cell of any one of claims 14-24, wherein the chimeric antigen receptor specifically binds to CD-19.

26. The vector or the cell of any one of claims 14-25, wherein the chimeric antigen receptor can be inserted in a human T cell membrane.

27. The cell of any one of claims 14-26, wherein the cell is a T cell.

28. A pharmaceutical composition comprising a vector or a cell of any one of claims 14-27.

29. Use of a vector or cell of any one of claims 17-27, or a pharmaceutical composition of claim 28, in the manufacture of a medicament for treating cancer, wherein the recombinant anti-PD-1 antigen-binding protein is a PD-1 antagonist.

30. The use of claim 29, wherein the recombinant anti-PD-1 antigen-binding protein inhibits, reduces, modulates or abolishes signal transduction mediated by PD-1.

31. Use of a combination of a nucleic acid encoding a recombinant anti-PD-1 antigen-binding protein as defined in any one of claims 1 to 7 and a nucleic acid encoding a chimeric antigen receptor in the manufacture of a pharmaceutical for treating cancer, wherein the use comprises that at least one T cell of the subject is to be transduced with the medicament, wherein said recombinant anti-PD-1 antigen-binding protein is not identical to said chimeric antigen receptor.

32. The use of claim 31, wherein the chimeric antigen receptor does not specifically bind to PD-1.

33. The antigen-binding protein or an antigen binding fragment thereof of any one of claims 1-7, a nucleic acid of claim 8, a vector of claim 9, a cell of claim 10, a pharmaceutical composition of claim 11 or 31 or a vector or cell of any one of claims 14 and 18-26 for use in therapy.