

include peptide, cell, vector or DNA-based vaccines, administration of monoclonal antibodies (mAb) or expression of a DNA-encoded mAb against PSMA (Muthumani, K. *et al.*, *Cancer Immunol. Immunother.* 2017, 66: 1577) and chimeric antigen receptor (CAR)-modified T cells (Junghans, RP *et al.*, *Prostate*. 2016, 76: 1257). Despite the reported expression of PSMA in normal tissues, anti-PSMA toxicities were not observed in the Phase I clinical study using anti-PSMA CAR T cells.

[0007] Accordingly, there remains a need in the art for agents (such as polypeptide constructs) that target PSMA for the diagnosis and/or treatment of cancer. The present application addresses these and other needs.

[0008] The disclosures of all publications, patents, patent applications and published patent applications referred to herein are hereby incorporated herein by reference in their entirety.

SUMMARY

[0009] In some examples, provided is an anti-prostate specific membrane antigen (PSMA) construct comprising an antibody moiety specifically recognizing an extracellular domain of a cell surface-bound PSMA that comprises an amino acid sequence set forth in SEQ ID NO: 44. In some examples according to (or as applied to) any of the examples above, the PSMA is expressed on the surface of a cancer cell. In some examples according to (or as applied to) any of the examples above, the cancer cell is a prostate cancer cell, a renal cell cancer cell, a uterine cancer cell, or a liver cancer cell. In some examples according to (or as applied to) any of the examples above, the cancer cell is a prostate cancer cell. In some examples according to (or as applied to) any of the examples above, the prostate cancer cell is a hormone refractory prostate cancer cell or a metastatic prostate cancer cell. In some examples according to (or as applied to) any of the examples above, the cancer cell is a renal cancer cell. In some examples according to (or as applied to) any of the examples above, the renal cancer cell is a clear cell renal cell carcinoma (CCRCC) cell. In some examples according to (or as applied to) any of the examples above, the PSMA is expressed on the surface of a cell selected from the group consisting of: LNCaP, MDA PCa 2b, VCaP, 22Rv1, Caki-1; HCC1482; and HuH-7.

In one aspect, the present disclosure refers to an anti-prostate specific membrane antigen (PSMA) construct comprising an anti-PSMA antibody moiety specifically recognizing an extracellular domain of a cell surface-bound PSMA, wherein the anti-PSMA antibody moiety comprises a) a heavy chain variable domain (V_H) comprising a heavy chain complementarity determining region (CDR-H) 1 comprising the amino acid sequence of SEQ ID NO: 1, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 3, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 5, and a light chain variable domain (V_L) comprising a light chain complementarity determining region (CDR-L) 1 comprising the amino acid sequence of SEQ ID NO: 7, a CDR-L2 comprising the amino acid sequence GNS, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 9; or b) a V_H comprising a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 2, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 4, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 6, and a V_L comprising a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 8, a CDR-L2 comprising the amino acid sequence SNN, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 10.

[0010] In one example, the present disclosure refers to an anti-prostate specific membrane antigen (PSMA) construct comprising an anti-PSMA antibody moiety specifically recognizing an extracellular domain of a cell surface-bound PSMA that comprises an amino acid sequence set forth in SEQ ID NO: 44, wherein the anti-PSMA antibody moiety comprises: i) a heavy chain variable domain (V_H) comprising a CDR-H1 comprising the amino acid sequence of any one of SEQ ID NOs: 1-2, or a variant thereof comprising up to about 5 amino acid substitutions, a CDR-H2 comprising the amino acid sequence of any one of SEQ ID NOs: 3-4, or a variant thereof comprising up to about 5 amino acid substitutions, and a CDR-H3 comprising the amino acid sequence of any one of SEQ ID NOs: 5-6, or a

variant thereof comprising up to about 5 amino acid substitutions; and ii) a light chain variable domain (V_L) comprising a CDR-L1 comprising the amino acid sequence of any one of SEQ ID NOs: 7-8, or a variant thereof comprising up to about 5 amino acid substitutions, a CDR-L2 comprising the amino acid sequence GNS or SSN, or a variant thereof comprising about 2 amino acid substitutions, and a CDR-L3 comprising the amino acid sequence of any one of SEQ ID NOs: 9-10, or a variant thereof comprising up to about 5 amino acid substitutions. In some examples according to (or as applied to) any of the examples above, the antibody moiety comprises: i) a heavy chain variable domain (V_H) comprising a CDR-H1 comprising the amino acid sequence of any one of SEQ ID NOs: 1-2, or a variant thereof comprising up to about 5 amino acid substitutions, a CDR-H2 comprising the amino acid sequence of any one of SEQ ID NOs: 3-4, or a variant thereof comprising up to about 5 amino acid substitutions, and a CDR-H3 comprising the amino acid sequence of any one of SEQ ID NOs: 5-6, or a variant thereof comprising up to about 5 amino acid substitutions; and ii) a light chain variable domain (V_L) comprising a CDR-L1 comprising the amino acid sequence of any one of SEQ ID NOs: 7-8, or a variant thereof

comprising up to about 5 amino acid substitutions, a CDR-L2 comprising the amino acid sequence GNS or SSN, or a variant thereof comprising about 2 amino acid substitutions, and a CDR-L3 comprising the amino acid sequence of any one of SEQ ID NOs: 9-10, or a variant thereof comprising up to about 5 amino acid substitutions. In some examples according to (or as applied to) any of the examples above, the antibody moiety comprises: i) a V_H comprising a CDR-H1 comprising the amino acid sequence of any one of SEQ ID NOs: 1-2, a CDR-H2 comprising the amino acid sequence of any one of SEQ ID NOs: 3-4, and a CDR-H3 comprising the amino acid sequence of any one of SEQ ID NOs: 5-6; and ii) a V_L comprising a CDR-L1 comprising the amino acid sequence of any one of SEQ ID NOs: 7-8, a CDR-L2 comprising the amino acid sequence of GNS or SNN, and a CDR-L3 comprising the amino acid sequence of any one of SEQ ID NOs: 9-10. In some examples according to (or as applied to) any of the examples above, the antibody moiety comprises i) a V_H comprising a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 1, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 3, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 5; and ii) a light chain variable domain (V_L) comprising a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 7, a CDR-L2 comprising the amino acid sequence GNS, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 9. In some examples according to (or as applied to) any of the examples above, the antibody moiety comprises i) a V_H comprising a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 2, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 4, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 6; and ii) a V_L comprising a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 8, a CDR-L2 comprising the amino acid sequence SNN, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 10.

[0011] In one example, the present disclosure refers to an anti-PSMA construct comprising an anti-PSMA antibody moiety specifically recognizing an extracellular domain of a cell surface-bound PSMA that comprises an amino acid sequence set forth in SEQ ID NO: 44, wherein the anti-PSMA antibody moiety comprises a CDR-H1, a CDR-H2, and a CDR-H3 of a V_H set forth in SEQ ID NO: 16 or 17 and a CDR-L1, a CDR-L2, and a CDR-L3 of a V_L set forth in SEQ ID NO: 18 or 19. In some examples according to (or as applied to) any of the examples above, the antibody moiety comprises a CDR-H1, a CDR-H2, and a CDR-H3 of a heavy chain variable domain (V_H) set forth in SEQ ID NO: 16 or 17 and a CDR-L1, a CDR-L2, and a CDR-L3 of a light chain variable domain (V_L) set forth in SEQ ID NO: 18 or 19. In some examples according to (or as applied to) any of the examples above, the antibody moiety comprises the CDR-H1, CDR-H2, and CDR-H3 of the V_H set forth in SEQ ID NO: 16 and the CDR-L1, the CDR-L2, and the CDR-L3 of the V_L set forth in SEQ ID NO: 18. In some examples according to (or as applied to) any of the examples above, the antibody moiety comprises the CDR-H1, CDR-H2, and CDR-H3 of the V_H set forth in SEQ ID NO: 17 and the CDR-L1, the CDR-L2, and the CDR-L3 of the V_L set forth in SEQ ID NO: 19. In some examples according to (or as applied to) any of the examples above, the antibody moiety comprises: i) a V_H comprising an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 16 or 17 and ii) a V_L comprising an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 18 or 19. In some examples

according to (or as applied to) any of the examples above, the antibody moiety comprises: i) a V_H comprising an amino acid sequence having at least about 90% sequence identity to SEQ ID NO: 16 or 17 and ii) a V_L comprising an amino acid sequence having at least about 90% sequence identity to SEQ ID NO: 18 or 19. In some examples according to (or as applied to) any of the examples above, the antibody moiety comprises: i) a V_H comprising an amino acid sequence having at least about 95% sequence identity to SEQ ID NO: 16 or 17 and ii) a V_L comprising an amino acid sequence having at least about 95% sequence identity to SEQ ID NO: 18 or 19. In some examples according to (or as applied to) any of the examples above, the antibody moiety comprises: a V_H comprising an amino acid sequence of SEQ ID NO: 16 and a V_L comprising the amino acid sequence of SEQ ID NO: 18. In some examples according to (or as applied to) any of the examples above, the antibody moiety comprises: a V_H comprising an amino acid sequence of SEQ ID NO: 17; and a V_L comprising the amino acid sequence of SEQ ID NO: 19. In one example, the present disclosure refers to an anti-PSMA construct comprising an anti-PSMA antibody moiety specifically recognizing an extracellular domain of a cell surface-bound PSMA that comprises an amino acid sequence set forth in SEQ ID NO: 44, wherein the anti-PSMA antibody moiety comprises: i) a V_H comprising the amino acid sequences of SEQ ID NOs: 1, 3, and 5, and a V_L comprising the amino acid sequences of SEQ ID NO: 7, GNS, and SEQ ID NO: 9; or ii) a V_H comprising the amino acid sequences of SEQ ID NOs: 2, 4, and 6, and a V_L comprising the amino acid sequences of SEQ ID NO: 8, SSN, and SEQ ID NO: 10. In some examples according to (or as applied to) any of the examples above, the antibody moiety comprises: i) a heavy chain variable domain (V_H) comprising the amino acid sequences of SEQ ID NOs: 1, 3, and 5, and a light chain variable domain (V_L) comprising the amino acid sequence of SEQ ID NO: 7, GNS, and SEQ ID NO: 9; or ii) a V_H comprising the amino acid sequences of SEQ ID NOs: 2, 4, and 6, and a V_L comprising the amino acid sequence of SEQ ID NO: 8, SSN, and SEQ ID NO: 10.

[0012] In some examples according to (or as applied to) any of the examples above, the antibody moiety specifically recognizing PSMA is chimeric, human, partially humanized, fully humanized, or semi-synthetic. In some examples according to (or as applied to) any of the examples above, the antibody moiety specifically recognizing PSMA is a full-length antibody, a Fab, a Fab', a F(ab')₂, an Fv, or a single chain Fv (scFv). In some examples according to (or as applied to) any of the examples above antibody moiety specifically recognizing PSMA is an scFv. In some examples according to (or as applied to) any of the examples above, the scFv comprises an amino acid sequence set forth in SEQ ID NO: 20. In some examples according to (or as applied to) any of the examples above, the scFv comprises an amino acid sequence set forth in SEQ ID NO: 21. In some examples according to (or as applied to) any of the examples above, the antibody moiety specifically recognizing PSMA is a Fab or Fab'. In some examples according to (or as applied to) any of the examples above, the antibody moiety specifically recognizing PSMA is fused to an Fc fragment optionally via a linker. In some examples according to (or as applied to) any of the examples above, the Fc fragment is a human IgG Fc fragment. In some examples according to (or as applied to) any of the examples above, the human IgG is an IgG1, IgG2, IgG3, or IgG4. In some examples according to (or as applied to) any of the examples above, the anti-PSMA antibody moiety is a full-length antibody. In some examples according to (or as applied to) any of the examples above, the full-length antibody

CLAIMS

1. An anti-prostate specific membrane antigen (PSMA) construct comprising an anti-PSMA antibody moiety specifically recognizing an extracellular domain of a cell surface-bound PSMA, wherein the anti-PSMA antibody moiety comprises

a) a heavy chain variable domain (V_H) comprising a heavy chain complementarity determining region (CDR-H) 1 comprising the amino acid sequence of SEQ ID NO: 1, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 3, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 5, and a light chain variable domain (V_L) comprising a light chain complementarity determining region (CDR-L) 1 comprising the amino acid sequence of SEQ ID NO: 7, a CDR-L2 comprising the amino acid sequence GNS, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 9; or

b) a V_H comprising a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 2, a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 4, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 6, and a V_L comprising a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 8, a CDR-L2 comprising the amino acid sequence SNN, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 10.

2. The anti-PSMA construct of claim 1, wherein the anti-PSMA antibody moiety comprises:

i) a V_H comprising the amino acid sequence of SEQ ID NO: 16, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 16, and a V_L comprising the amino acid sequence of SEQ ID NO: 18, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 18;

ii) a V_H comprising the amino acid sequence of SEQ ID NO: 17, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 17, and a V_L comprising the amino acid sequence of SEQ ID NO: 19, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 19;

iii) a V_H comprising the amino acid sequence of SEQ ID NO: 16, and a V_L comprising the amino acid sequence of SEQ ID NO: 18; or

iv) a V_H comprising the amino acid sequence of SEQ ID NO: 17, and a V_L comprising the amino acid sequence of SEQ ID NO: 19.

3. The anti-PSMA construct of claim 1 or 2, wherein the anti-PSMA antibody moiety is chimeric, human, partially humanized, fully humanized, or semi-synthetic.

4. The anti-PSMA construct of any one of claims 1-3, wherein the anti-PSMA antibody moiety is a full-length antibody, a Fab, a Fab', a $F(ab')_2$, an Fv, or a single chain Fv (scFv).

5. The anti-PSMA construct of claim 4, wherein the anti-PSMA antibody moiety is an anti-PSMA scFv.
6. The anti-PSMA construct of claim 5, wherein the anti-PSMA scFv comprises:
 - i) the amino acid sequence of SEQ ID NO: 20, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 20; or
 - ii) the amino acid sequence of SEQ ID NO: 21, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 21.
7. The anti-PSMA construct of claim 4, wherein the anti-PSMA antibody moiety is a full-length anti-PSMA antibody.
8. The anti-PSMA construct of claim 7, wherein the full-length anti-PSMA antibody comprises:
 - i) a heavy chain comprising the amino acid sequence of SEQ ID NO: 39, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 39, and a light chain comprising the amino acid sequence of SEQ ID NO: 40, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 40; or
 - ii) a heavy chain comprising the amino acid sequence of SEQ ID NO: 41, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 41, and a light chain comprising the amino acid sequence of SEQ ID NO: 42, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 42.
9. The anti-PSMA construct of any one of claims 1-8, wherein the anti-PSMA construct is monospecific.
10. The anti-PSMA construct of any one of claims 1-8, wherein the anti-PSMA construct is multispecific.
11. The anti-PSMA construct of claim 10, wherein the anti-PSMA construct is bispecific.
12. The anti-PSMA construct of claim 10 or 11, wherein the anti-PSMA construct is a tandem scFv, a diabody (Db), a single chain diabody (scDb), a dual-affinity retargeting (DART) antibody, a F(ab')₂, a dual variable domain (DVD) antibody, a knob-into-hole (KiH) antibody, a dock and lock (DNL) antibody, a chemically cross-linked antibody, a heteromultimeric antibody, or a heteroconjugate antibody.
13. The anti-PSMA construct of any one of claims 10-12, wherein the anti-PSMA construct further comprises a second antibody moiety specifically recognizing a second antigen.

14. The anti-PSMA construct of claim 13, wherein the second antigen is an antigen on the surface of a B cell, a natural killer cell, a dendritic cell, a macrophage, a monocyte, a neutrophil, or a T cell.
15. The anti-PSMA construct of claim 13, wherein the second antigen is an antigen on the surface of a T cell.
16. The anti-PSMA construct of claim 15, wherein the antigen on the surface of the T cell is selected from the group consisting of CD3 γ , CD3 δ , CD3 ϵ , CD3 ζ , CD28, OX40, GITR, CD137, CD27, CD40L, and HVEM.
17. The anti-PSMA construct of any one of claims 1-13, wherein the anti-PSMA construct is an anti-PSMA chimeric antigen receptor (CAR) comprising:
- (a) an extracellular domain comprising the anti-PSMA antibody moiety;
 - (b) a transmembrane domain; and
 - (c) an intracellular signaling domain.
18. The anti-PSMA construct of claim 17, wherein the intracellular signaling domain comprises a primary immune cell signaling sequence derived from CD3 ζ , TCR ζ , FcR γ , FcR β , CD3 γ , CD3 δ , CD3 ϵ , CD5, CD22, CD79a, CD79b, or CD66d.
19. The anti-PSMA construct of claim 18, wherein the intracellular signaling domain further comprises a costimulatory signaling sequence derived from CD27, CD28, 4-1BB, ICOS, OX40, CD30, CD40, PD-1, lymphocyte function-associated antigen-1 (LFA-1), CD2, CD7, LIGHT, NKG2C, B7-H3, or a ligand that specifically binds with CD83.
20. The anti-PSMA construct of claim 18 or 19, wherein the intracellular signaling domain comprises a primary immune cell signaling sequence derived from CD3 ζ and a costimulatory signaling sequence derived from CD28.
21. The anti-PSMA construct of any one of claims 17-20, wherein the anti-PSMA CAR comprises:
- i) the amino acid sequence of SEQ ID NO: 29, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 29; or
 - ii) the amino acid sequence of SEQ ID NO: 30, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 30.
22. The anti-PSMA construct of any one of claims 1-13, wherein the anti-PSMA construct is an anti-PSMA chimeric antibody T-cell receptor (TCR) (caTCR) comprising:
- (a) an extracellular domain comprising the anti-PSMA antibody moiety; and

(b) a TCR module (TCRM), wherein the TCRM comprises a first TCR domain (TCRD) comprising a first TCR transmembrane domain (TCR-TM) and a second TCRD comprising a second TCR-TM, wherein the TCRM facilitates recruitment of at least one TCR-associated signaling molecule.

23. The anti-PSMA construct of claim 22, wherein:

- i) the first TCR-TM is derived from TCR γ and the second TCR-TM is derived from TCR δ ; or
- ii) the first TCR-TM is derived from TCR δ and the second TCR-TM is derived from TCR γ .

24. The anti-PSMA construct of claim 22, wherein:

- i) the first TCR-TM is derived from TCR α and the second TCR-TM is derived from TCR β ; or
- ii) the first TCR-TM is derived from TCR β and the second TCR-TM is derived from TCR α .

25. The anti-PSMA construct of any one of claims 22-24, wherein the anti-PSMA construct comprises:

- i) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 31, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 31, and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 32, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 32;

- ii) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 34, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 34, and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 35, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 35;

- iii) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 165, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 165, and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 166, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 166;

- iv) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 167, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 167, and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 168, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 168;

- v) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 169, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 169, and a

second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 170, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 170;

vi) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 171, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 171, and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 172, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 172;

vii) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 173, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 173, and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 174, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 174;

viii) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 175, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 175, and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 176, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 176;

ix) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 177, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 177, and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 178, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 178; or

x) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 179, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 179, and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 180, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 180.

26. The anti-PSMA construct of any one of claims 22-25, wherein the TCR-associated signaling molecule is selected from the group consisting of CD3 $\delta\epsilon$, CD3 $\gamma\epsilon$, and CD3 $\zeta\zeta$.

27. The anti-PSMA construct of any one of claims 22-26, wherein the caTCR lacks a functional primary immune cell signaling domain.

28. The anti-PSMA construct of any one of claims 1-13, wherein the anti-PSMA construct is an anti-PSMA chimeric signaling receptor (CSR) comprising:

- (a) a ligand-binding module comprising the anti-PSMA antibody moiety;
- (b) a transmembrane module; and
- (c) a co-stimulatory immune cell signaling module,

wherein the CSR lacks a functional primary immune cell signaling domain.

29. The anti-PSMA construct of claim 28, wherein the CSR lacks any primary immune cell signaling sequences.

30. The anti-PSMA construct of claim 28 or 29, wherein the transmembrane module of the CSR and the co-stimulatory immune cell signaling module of the CSR are derived from the same molecule.
31. The anti-PSMA construct of claim 28 or 29, wherein the transmembrane module of the CSR and the co-stimulatory immune cell signaling module of the CSR are derived from different molecules.
32. The anti-PSMA construct of claim 30 or 31, wherein the molecule is selected from the group consisting of CD28, 4-1BB (CD137), OX40, CD30, CD27, CD40, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1), CD2, CD7, LIGHT, NKG2C, B7-H3, and a ligand that specifically binds with CD83.
33. The anti-PSMA construct of any one of claims 28-32, wherein the transmembrane module of the CSR comprises:
- i) a transmembrane domain derived from CD28, CD3 ϵ , CD3 ζ , CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD27, CD30, CD33, CD37, CD64, CD80, CD86, CD134, CD137, CD154, 4-1BB, OX40, or the α , β , δ , γ , or ζ chain of a TCR; and/or
 - ii) the amino acid sequence of any one of SEQ ID NOs: 94-99, or an amino acid sequence having at least about 85% sequence identity to any one of SEQ ID NOs: 94-99.
34. The anti-PSMA construct of any one of claims 28-33, wherein the co-stimulatory immune cell signaling module of the CSR is derived from the intracellular domain of a co-stimulatory receptor of a TCR.
35. The anti-PSMA construct of claim 34, wherein the co-stimulatory immune cell signaling module of the CSR:
- i) is derived from a molecule selected from the group consisting of 4-1BB, CD27, CD28, CD30, OX40, ICOS, CD40; and/or
 - ii) comprises the amino acid sequence of any one of SEQ ID NOs: 100-103 and 183, or an amino acid sequence having at least about 85% sequence identity to any one of SEQ ID NOs: 100-103 and 183.
36. The anti-PSMA construct of claim 28 or 29, wherein the anti-PSMA CSR comprises the amino acid sequence of any one of SEQ ID NOs: 37, 38, 51-84, 93, and 184-186, or an amino acid sequence having at least about 85% sequence identity to any one of SEQ ID NOs: 37, 38, 51-84, 93, and 184-186.
37. The anti-PSMA construct of any one of claims 28-36, wherein the anti-PSMA construct further comprises a signal peptide.

38. The anti-PSMA construct of claim 37, wherein the signal peptide comprises the amino acid sequence of SEQ ID NO: 128.

39. The anti-PSMA construct of any one of claims 1-15, wherein the anti-PSMA construct is conjugated to an effector molecule, and wherein the effector molecule is a detectable label or a therapeutic agent selected from the group consisting of: a drug, a toxin, a radioisotope, a protein, a peptide, and a nucleic acid.