

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.

[0010] 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 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 aspect, 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 aspect, 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

comprises a heavy chain comprising an amino acid sequence set forth in SEQ ID NO: 39 and a light chain comprising an amino acid sequence set forth in SEQ ID NO: 40. In some examples according to (or as applied to) any of the examples above, the full-length antibody comprises a heavy chain comprising an amino acid sequence set forth in SEQ ID NO: 41 and a light chain comprising an amino acid sequence set forth in SEQ ID NO: 42. In some examples according to (or as applied to) any of the examples above, the anti-PSMA construct is monospecific. In some examples according to (or as applied to) any of the examples above the anti-PSMA construct is multispecific. In some examples according to (or as applied to) any of the examples above the anti-PSMA construct is bispecific. In some examples according to (or as applied to) any of the examples above 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.

[0013] In some examples according to (or as applied to) any of the examples above the anti-PSMA construct is a tandem scFv comprising two scFvs linked by a peptide linker. In some examples according to (or as applied to) any of the examples above the anti-PSMA construct further comprises a second antibody moiety specifically recognizing a second antigen. In some examples according to (or as applied to) any of the examples above, the second antigen is an antigen on the surface of a T cell. In some examples according to (or as applied to) any of the examples above, the T cell is selected from the group consisting of a cytotoxic T cell, a helper T cell, and a natural killer T cell. In some examples according to (or as applied to) any of the examples above, the second antigen is selected from the group consisting of CD3 γ , CD3 δ , CD3 ϵ , CD3 ζ , CD28, OX40, GITR, CD137, CD27, CD40L, and HVEM. In some examples according to (or as applied to) any of the examples above, the second antigen is CD3 ϵ . In some examples according to (or as applied to) any of the examples above, the anti-PSMA construct is a tandem scFv comprising an N-terminal scFv specifically recognizing PSMA and a C-terminal scFv specifically recognizing CD3 ϵ . In some examples according to (or as applied to) any of the examples above, the anti-PSMA construct comprises an amino acid sequence set forth in SEQ ID NO: 25 or 26. In some examples according to (or as applied to) any of the examples above, the anti-PSMA construct comprises an amino acid sequence set forth in SEQ ID NO: 27 or 28. In some examples according to (or as applied to) any of the examples above, the expression of the anti-PSMA construct is induced by the activation of an engineered T cell. In some examples according to (or as applied to) any of the examples above, the engineered T cell is a T cell comprising a chimeric antigen receptor (CAR). In some examples according to (or as applied to) any of the examples above, the CAR specifically binds to PSMA. In some examples

according to (or as applied to) any of the examples above, the CAR binds to an antigen other than PSMA. In some examples according to (or as applied to) any of the examples above, the engineered T cell is a T cell comprising a chimeric antibody-T cell receptor (TCR) construct (caTCR). In some examples according to (or as applied to) any of the examples above, the caTCR specifically binds to PSMA. In some examples according to (or as applied to) any of the examples above, the caTCR binds to an antigen other than PSMA. In some examples according to (or as applied to) any of the examples above, the second antigen bound by the second antibody moiety of the anti-PSMA construct is an antigen on the surface of a B cell, a natural killer cell, a dendritic cell, a macrophage, a monocyte, or a neutrophil.

[0014] In some examples according to (or as applied to) any of the examples above, the anti-PSMA construct is a CAR comprising: (a) an extracellular domain comprising the anti-PSMA antibody moiety; (b) a transmembrane domain; and (c) an intracellular signaling domain. In some examples according to (or as applied to) any of the examples above, 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. In some examples according to (or as applied to) any of the examples above, the intracellular signaling domain further comprises a costimulatory signaling sequence derived from CD28, 4-1BB, ICOS, or OX40. In some examples according to (or as applied to) any of the examples above, the intracellular signaling domain comprises a CD3 ζ intracellular signaling sequence and a CD28 intracellular signaling sequence. In some examples according to (or as applied to) any of the examples above, the anti-PSMA construct comprises an amino acid sequence set forth in SEQ ID NO: 29. In some examples according to (or as applied to) any of the examples above, the anti-PSMA construct comprises an amino acid sequence set forth in SEQ ID NO: 30.

[0015] In some examples according to (or as applied to) any of the examples above, the anti-PSMA construct is a caTCR comprising: (a) an extracellular domain comprising the anti-PSMA antibody moiety; and (b) a T cell receptor module (TCRM) comprising 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. In some examples according to (or as applied to) any of the examples above, the first TCR-TM is derived from one of the transmembrane domains of a first naturally occurring TCR and the second TCR-TM is derived from the other transmembrane domain of the first naturally occurring TCR. In some examples according to (or as applied to) any of the examples above, the at least one of the TCR-TMs is non-naturally occurring. In some examples according to (or as applied to) any of the examples above, the TCRM comprising the at least one non-naturally

occurring TCR-TM allows for enhanced recruitment of the at least one TCR-associated signaling molecule as compared to a TCRM comprising the first naturally occurring T cell receptor transmembrane domains. In some examples according to (or as applied to) any of the examples above, the first and second TCR-TMs are naturally occurring. In some examples according to (or as applied to) any of the examples above, the first naturally occurring TCR is a γ/δ TCR. In some examples according to (or as applied to) any of the examples above, the anti-PSMA construct comprises a first polypeptide chain comprising an amino acid sequence set forth in SEQ ID NO: 31 and a second polypeptide chain comprising an amino acid sequence set forth in SEQ ID NO: 32. In some examples according to (or as applied to) any of the examples above, the anti-PSMA construct comprises a first polypeptide chain comprising an amino acid sequence set forth in SEQ ID NO: 34 and a second polypeptide chain comprising an amino acid sequence set forth in SEQ ID NO: 35. In some examples according to (or as applied to) any of the examples above, the first naturally occurring TCR is an α/β TCR. In some examples according to (or as applied to) any of the examples above, the TCR-associated signaling molecule is selected from the group consisting of CD3 $\delta\epsilon$, CD3 $\gamma\epsilon$, and CD3 $\zeta\zeta$. In some examples according to (or as applied to) any of the examples above, the caTCR lacks a functional primary immune cell signaling domain. In some examples according to (or as applied to) any of the examples above, the caTCR lacks any primary immune cell signaling sequences.

[0016] In some examples according to (or as applied to) any of the examples above, the anti-PSMA construct is a chimeric signaling receptor (CSR) comprising: i) a ligand-binding module that is capable of binding or interacting with PSMA; ii) a transmembrane module; and iii) a co-stimulatory immune cell signaling module that is capable of providing a co-stimulatory signal to the effector cell, wherein the ligand-binding module and the co-stimulatory immune cell signaling module are not derived from the same molecule, and wherein the CSR lacks a functional primary immune cell signaling domain. In some examples according to (or as applied to) any of the examples above, the CSR lacks any primary immune cell signaling sequences. In some examples according to (or as applied to) any of the examples above, the ligand-binding module comprises the anti-PSMA construct as disclosed herein. In some examples according to (or as applied to) any of the examples above, the transmembrane module of the CSR comprises transmembrane domains derived from CD28, CD3 ϵ , CD3 ζ , CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD137, or CD154. In some examples according to (or as applied to) any of the examples above, the co-stimulatory immune cell signaling module is derived from the intracellular domain of a co-stimulatory receptor of a TCR. In some examples according to (or as applied to) any of the examples above, the co-stimulatory receptor is selected from the group consisting of CD28, 4-1BB, OX40, ICOS, CD27, and CD40. In some examples according to (or

as applied to) any of the examples above, the expression of the CSR is inducible upon activation of an engineered T cell. In some examples according to (or as applied to) any of the examples above, the engineered T cell is a T cell comprising a CAR. In some examples according to (or as applied to) any of the examples above, the CAR specifically binds to PSMA. In some examples according to (or as applied to) any of the examples above, the CAR binds to an antigen other than PSMA. In some examples according to (or as applied to) any of the examples above, the engineered T cell is a T cell comprising a caTCR. In some examples according to (or as applied to) any of the examples above, the caTCR specifically binds to PSMA. In some examples according to (or as applied to) any of the examples above, the caTCR binds to an antigen other than PSMA. In some examples according to (or as applied to) any of the examples above, the anti-PSMA construct comprises an amino acid sequence set forth in SEQ ID NO 37. In some examples according to (or as applied to) any of the examples above, the anti-PSMA construct comprises an amino acid sequence set forth in SEQ ID NO 38.

[0017] In some examples according to (or as applied to) any of the examples above, the anti-PSMA construct is conjugated to an effector molecule. In some examples according to (or as applied to) any of the examples above, the effector molecule is a therapeutic agent selected from the group consisting of: a drug, a toxin, a radioisotope, a protein, a peptide, and a nucleic acid. In some examples according to (or as applied to) any of the examples above, the therapeutic agent is a drug or a toxin. In some examples according to (or as applied to) any of the examples above, the effector molecule is a detectable label.

[0018] In another example of the current disclosure, provided is an effector cell that has been genetically modified with one or more nucleic acids encoding the anti-PSMA CAR according to (or as applied to) any of the examples above or the anti-PSMA caTCR according to (or as applied to) any of the examples above. In some examples according to (or as applied to) any of the examples above, the one or more nucleic acids encoding the anti-PSMA CAR or anti-PSMA caTCR also encode a CSR comprising a ligand binding module that binds a target antigen. In some examples according to (or as applied to) any of the examples above, the effector cell has been genetically modified with one or more additional nucleic acids encoding a CSR comprising a ligand binding module that binds a target antigen. In some examples according to (or as applied to) any of the examples above, the target antigen is PSMA. In some examples according to (or as applied to) any of the examples above, the target antigen is an antigen other than PSMA. In some examples according to (or as applied to) any of the examples above, the one or more nucleic acids encoding the anti-PSMA CAR or anti-PSMA caTCR also encode a tandem scFv that comprises a first scFv that binds a target antigen. In some examples according to (or as applied to) any of

the examples above, the effector cell has been genetically modified with one or more additional nucleic acids encoding a tandem scFv that comprises a first scFv that binds a target antigen. In some examples according to (or as applied to) any of the examples above, the target antigen is PSMA. In some examples according to (or as applied to) any of the examples above, the target is an antigen other than PSMA. In some examples according to (or as applied to) any of the examples above, provided is an effector cell that has been genetically modified with one or more nucleic acids encoding the anti-PSMA tandem scFv according to (or as applied to) any of the examples above or the anti-PSMA CSR according to (or as applied to) any of the examples above. In some examples according to (or as applied to) any of the examples above, the one or more nucleic acids encoding the anti-PSMA tandem scFv or anti-PSMA CSR also encode a CAR. In some examples according to (or as applied to) any of the examples above, the effector cell has been genetically modified with one or more additional nucleic acids encoding a CAR. In some examples according to (or as applied to) any of the examples above, the CAR specifically binds PSMA. In some examples according to (or as applied to) any of the examples above, the CAR specifically binds an antigen other than PSMA. In some examples according to (or as applied to) any of the examples above, the one or more nucleic acids encoding the anti-PSMA tandem scFv or anti-PSMA CSR also encode a caTCR. In some examples according to (or as applied to) any of the examples above, the effector cell has been genetically modified with one or more additional nucleic acids encoding a caTCR. In some examples according to (or as applied to) any of the examples above, the caTCR specifically binds PSMA. In some examples according to (or as applied to) any of the examples above, the caTCR specifically binds an antigen other than PSMA. In some examples according to (or as applied to) any of the examples above, the effector cell is an immune cell. In some examples according to (or as applied to) any of the examples above, the immune cell is a T cell. In some examples according to (or as applied to) any of the examples above, the T cell is a cytotoxic T cell, a helper T cell, or a natural killer T cell.

[0019] In another example of the current disclosure, provided is a method of producing an effector cell, comprising genetically modifying a cell with one or more nucleic acids encoding the anti-PSMA CAR according to (or as applied to) any of the examples above, or the anti-PSMA caTCR according to (or as applied to) any of the examples above. In some examples according to (or as applied to) any of the examples above, the one or more nucleic acids encoding the anti-PSMA CAR or anti-PSMA caTCR also encode a CSR comprising a ligand binding module that binds a target antigen. In some examples according to (or as applied to) any of the examples above, the method comprises further genetically modifying the cell with one or more additional nucleic acids encoding a CSR comprising a ligand binding module that binds a target antigen. In some

examples according to (or as applied to) any of the examples above, the target antigen is PSMA. In some examples according to (or as applied to) any of the examples above, the target antigen is an antigen other than PSMA. In some examples according to (or as applied to) any of the examples above, the one or more nucleic acids encoding the anti-PSMA CAR or anti-PSMA caTCR also encode a tandem scFv that comprises a first scFv that binds a target antigen. In some examples according to (or as applied to) any of the examples above, the method comprises further genetically modifying the cell with one or more additional nucleic acids encoding a tandem scFv that comprises a first scFv that binds a target antigen. In some examples according to (or as applied to) any of the examples above, the target antigen is PSMA. In some examples according to (or as applied to) any of the examples above, the target is an antigen other than PSMA. In some examples according to (or as applied to) any of the examples above, provided is a method of producing an effector cell, comprising genetically modifying a cell with one or more nucleic acids encoding the anti-PSMA tandem scFv according to (or as applied to) any of the examples above, or the anti-PSMA CSR according to (or as applied to) any of the examples above. In some examples according to (or as applied to) any of the examples above, the one or more nucleic acids encoding the anti-PSMA tandem scFv or anti-PSMA CSR also encode a CAR. In some examples according to (or as applied to) any of the examples above, the method comprises further genetically modifying the cell with one or more additional nucleic acids encoding a CAR. In some examples according to (or as applied to) any of the examples above, the CAR specifically binds PSMA. In some examples according to (or as applied to) any of the examples above, the CAR specifically binds an antigen other than PSMA. In some examples according to (or as applied to) any of the examples above, the one or more nucleic acids encoding the anti-PSMA CAR or anti-PSMA caTCR also encode a caTCR. In some examples according to (or as applied to) any of the examples above, the method comprises further genetically modifying the cell with one or more additional nucleic acids encoding a caTCR. In some examples according to (or as applied to) any of the examples above, the caTCR specifically binds PSMA. In some examples according to (or as applied to) any of the examples above, the caTCR specifically binds an antigen other than PSMA. In some examples according to (or as applied to) any of the examples above, the effector cell is an immune cell. In some examples according to (or as applied to) any of the examples above, the immune cell is a T cell. In some examples according to (or as applied to) any of the examples above, the T cell is a cytotoxic T cell, a helper T cell, or a natural killer T cell.

[0020] In another example of the current disclosure, provided is nucleic acid encoding the polypeptide portion(s) of the anti-PSMA construct according to (or as applied to) any of the examples above. Also provided is a vector comprising the nucleic acid according to (or as applied

to) any of the examples above. Also provided is a host cell comprising the nucleic acid or the vector according to (or as applied to) any of the examples above.

[0021] Also provided is a method of producing the anti-PSMA construct according to (or as applied to) any of the examples above, comprising culturing the host cell according to (or as applied to) any of the examples above under conditions where the anti-PSMA construct is expressed, and recovering the anti-PSMA construct produced by the host cell.

[0022] In another example of the current disclosure, provided is a pharmaceutical composition comprising the anti-PSMA construct according to (or as applied to) any of the examples above, the effector cell according to (or as applied to) any of the examples above, the nucleic acid according to (or as applied to) any of the examples above, or the vector according to (or as applied to) any of the examples above, and a pharmaceutical acceptable carrier.

[0023] In another example of the current disclosure, provided is a kit comprising the anti-PSMA construct of according to (or as applied to) any of the examples above, the effector cell according to (or as applied to) any of the examples above, the nucleic acid according to (or as applied to) any of the examples above, the vector according to (or as applied to) any of the examples above and/or the host cell of according to (or as applied to) any of the examples above.

[0024] Another example of the current disclosure provides a method of detecting PSMA in a sample, comprising contacting the sample with the anti-PSMA construct according to (or as applied to) any of the examples above conjugated to a detectable label, and detecting the presence of the label. In some examples according to (or as applied to) any of the examples above, provided the sample comprises cells expressing PSMA.

[0025] Another example of the current disclosure provides a method of treating an individual having a PSMA-associated disease or disorder, comprising administering to the individual an effective amount of the pharmaceutical composition according to (or as applied to) any of the examples above. In some examples according to (or as applied to) any of the examples above, provided is a method of treating an individual having a PSMA-associated disease or disorder, comprising administering to the individual an effector cell that has been genetically modified with one or more nucleic acids that encode the anti-PSMA CAR according to (or as applied to) any of the examples above, or the anti-PSMA caTCR according to (or as applied to) any of the examples above. In some examples according to (or as applied to) any of the examples above, the method comprises genetically modifying the effector cell with the one or more nucleic acids prior to administration. In some examples according to (or as applied to) any of the examples above, the one or more nucleic acids that encode the anti-PSMA CAR or the anti-PSMA caTCR also encode a CSR or a tandem scFv. In some examples according to (or as applied to) any of the

examples above, the method comprises further genetically modifying the effector cell with one or more additional nucleic acids encoding a CSR or a tandem scFv. In some examples according to (or as applied to) any of the examples above, the tandem scFv specifically binds PSMA. In some examples according to (or as applied to) any of the examples above, the tandem scFv specifically binds an antigen other than PSMA. In some examples according to (or as applied to) any of the examples above, the CSR specifically binds PSMA. In some examples according to (or as applied to) any of the examples above, the CSR specifically binds an antigen other than PSMA. In some examples according to (or as applied to) any of the examples above, provided is a method of treating an individual having a PSMA-associated disease or disorder, comprising administering to the individual an effector cell that has been genetically modified with one or more nucleic acids that encode the anti-PSMA tandem scFv according to (or as applied to) any of the examples above, or anti-PSMA CSR according to (or as applied to) any of the examples above. In some examples according to (or as applied to) any of the examples above, the method comprises genetically modifying the effector cell with the one or more nucleic acids prior to administration. In some examples according to (or as applied to) any of the examples above, the one or more nucleic acids that encode the anti-PSMA CSR or anti-PSMA tandem scFv also encode a CAR or a caTCR. In some examples according to (or as applied to) any of the examples above, the method comprises further genetically modifying the effector cell with one or more additional nucleic acids encoding a CAR or a caTCR. In some examples according to (or as applied to) any of the examples above, the CAR specifically binds PSMA. In some examples according to (or as applied to) any of the examples above, the CAR specifically binds an antigen other than PSMA. In some examples according to (or as applied to) any of the examples above, the caTCR specifically binds PSMA. In some examples according to (or as applied to) any of the examples above, the caTCR specifically binds an antigen other than PSMA. In some examples according to (or as applied to) any of the examples above, the effector cell is an immune cell. In some examples according to (or as applied to) any of the examples above, the immune cell is a T cell. In some examples according to (or as applied to) any of the examples above, the T cell is a cytotoxic T cell, a helper T cell, or a natural killer T cell. In some examples according to (or as applied to) any of the examples above, the method further comprises obtaining an effector cell from an individual prior to genetically modifying and administering the effector cell. In some examples according to (or as applied to) any of the examples above, the individual from whom the effector cell is obtained is the individual to whom the genetically modified effector cell is administered. In some examples according to (or as applied to) any of the examples above, the individual from whom the effector cell is obtained is not the individual to whom the genetically modified effector cell is administered. In some

examples according to (or as applied to) any of the examples above, the genetically modified effector cell is allogenic with respect to the individual to whom the genetically modified effector cell is administered. In some examples according to (or as applied to) any of the examples above, the genetically modified effector cell is syngeneic with respect to the individual to whom the genetically modified effector cell is administered. In some examples according to (or as applied to) any of the examples above, the genetically modified effector cell is xenogeneic respect to the individual to whom the genetically modified effector cell is administered. In some examples according to (or as applied to) any of the examples above, the method of treating the individual having the PSMA-associated disease or disorder comprises administering an additional therapy to the individual. In some examples according to (or as applied to) any of the examples above, the PSMA-associated disease or disorder is cancer. In some examples according to (or as applied to) any of the examples above, the cancer is selected from the group consisting of: prostate cancer, renal cancer cell, uterine cancer, and liver cancer. In some examples according to (or as applied to) any of the examples above, the cancer is prostate cancer. In some examples according to (or as applied to) any of the examples above, the prostate cancer is hormone-refractory prostate cancer or metastatic prostate cancer. In some examples according to (or as applied to) any of the examples above, the cancer is renal cancer. In some examples according to (or as applied to) any of the examples above, the renal cancer is clear cell renal cell cancer (CCRCC). In some examples according to (or as applied to) any of the examples above, the individual having the PSMA-associated disease or disorder is a mammal. In some examples according to (or as applied to) any of the examples above, the mammal is a human.

[0026] Another example of the current disclosure provides a method of diagnosing an individual suspected of having a PSMA-associated disease or disorder, comprising: a) administering an effective amount of the anti-PSMA construct according to (or as applied to) any of the examples above conjugated to a detectable label to the individual; and b) determining the level of the label in the individual, wherein a level of the label above a threshold level indicates that the individual has the PSMA-associated disease or disorder. In some examples according to (or as applied to) any of the examples above, provided is a method of diagnosing an individual suspected of having a PSMA-associated disease or disorder, comprising: a) contacting a sample derived from the individual with the anti-PSMA construct according to (or as applied to) any of the examples above conjugated to a detectable label; and b) determining the number of cells bound with the anti-PSMA construct in the sample, wherein a value for the number of cells bound with the anti-PSMA construct above a threshold level indicates that the individual has the PSMA-associated disease or disorder. In some examples according to (or as applied to) any of the examples above, the PSMA-associated disease or disorder is cancer. In some examples according to (or as applied to) any of the

examples above, the cancer is selected from the group consisting of: prostate cancer, renal cancer cell, uterine cancer, and liver cancer. In some examples according to (or as applied to) any of the examples above, the cancer is prostate cancer. In some examples according to (or as applied to) any of the examples above, the prostate cancer is hormone-refractory prostate cancer or metastatic prostate cancer. In some examples according to (or as applied to) any of the examples above, the cancer is renal cancer. In some examples according to (or as applied to) any of the examples above, the renal cancer is clear cell renal cell cancer (CCRCC). In some examples according to (or as applied to) any of the examples above, the individual suspected of having a disease or disorder associated with expression, aberrant expression, and/or aberrant activity of PSMA is a mammal. In some examples according to (or as applied to) any of the examples above, the mammal is a human.

BRIEF DESCRIPTION OF THE DRAWINGS

[0027] FIG. 1 shows the results of flow cytometry experiments that were performed to assess the binding phage clones A and B to PSMA-positive and PSMA-negative cells.

[0028] FIG. 2 shows the results experiments that were performed to assess specific killing of target cells by T cells expressing a CAR comprising an scFv moiety derived from Clone A or Clone B.

[0029] FIG. 3 shows the results experiments that were performed to assess specific IFN gamma release by T cells expressing a CAR comprising an scFv moiety derived from Clone A or Clone B.

[0030] FIG. 4 provides a schematic depiction of an exemplary caTCR. The Fab fragment is derived from Clone A or Clone B.

[0031] FIG. 5 shows the results of flow cytometry experiments confirming that Clone A and Clone B can be used in multiple receptor configurations (e.g., CAR or caTCR + CSR) to stimulate T-cell proliferation in response to antigen.

[0032] FIG. 6 shows the results of experiments performed to assess the specific killing of three PSMA⁺ target cell lines by T cells expressing Clone A and/or Clone B in different anti-PSMA construct configurations and construct combinations.

[0033] FIG. 7 shows the results of additional experiments performed to assess the specific killing of three PSMA⁺ target cell lines by T cells expressing Clone A and/or Clone B in different anti-PSMA construct configurations and construct combinations.

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 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.

2. The anti-PSMA construct of claim 1, wherein the anti-PSMA 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.

3. 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.

4. The anti-PSMA construct of claim 3, wherein the anti-PSMA antibody moiety comprises: (a) 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; or

(b) 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.

5. 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.

6. The anti-PSMA construct of any one of claims 1-5, wherein the anti-PSMA antibody moiety comprises

a) 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 a 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; 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.

7. The anti-PSMA construct of any one of claims 1-6, wherein the anti-PSMA antibody moiety comprises:

i) a V_H comprising the amino acid sequence of SEQ ID NO: 16 or 17, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 16 or 17, and a V_L comprising the amino acid sequence of SEQ ID NO: 18 or 19, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 18 or 19;

ii) 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;

iii) 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;

iv) 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

v) 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.

8. The anti-PSMA construct of any one of claims 1-8, wherein the anti-PSMA antibody moiety is chimeric, human, partially humanized, fully humanized, or semi-synthetic.

9. The anti-PSMA construct of any one of claims 1-8, 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).

10. The anti-PSMA construct of claim 9, wherein the anti-PSMA antibody moiety is an scFv.

11. The anti-PSMA construct of claim 10, wherein the scFv comprises:

i) the amino acid sequence set forth in 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 set forth in SEQ ID NO: 21, or an amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 21.

12. The anti-PSMA construct of claim 9, wherein the anti-PSMA construct is a full-length antibody.

13. The anti-PSMA construct of claim 12, wherein the full-length antibody comprises:

i) a V_H 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 V_L comprising the amino acid sequence of SEQ ID NO: 40, or amino acid sequence having at least about 85% sequence identity to SEQ ID NO: 40; or

ii) a V_H 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 V_L 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.

14. The anti-PSMA construct of any one of claims 1-13, wherein the anti-PSMA construct is monospecific.

15. The anti-PSMA construct of any one of claims 1-13, wherein the anti-PSMA construct is multispecific.

16. The anti-PSMA construct of claim 15, wherein the anti-PSMA construct is bispecific.

17. The anti-PSMA construct of claim 15 or 16, 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.
18. The anti-PSMA construct of any one of claims 15-17, wherein the anti-PSMA construct further comprises a second antibody moiety specifically recognizing a second antigen.
19. The anti-PSMA construct of claim 18, 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.
20. The anti-PSMA construct of claim 19, 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.
21. The anti-PSMA construct of any one of claims 1-11, wherein the anti-PSMA construct is a CAR comprising:
- (a) an extracellular domain comprising the anti-PSMA antibody moiety;
 - (b) a transmembrane domain; and
 - (c) an intracellular signaling domain.
22. The anti-PSMA construct of claim 21, 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.
23. The anti-PSMA construct of claim 22, wherein the intracellular signaling domain further comprise a costimulatory signaling sequence derived from CD28, 4-1BB, ICOS, or OX40.
24. The anti-PSMA construct of any one of claims 21-23, wherein the intracellular signaling domain comprises a primary immune cell signaling sequence derived from CD3 ζ and a costimulatory signaling sequence derived from CD28.
25. The anti-PSMA construct of any one of claims 21-24, comprising:
- 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.

26. The anti-PSMA construct of any one of claims 1-8, wherein the anti-PSMA construct is a caTCR comprising:

(a) an extracellular domain comprising the anti-PSMA antibody moiety; and

(b) a T cell receptor module (TCRM) comprising 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.

27. The anti-PSMA construct of claim 26, wherein the first TCR-TM and the second TCR-TM are derived from a γ/δ TCR.

28. The anti-PSMA construct of claim 27, wherein:

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

ii) the first TCR-TM is derived from a TCR δ chain and the second TCR-TM is derived from a TCR γ chain.

29. The anti-PSMA construct of any one of claims 26-28, 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.

30. The anti-PSMA construct of any one of claims 26-29, wherein the TCR-associated signaling molecule is selected from the group consisting of CD3 $\delta\epsilon$, CD3 $\gamma\epsilon$, and CD3 $\zeta\zeta$.

31. The anti-PSMA construct of any one of claims 26-30, wherein the caTCR lacks a functional primary immune cell signaling domain.

32. The anti-PSMA construct of any one of claims 1-8, wherein the anti-PSMA construct is a chimeric signaling receptor (CSR) comprising:

- i) a ligand-binding module that is capable of binding or interacting with PSMA;
- ii) a transmembrane module; and
- iii) a co-stimulatory immune cell signaling module,

wherein the ligand-binding module and the co-stimulatory immune cell signaling module are not derived from the same molecule, and wherein the CSR lacks a functional primary immune cell signaling domain.

33. The anti-PSMA construct of claim 32, wherein the CSR lacks any primary immune cell signaling sequences.
34. The anti-PSMA construct of claim 32 or 33, wherein the ligand-binding module comprises the anti-PSMA construct of any one of claims 1-25.
35. The anti-PSMA construct of any one of claims 32-34, wherein the transmembrane module of the CSR and the co-stimulatory immune cell signaling module of the CSR are from the same molecule.
36. The anti-PSMA construct of claim 25, 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.
37. The anti-PSMA construct of any one of claims 32-36, wherein the transmembrane module of the CSR and the co-stimulatory immune cell signaling module of the CSR are from different molecules.
38. The anti-PSMA construct of any one of claims 32-37, wherein the transmembrane module of the CSR comprises 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, the α , β , δ , γ , or ζ chain of the T-cell receptor, a sequence comprising 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.
39. The anti-PSMA construct of any one of claims 32-38, wherein the co-stimulatory immune cell signaling module is derived from the intracellular domain of a co-stimulatory receptor of a TCR.
40. The anti-PSMA construct of claim 39, wherein the co-stimulatory receptor is selected from the group consisting of 4-1BB, CD27, CD28, CD30, OX40, ICOS, CD40, a sequence comprising 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.
41. The anti-PSMA construct of any one of claims 33-40, comprising the amino acid sequence of any one of SEQ ID NOS: 37-38, 55-84, 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, 55-84, 93, and 184-186.
42. The anti-PSMA construct of any one of claims 32-41, wherein the anti-PSMA construct further comprising a signal peptide.

43. The anti-PSMA construct of claim 42, wherein the signal peptide comprises the amino acid sequence of SEQ ID NO: 128.

44. The anti-PSMA construct of any one of claims 1-20, wherein the anti-PSMA construct is conjugated to an effector molecule, 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.