

[0015a] In another aspect, provided herein is a prostate specific membrane antigen (PSMA) wherein said protein comprises the amino acid sequence of SEQ ID NO: 146 or 147.

[0015b] In another aspect, provided herein is a use of an effective amount of the pharmaceutical composition as disclosed herein in the manufacture of a medicament for treating an individual in need of treatment of cancer.

INCORPORATION BY REFERENCE

[0016] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF THE DRAWINGS

[0017] The novel features of the invention are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings of which:

[0018] **Figure 1** is schematic representation of an exemplary PSMA targeting trispecific antigen-binding protein where the protein has a constant core element comprising an anti-CD3 ϵ single chain variable fragment (scFv) and an anti-HSA variable heavy chain region; and a PSMA binding domain that can be a VH, scFv, a non-Ig binder, or ligand.

[0019] **Figures 2A-B** compare the ability of exemplary PSMA targeting trispecific proteins (PSMA targeting TriTAC molecules) with different affinities for CD3 to induce T cells to kill human prostate cancer cells.

Figure 2A shows killing by different PSMA targeting TriTAC molecules in prostate cancer model LNCaP.

Figure 2B shows killing by different PSMA targeting TriTAC molecules in prostate cancer model 22Rv1.

Figure 2C shows EC50 values for PSMA targeting TriTAC in LNCaP and 22Rv1 prostate cancer models.

[0020] **Figure 3** shows the serum concentration of PSMA targeting TriTAC C236 in Cynomolgus monkeys after i.v. administration (100 μ g/kg) over three weeks.

[0021] **Figure 4** shows the serum concentration of PSMA targeting TriTAC molecules with different CD3 affinities in Cynomolgus monkeys after i.v. administration (100 μ g/kg) over three weeks.

[0022] **Figures 5A-C** show the ability of PSMA targeting TriTAC molecules with different affinities for PSMA to induce T cells to kill the human prostate cancer cell line LNCaP. **Figure 5A** shows the experiment performed in the absence of human serum albumin with a PSMA targeting BiTE as positive control. **Figure 5B** shows the experiment performed in the presence of human serum albumin with a PSMA targeting BiTE as positive control. **Figure 5C** shows EC50 values for PSMA targeting TriTAC in the presence or absence of HSA with a PSMA targeting BiTE as a positive control in LNCaP prostate cancer models.

[0023] **Figure 6** demonstrates the ability of PSMA targeting TriTAC molecules to inhibit tumor growth of human prostate cancer cells in a mouse xenograft experiment.

CLAIMS

WHAT IS CLAIMED IS:

1. A prostate specific membrane antigen (PSMA) targeting trispecific protein, wherein said protein comprises the amino acid sequence of SEQ ID NO: 146 or 147.
2. A pharmaceutical composition comprising (i) the PSMA targeting trispecific protein according to claim 1 and (ii) a pharmaceutically acceptable carrier.
3. Use of an effective amount of the pharmaceutical composition of claim 2 in the manufacture of a medicament for treating an individual in need of treatment of cancer.
4. The use of claim 3, wherein the cancer is prostate cancer or renal cancer.