

WHAT IS CLAIMED IS:

1. A protein comprising a transmembrane domain of an alpha chain of interleukin-7 receptor, with one or more modifications, wherein the transmembrane domain with one or more modifications has a sequence of SEQ ID NO: 2, or SEQ ID NO: 4, 6 or 8.

2. The protein of claim 1, wherein the protein further comprises an intracellular domain of an alpha chain of interleukin-7 receptor.

3. The protein of claim 2, wherein the intracellular domain comprises a sequence of SEQ ID NO: 45.

4. The protein of any one of claims 1 to 3, wherein the protein further comprises an extracellular domain of an alpha chain of interleukin-7 receptor.

5. The protein of claim 4, wherein the extracellular domain comprises a sequence of SEQ ID NO: 11.

6. The protein of claim 1, further comprising
an extracellular interleukin-15 domain; and
an extracellular sushi domain from an alpha chain of interleukin-15 receptor.

7. The protein of claim 6, wherein the extracellular interleukin-15 domain comprises a sequence of SEQ ID NO: 22 or SEQ ID NO: 24.

8. ~~The protein of claim 6,~~ and/or wherein the extracellular sushi domain of the alpha chain of interleukin-15 receptor comprises SEQ ID NO: 36 or SEQ ID NO: 37.

~~98.~~ A nucleic acid encoding a protein of any one of claims 1 to 7.

~~109.~~ A vector comprising the nucleic acid of claim ~~98.~~

~~11~~10. The vector of claim ~~109~~, further comprising a promoter operably linked to the nucleic acid, ~~and optionally, or both a promoter operably linked to the nucleic acid and~~ an enhancer sequence operably linked to the nucleic acid.

~~12~~11. The vector of claim ~~9 or 10~~10, further comprising a sequence encoding a chimeric antigen receptor which binds specifically to a tumor antigen.

~~13~~12. The vector of claim ~~12~~11, wherein the tumor antigen is selected from the group consisting of: glypican-3, BCMA, MAGE, MUC16, CD19, WT-1, CD22, LI-CAM, ROR-1, CEA, 4-1BB, ETA, 5T4, adenocarcinoma antigen, alpha-fetoprotein (AFP), BAFF, B-lymphoma cell, C242 antigen, CA-125, carbonic anhydrase 9 (CA- IX), C-MET, CCR4, CD152, CD20, CD125 CD200, CD221, CD23 (IgE receptor), CD28, CD30 (TNFRSF8), CD33, CD4, CD40, CD44 v6, CD51, CD52, CD56, CD74, CD80, CEA, CNT0888, CTLA-4, DR5, EGFR, EpCAM, CD3, FAP, fibronectin extra domain-B, folate receptor 1, GD2, GD3 ganglioside, glycoprotein 75, GPNMB, HER2/neu, HGF, human scatter factor receptor kinase, IGF-1 receptor, IGF-I, IgG1, IL-13, IL-6, insulin-like growth factor I receptor, integrin $\alpha 5 \beta 1$, integrin $\alpha \nu \beta 3$, MORAb-009, MS4A1, MUC1, mucin CanAg, N-glycolylneuraminic acid, NPC-1C, PDGF-R a, PDL192, phosphatidylserine, prostatic carcinoma cells, RANKL, RON, SCH 900105, SDC1, SLAMF7, TAG-72, tenascin C, TGF beta 2, TGF- β , TRAIL-R1, TRAIL-R2, tumor antigen CTAA16.88, VEGF-A, VEGFR-1, VEGFR2, and vimentin.

~~14~~13. The vector of ~~claim of any one of claims 109 to 12~~, wherein the chimeric antigen receptor comprises one or more co-stimulatory signaling domains selected from the group consisting of: 4-1BB, CD27, OX40, CD40, CD28, GITR, CD2, CD5, ICAM-1, CD11a, Lck, TNFR-I, TNFR-II, FasR, CD30, ICOS, LIGHT, NKG2C, B7-H3, DAP-10, and DAP-12.

~~15~~14. The vector of ~~any one of claims 9 to 13~~10, wherein the vector is a lentiviral or an adenoviral vector.

1615. An isolated mammalian cell comprising a vector of any one of claims 9 to 1410.

1716. The mammalian cell of claim 1615, wherein the mammalian cell is an immune cell.

1817. The mammalian cell of claim 1716, wherein the immune cell is selected from the group consisting of: a CD4⁺ T cell, a CD8⁺ T cell, a B cell, a monocyte, a natural killer cell, a dendritic cell, a macrophage, a regulatory T cell, and a helper T cell.

1918. A pharmaceutical composition comprising a vector of any one of claims 9 to 1410 and a pharmaceutically acceptable carrier.

2019. A pharmaceutical composition comprising a mammalian cell of any one of claims 15 to 1746.

20. Use of a therapeutically effective amount of the cell of any one of claims 15 to 18, or the composition of claim 19, in the manufacture of a medicament for inducing cell death in a cancer cell in a subject in need thereof.

21. Use of a therapeutically effective amount of the cell of any one of claims 15 to 18, or the composition of claim 19, in the manufacture of a medicament for decreasing the risk of developing a metastasis or an additional metastasis in a subject having a cancer.

22. The use of claim 20 or 21, wherein the cancer is selected from: hepatocellular carcinoma, acute lymphoblastic leukemia, acute myeloid leukemia, adrenocortical carcinoma, Kaposi sarcoma, lymphoma, anal cancer, appendix cancer, teratoid/rhabdoid tumor, basal cell carcinoma, bile duct cancer, bladder cancer, bone cancer, brain cancer, breast cancer, bronchial tumor, carcinoid tumor, cardiac tumor, cervical cancer, chordoma, chronic lymphocytic leukemia, chronic myeloproliferative neoplasm, colon cancer, colorectal cancer, craniopharyngioma, bile duct cancer,

endometrial cancer, ependymoma, esophageal cancer, esthesioneuroblastoma, Ewing sarcoma, eye cancer, fallopian tube cancer, gallbladder cancer, gastric cancer, gastrointestinal carcinoid tumor, gastrointestinal stromal tumor, germ cell tumor, hairy cell leukemia, head and neck cancer, heart cancer, liver cancer, hypopharyngeal cancer, pancreatic cancer, kidney cancer, laryngeal cancer, chronic myelogenous leukemia, lip and oral cavity cancer, lung cancer, melanoma, Merkel cell carcinoma, mesothelioma, mouth cancer, oral cancer, osteosarcoma, ovarian cancer, penile cancer, pharyngeal cancer, prostate cancer, rectal cancer, salivary gland cancer, skin cancer, small intestine cancer, soft tissue sarcoma, gastric cancer, testicular cancer, throat cancer, thyroid cancer, urethral cancer, uterine cancer, vaginal cancer, and vulvar cancer.