

What is claimed is:

1. A virus-like particle (VLP), ~~comprising~~consisting of, in order from amino terminus to carboxy terminus as a single peptide:

at least one capsid protein; and

a fusion protein, ~~comprising~~consisting of: at least one protease cleavage peptide sequence, and at least one ~~recall-protein~~epitope that is from 8 to 17 amino acids in length,

wherein:

~~said recall-protein comprises at least one epitope,~~

said fusion protein is 45 amino acids or less in length,

~~the fusion protein is attached to the capsid protein, and~~

~~the protease cleavage peptide sequence is positioned between the capsid protein and the recall-protein~~

when the VLP is contacted by a protease that recognizes and cleaves the at least one protease cleavage peptide sequence, then the at least one epitope is released from the VLP resulting in complexation of the epitope with a major histocompatibility (MHC) molecule present on a tumor cell surface in a tumor microenvironment, resulting in activation of T cells, thereby inhibiting growth, proliferation, and/or metastasis of the tumor cell.

2. The VLP of claim 1, wherein the at least one epitope:

~~is a pathogen epitope,~~

~~comprises a peptide sequence that complexes with a major histocompatibility (MHC) molecule, and/or~~

has a sequence selected from one or more of SEQ ID NOS: 1 to 83.

3. The VLP of claim 1 or claim 2, wherein the capsid protein is a *Papillomavirus* L1 and/or L2 capsid protein.

4. The VLP of claim 3, wherein the L1 protein is from Bovine papilloma virus (BPV), Human papilloma virus (HPV), Rabbit papilloma virus (RPV), or Mouse papilloma virus (MPV).

5. The VLP of claim 31, wherein the L1 protein is from a bacteriophage or from a plant.

6. The VLP of any one of claims 1 to 5, wherein the at least one recall protein is attached to the at least one capsid protein via conjugation through: a disulfide bond, an ester bond, an amide bond, or a chemical linkage created by exposure of the at least one recall protein and at least one capsid protein simultaneously to a cross-linking agent under conditions amenable to formation of a chemical cross-link.

7. The VLP of any one of claims 1 to 5, wherein the fusion protein comprises at least two recall proteins or wherein the VLP comprises at least two fusion proteins each comprising different recall proteins.

8. The VLP of any one of claims 1 to 7, wherein the at least one epitope is a human T cell epitope.

9. The VLP of any one of claims 1 to 8, wherein the epitope sequence is from a childhood vaccine.

10. The VLP of claim 9, wherein the capsid protein is from human papilloma virus, hepatitis B virus, bacteriophage MS2, bacteriophage Q β , bacteriophage P22, cowpea chlorotic mottle virus, cowpea mosaic virus, influenza virus, parvovirus, Norwalk virus, hamster polyoma virus, *Macrobrachium Rosenbergii Nodavirus*, hepatitis C virus, or a retrovirus.

11. The VLP of any one of claims 1 to 10, wherein the fusion protein is conjugated to the L1 protein via a cysteine, lysine, or arginine residue of the at least one capsid protein.

12. The VLP of claim 11, wherein ~~about~~ 20 to ~~about~~ 100 percent of the cysteine, lysine, and/or arginine residues of the at least one the at least one capsid protein are conjugated to at least one of the fusion proteins.

13. The VLP of any one of claims 1 to 12, wherein the at least one protease cleavage peptide sequence is recognized by a tumor microenvironment protease selected from one or more of: cathepsins, kallikreins, serine proteases, caspases, matrix metalloproteinases, and disintegrin and metalloproteinases (ADAMs).

14. The VLP of any one of claims 1 to 13, wherein the at least one epitope is a viral epitope and is from a vaccinia virus, varicella zoster virus, a herpes zoster virus, rubella, a hepatitis virus, an influenza virus, a measles virus, a mumps virus, a poliovirus, a variola virus, a rabies virus, dengue virus, Ebola virus, West Nile virus, a yellow fever virus, a zika virus, a cytomegalovirus, or an Epstein–Barr virus.

15. The VLP of any one of claims 1 to 14, wherein the at least one epitope is a bacterial epitope and is from *Bordetella pertussis*, *Clostridium tetani*, *Chlamydia trachomatis*, diphtheria, *Hemophilus influenza*, *Meningococcus*, *Pneumococcus*, *Vibrio cholera*, *Mycobacterium tuberculosis*, *Bacillus Calmette-Guérin* (BCG), typhoid, *Escherichia coli*, *Salmonella*, *Legionella pneumophila*, *Rickettsia*, *Treponema pallidum pallidum*, *Streptococcus*, *Bacillus anthracis*, *Clostridium botulinum*, or *Yersinia*.

16. The VLP of any one of claims 1 to 14, wherein the at least one epitope is a parasitic epitope and is from *Entamoeba histolytica*, *Toxoplasma gondii*, *Trichinella*, *Trichomonas*, *Trypanosoma*, *Trypanosoma brucei rhodesiense*, *Trypanosoma cruzi*, or *Plasmodium*.

17. The VLP of any one of claims 1 to 16, wherein the at least one capsid protein exhibits tropism for a specific type of tissue.

18. The VLP of claim 17, wherein the tropism is a tropism for cells or tissues expressing heparin sulfate proteoglycan (HSPG).

19. The VLP of any one of claims 1 to 18, for use in the treatment of cancer, [and wherein the epitope is as defined in any one of claims 2, 8 to 10, and 14 to 16.](#)

20. The VLP for use of claim 19, wherein the VLP is capable of eliciting a T cell response at a threshold of at least 2-fold above a baseline of total CD8⁺ T cells in the subject.

21. The VLP for use of claim 20, wherein the CD8⁺ T cells comprise CD69⁺ cells.

22. Use of the VLP of any one of claims 1 to 18, in the manufacture of a medicament for the treatment of cancer, [wherein the epitope is as defined in any one of claims 2, 8 to 10, and 14 to 16.](#)

23. The VLP for use or the use of any one of claims 19 to 22, wherein the VLP for use or the use inhibits the growth, progression, or metastasis of a tumor.

24. The VLP for use or the use of any one of claims 19 to 23, wherein the cancer is one or more of a small lung cell cancer, hepatocellular carcinoma, liver cancer, hepatocellular carcinoma, melanoma, metastatic melanoma, adrenal cancer, anal cancer, aplastic anemia, bile duct cancer, bladder cancer, bone cancer, brain or central nervous system cancer, breast cancer, cervical cancer, colon or rectum cancer, endometrial cancer, esophagus cancer, Ewing's tumor, eye cancer, gallbladder cancer, gastrointestinal carcinoid tumors, gastrointestinal stromal tumor, gestational trophoblastic disease, Hodgkin disease, Kaposi sarcoma, kidney cancer, laryngeal and hypopharyngeal cancer, leukemia, liver cancer, lung cancer, lymphoma, malignant mesothelioma, multiple myeloma, myelodysplastic syndrome, nasal cavity and paranasal sinus cancer, nasopharyngeal cancer, neuroblastoma, oral cavity and oropharyngeal cancer, osteosarcoma, ovarian cancer, pancreatic cancer, penile cancer, pituitary tumors, prostate cancer, retinoblastoma, rhabdomyosarcoma, salivary gland cancer, sarcoma, skin cancer, stomach cancer, testicular cancer, thymus cancer, thyroid cancer, uterine sarcoma, vaginal cancer, vulvar cancer, Waldenstrom Macroglobulinemia, Wilms Tumor, non-Hodgkin lymphoma, Hodgkin lymphoma, Burkitt's lymphoma, lymphoblastic lymphomas, mantle cell lymphoma, multiple myeloma, small lymphocytic lymphoma, splenic marginal zone lymphoma, marginal zone lymphoma, mixed cell type diffuse aggressive lymphomas of adults, large cell type diffuse aggressive lymphomas of adults, large cell immunoblastic diffuse aggressive lymphomas of adults, small non-cleaved cell diffuse aggressive lymphomas of adults, or follicular lymphoma, head and neck cancer,

endometrial or uterine carcinoma, non-small cell lung cancer, osteosarcoma, glioblastoma, or metastatic cancer.