

CLAIMS

1. An oncolytic adenoviral vector comprising
5 a deletion of a nucleic acid sequence in the E3 region, and
a nucleic acid sequence encoding a bispecific monoclonal antibody
in the place of the deleted nucleic acid sequence in E3 region, wherein the
bispecific monoclonal antibody comprises a single chain variable fragment
(scFv) specific for a cell surface molecule and a scFv specific for a tumor anti-
10 gen.
2. The oncolytic adenoviral vector according to claim 1, wherein a
backbone of the adenoviral vector is an adenovirus serotype 5 (Ad5) or serotype
3 (Ad3) nucleic acid backbone.
3. The oncolytic adenoviral vector according to any one of the previ-
15 ous claims, wherein the vector further comprises E2F1 promoter for tumor spe-
cific expression of E1A.
4. The oncolytic adenoviral vector according to any one of the previ-
ous claims, wherein the vector further comprises a 24 bp deletion (D24) in the
Rb binding constant region 2 of adenoviral E1.
- 20 5. The oncolytic adenoviral vector according to any one of the previ-
ous claims, wherein the deletion of a nucleic acid sequence in the E3 region is
a deletion of viral *gp19k* and *6.7k* reading frames.
6. The oncolytic adenoviral vector according to any one of the previ-
ous claims, wherein the vector comprises:
25 1) E2F1 promoter for tumor specific expression of E1A
2) a 24 bp deletion (D24) in the Rb binding constant region 2 of ade-
noviral E1;
3) a nucleic acid sequence deletion of viral *gp19k* and *6.7k* reading
frames; and
30 4) a nucleic acid sequence encoding a bipartite molecule comprising
a single chain variable fragment (scFv) specific for a cell surface molecule and
a scFv specific for a tumor antigen in the place of the deleted nucleic acid se-
quence as defined in point 3).
7. The oncolytic adenoviral vector according to any one of the previ-
35 ous claims, wherein the backbone is Ad5 nucleic acid backbone and the vector
further comprises an Ad3 fiber knob.

8. The oncolytic adenoviral vector according to any one of the previous claims, wherein the cell surface molecule is on immunological effector cells.

9. The oncolytic adenoviral vector according to claim 8, wherein the effector cells are T lymphocytes.

5 10. The oncolytic adenoviral vector according to any one of the previous claims, wherein the tumor antigen is selected from Table 1 or from the group consisting of mesothelin, EpCAM1 and MUC1.

10 11. The oncolytic adenoviral vector according to any one of the previous claims, wherein the cell surface molecule is selected from CD3, CD8 and CD4.

12. The oncolytic adenoviral vector according to any one of the previous claims, wherein the tumor antigen is mesothelin and the cell surface molecule is CD3; the tumor antigen is EpCAM1 and the cell surface molecule is CD3; or the tumor antigen is MUC1 and the cell surface molecule is CD3.

15 13. The oncolytic adenoviral vector according to any one of the previous claims, wherein the oncolytic adenoviral vector codes for two or more transgenes.

14. The oncolytic adenoviral vector according to any one of the previous claims, further comprising IL-2, TNFalpha or CD40L transgene.

20 15. A pharmaceutical composition comprising an oncolytic adenoviral vector according to any one of claims 1-14.

16. An oncolytic adenoviral vector according to any one of claims 1-14 for use in treatment of cancer.

25 17. An oncolytic adenoviral vector for use according to claim 16 together with an adoptive cell therapeutic composition.

18. A method of treating cancer in a subject, wherein the method comprises administration of an oncolytic adenoviral vector according to any one of claims 1-14 to a subject.

30 19. The method according to claim 18, wherein the method further comprises administration of adoptive cell therapeutic composition to the subject.

20. The method or the oncolytic adenoviral vector for use according to claim 17 or 19, wherein the adoptive cell therapeutic composition comprises a cell type selected from a group consisting of a tumor infiltrating lymphocyte (TIL), T-cell receptor modified lymphocytes and chimeric antigen receptor modified lymphocytes.

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21. The method or the oncolytic adenoviral vector for use according to any one of claims 17 or 19-20, wherein the adoptive cell therapeutic composition comprises a cell type selected from a group consisting of T-cells, CD8+ cells, CD4+ cells, NK-cells, delta-gamma T-cells, regulatory T-cells, and peripheral blood mononuclear cells.

22. The method or the oncolytic adenoviral vector for use according to any one of claims 17 or 19-21, wherein the adoptive cell therapeutic composition comprises T-cells.

23. The method or the oncolytic adenoviral vector for use according to any one of claims 16-22, wherein the cancer is selected from a group consisting of nasopharyngeal cancer, synovial cancer, hepatocellular cancer, renal cancer, cancer of connective tissues, melanoma, lung cancer, bowel cancer, colon cancer, rectal cancer, colorectal cancer, brain cancer, throat cancer, oral cancer, liver cancer, bone cancer, pancreatic cancer, choriocarcinoma, gastrinoma, pheochromocytoma, prolactinoma, T-cell leukemia/lymphoma, neuroroma, von Hippel-Lindau disease, Zollinger-Ellison syndrome, adrenal cancer, anal cancer, bile duct cancer, bladder cancer, ureter cancer, brain cancer, oligodendroglioma, neuroblastoma, meningioma, spinal cord tumor, bone cancer, osteochondroma, chondrosarcoma, Ewing's sarcoma, cancer of unknown primary site, carcinoid, carcinoid of gastrointestinal tract, fibrosarcoma, breast cancer, Paget's disease, cervical cancer, colorectal cancer, rectal cancer, esophagus cancer, gall bladder cancer, head cancer, eye cancer, neck cancer, kidney cancer, Wilms' tumor, liver cancer, Kaposi's sarcoma, prostate cancer, lung cancer, testicular cancer, Hodgkin's disease, non-Hodgkin's lymphoma, oral cancer, skin cancer, mesothelioma, multiple myeloma, ovarian cancer, endocrine pancreatic cancer, glucagonoma, pancreatic cancer, parathyroid cancer, penis cancer, pituitary cancer, soft tissue sarcoma, retinoblastoma, small intestine cancer, stomach cancer, thymus cancer, thyroid cancer, trophoblastic cancer, hydatidiform mole, uterine cancer, endometrial cancer, vagina cancer, vulva cancer, acoustic neuroma, mycosis fungoides, insulinoma, carcinoid syndrome, somatostatinoma, gum cancer, heart cancer, lip cancer, meninges cancer, mouth cancer, nerve cancer, palate cancer, parotid gland cancer, peritoneum cancer, pharynx cancer, pleural cancer, salivary gland cancer, tongue cancer and tonsil cancer.

24. The method or the oncolytic adenoviral vector for use according to any one of claims 16-23, wherein the administration(s) of oncolytic viral vectors and an adoptive cell therapeutic composition to a subject is(are) conducted simultaneously or consecutively, in any order.

5 25. The method or the oncolytic adenoviral vector for use according to any one of claims 16-24, further comprising administration of concurrent or sequential radiotherapy, monoclonal antibodies, chemotherapy or other anti-cancer drugs or interventions to a subject.

10 26. The oncolytic adenoviral vector according to any one of claims 1-14 for use in increasing the efficacy of adoptive cell therapy in a subject.

 27. A method of increasing the efficacy of adoptive cell therapy in a subject by administering an oncolytic adenoviral vector according to any one of claims 1-14 to a subject in need thereof, wherein the subject has been administered or is to be administered with adoptive cell therapy.