

CLAIMS

1. An oncolytic adenoviral vector comprising a nucleic acid sequence encoding a variant interleukin 2 (vIL-2) polypeptide as a transgene.

2. The oncolytic viral vector according to claim 1, wherein said variant IL-2 exhibits reduced binding to receptor subunit IL-2R α but retains the IL-2R β and IL-2R γ binding activity or has improved IL-2R β and IL-2R γ binding activity.

3. The oncolytic vector according to claim 2, wherein a backbone of the oncolytic adenoviral vector is an adenovirus serotype 5 (Ad5) or serotype 3 (Ad3) nucleic acid backbone or adenovirus serotype 5 (Ad5) backbone with the fiber knob of adenovirus serotype 3 (Ad3)

4. The oncolytic vector according to claim 2 or 3, wherein said nucleic acid sequence encoding a variant interleukin 2 (vIL-2) polypeptide is in the place of a deleted nucleic acid sequence in the E3 region of said oncolytic adenoviral vector.

5. The oncolytic vector according to claim 4, 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 vector according to any one of claims 1-5, wherein the vector comprises a 24 bp deletion ($\Delta 24$) in the adenoviral E1 sequence of said oncolytic adenoviral vector.

7. The oncolytic vector according to any one of claims 1-6, wherein the vector comprises an Ad5/3 fiber knob.

8. The oncolytic vector according to any one of claims 1-7, wherein the vector comprises Ad5/3-E2F-d24 backbone.

9. The oncolytic vector according to any one of claims 1-8, wherein the vector has the structure Ad5/3-E2F-d24-vIL-2.

10. The oncolytic vector according to any one of claims 1-9, wherein said nucleic acid sequence encodes for the variant IL-2 polypeptide comprising the substitutions L80F, R81D, L85V, I86V and I92F, the positions defined as in SEQ ID NO:2.

11. The oncolytic vector according to any one of claims 1-10, wherein the vector comprises nucleic acid sequence encoding a further transgene.

12. The oncolytic vector according to claim 11, wherein the further transgene is encoding a cytokine.

13. The oncolytic vector according to claim 12, wherein the cytokine is selected from the list consisting of: TNFalpha, interferon alpha, interferon beta, interferon gamma, complement C5a, CD40L, IL12, IL-23, IL15, IL17, CCL1, CCL11, CCL12, CCL13, CCL14-1, CCL14-2, CCL14-3, CCL15-1, CCL15-2, CCL16, CCL17, CCL18, CCL19, CCL2, CCL20, CCL21, CCL22, CCL23-1, CCL23-2, CCL24, CCL25-1, CCL25-2, CCL26, CCL27, CCL28, CCL3, CCL3L1, CCL4, CCL4L1, CCL5 (=RANTES), CCL6, CCL7, CCL8, CCL9, CCR10, CCR2, CCR5, CCR6, CCR7, CCR8, CCRL1, CCRL2, CX3CL1, CX3CR, CXCL1, CXCL10, CXCL11, CXCL12, CXCL13, CXCL14, CXCL15, CXCL16, CXCL2, CXCL3, CXCL4, CXCL5, CXCL6, CXCL7, CXCL8, CXCL9, CXCR1, CXCR2, CXCR4, CXCR5, CXCR6, CXCR7 and XCL2.

14. The oncolytic vector according to claim 12, wherein the cytokine is TNFalpha.

15. A pharmaceutical composition comprising an oncolytic adenoviral vector according to any one of claims 1-14 and at least one of the following: physiologically acceptable carriers, buffers, excipients, adjuvants, additives, antiseptics, preservatives, filling, stabilising and/or thickening agents.

16. An oncolytic adenoviral vector according to any one of claims 1-14 or a pharmaceutical composition according to claim 15 for use in the treatment of cancer or tumor, preferably a solid tumor.

17. The oncolytic vector or pharmaceutical composition for use in treatment of cancer or tumor according to claim 16, wherein the cancer or tumor 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, pheo-chromocytoma, prolactinoma, T-cell leukemia/lymphoma, neuroma, 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, esophagus cancer, gall bladder cancer, head cancer, eye cancer, neck cancer, kidney cancer, Wilms' tumor, Kaposi's sarcoma, prostate 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,
5 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.

18. The oncolytic vector or pharmaceutical composition for use in
10 treatment of cancer according to claim 16 or 17 together with an adoptive cell therapeutic composition.

19. The oncolytic vector or pharmaceutical composition for use in treatment of cancer according to claim 18 for increasing the efficacy of adoptive cell therapy in a subject.

15 20. The oncolytic vector or pharmaceutical composition for use in treatment of cancer according to any one of claims 16-19 together with radiotherapy, monoclonal antibodies, chemotherapy, small molecular inhibitors, hormonal therapy or other anti-cancer drugs or interventions to a subject.

21. A method of treating cancer or tumor in a subject, wherein a
20 pharmaceutically effective amount of an oncolytic adenoviral vector according to any one of claims 1-14 or a pharmaceutical composition according to claim 15 is administered to a subject.

22. The method according to claim 21, wherein the cancer or tumor is selected from a group consisting of nasopharyngeal cancer, synovial cancer,
25 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, pheo-chromocytoma, prolactinoma, T-cell leukemia/lymphoma, neuroma, von Hippel-Lindau disease, Zollinger-Ellison
30 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, esophagus cancer, gall bladder
35 cancer, head cancer, eye cancer, neck cancer, kidney cancer, Wilms' tumor, 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, parathyroid cancer, penis cancer, pituitary cancer, soft tissue sarcoma, retinoblastoma, small intestine cancer, stomach cancer, thymus cancer, thyroid cancer, trophoblastic cancer,
5 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
10 cancer.

23. The method according to claim 21 or 22, wherein said vector is administered together with an adoptive cell therapeutic composition.

24. The method according to claim 23, wherein the administration(s) of an adoptive cell therapeutic composition and an oncolytic viral vector to a subject is
15 (are) conducted simultaneously or consecutively, in any order.

25. The method according to any one of claims 21-24 further comprising administration of concurrent or sequential radiotherapy, monoclonal antibodies, chemotherapy, small molecular inhibitors, hormonal therapy, adoptive cell therapy or other anti-cancer drugs or interventions to a subject.

20 26. Use of an oncolytic vector according to any one of claims 1-14 for the manufacture of a medicament for the treatment of cancer or tumor.