

Claims

1. A replication deficient oncolytic viral vector or replication capable group B oncolytic adenovirus selected from the group consisting of Ad11 and enadenotucirev, wherein the virus encodes an antibody or a binding fragment thereof for expression on the surface of a cancer cell, wherein said antibody or binding fragment is specific to a CD3 protein of a T-cell receptor complex (TCR), wherein the virus does not encode a B7 protein or an active fragment thereof.
2. A replication deficient oncolytic viral vector or replication capable group B oncolytic adenovirus according to claim 1 wherein the virus is Ad11.
3. A replication deficient oncolytic viral vector or replication capable oncolytic virus according to claim 1 or claim 2, wherein the virus is replication competent.
4. A replication deficient oncolytic viral vector or replication capable oncolytic virus s according to claim 1 or claim 2, wherein the virus is replication deficient.
5. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to any one of claims 1 to 4 wherein the encoded antibody further comprises a transmembrane domain or a GPI anchor.
6. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to claim 5, wherein the transmembrane domain is selected from a sequence shown in SEQ ID NO: 10 to 14.
7. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to any one of claims 1 to 6, wherein the oncolytic adenovirus is EnAd.
8. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to any one of claims 1 to 7, wherein the antibody or binding fragment is selected from the group comprising a full length antibody, a Fab, modified Fab, Fab', modified Fab', F(ab')₂, Fv, single domain antibodies, scFv, bi, tri or tetra-valent antibodies, Bis-scFv, diabodies, triabodies, tetrabodies, ,humabodies, disulfide stabilised forms of any one of the same and epitope-binding fragments thereof.
9. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to claims 1 to 8, wherein the antibody binding fragment is a single chain Fv.
10. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to any one of claims 1 to 9, wherein the oncolytic virus encodes at least one further transgene.
11. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to claim 10, wherein the oncolytic virus encodes at least two further transgenes.
12. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to claim 10 or 11, wherein the further transgene(s) encode(s) a protein independently selected from the group comprising a cytokine, a chemokine, an antagonistic antibody molecule or binding fragment thereof, an agonistic antibody molecule or binding fragment thereof, an immunomodulator and combinations thereof.

13. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to claim 12, wherein at least one further transgene encodes an antibody molecule or a binding fragment thereof (for example which may be in a surface expressed form and/or secreted form).
14. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to claim 13, wherein the antibody molecule or binding fragment is an inhibitor.
15. A replication deficient oncolytic viral vector or a replication competent oncolytic virus according to claim 14, wherein the inhibitor is an inhibitor of an angiogenesis factor or an inhibitor of a T cell deactivating factor.
16. A replication deficient oncolytic viral vector or a replication competent oncolytic virus according to any one of claims 13 to 15, wherein antibody molecule or binding fragment is an agonist.
17. A replication deficient oncolytic viral vector or a replication competent oncolytic virus according to claim 16, wherein the agonist is independently selected from the group comprising antibodies to CD40, GITR, OX40, CD27 and 4-1BB.
18. A replication deficient oncolytic viral vector or a replication competent oncolytic virus according to any one of claims 12 to 17 where the immunomodulator is a membrane-associated protein ligand for immune cell surface receptors selected from the group comprising CTLA-4, PD-1, PD-L1, PD-L2, VISTA, B7-H3, B7-H4, HVEM, ILT-2, ILT-3, ILT-4, TIM-3, LAG-3, BTLA, LIGHT or CD160, for example CTLA-4, PD-1, PD-L1, PD-L2, CD16, CD25, CD33, CD332, CD127, CD31, CD43, CD44, CD162, CD301a, CD301b and Galectin-3, FLT-3, FLT-3 ligand, TLRs, TLR ligands, CCR7, CD1a, CD1c, CD11b, CD11c, CD80, CD83, CD86, CD123, CD172a, CD205, CD207, CD209, CD273, CD281, CD283, CD286, CD289, CD287, CXCR4, GITR Ligand, IFN- α 2, IL-12, IL-23, ILT1, ILT2, ILT3, ILT4, ILT5, ILT7, TSLP Receptor, CD141, CD303, CADM1, CLEC9a, XCR1 and CD304, OX40, OX40 ligand, CD27, CD28, CD30, CD40, CD40 ligand, CD70, CD137, GITR, 4-1BB, ICOS and ICOS ligand.
19. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to any one of claims 10 to 18, wherein at least one further transgene encodes a cytokine (including secreted or cell membrane associated molecules).
20. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to any one of claims 11 to 19, wherein a second further transgene encodes a cytokine (including secreted or cell membrane associated molecules).
21. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to any one claims 19 or 20, wherein the encoded cytokine is independently selected from TNF alpha super family (TNFSF includes TNF-alpha, TNF-C, OX40L, CD154, FasL, LIGHT, TL1A, CD70, Siva, CD153, 4-1BB ligand, TRAIL, RANKL, TWEAK, APRIL, BAFF, CAMLG, NGF, BDNF, NT-3, NT-4, GITR ligand, EDA-A, EDA-A2), TGF-beta superfamily, IL-1 family (i.e. IL-1 and IL-18), IL-2 family, IL-10 family, IL-17 family, interferon family.

22. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to claim 21, wherein the encoded cytokine is independently selected from TNF-alpha, IL-1, IL-8, IL-10, IL-17, interferon, LIGHT, TL1A, Siva, TRAIL, RANKL, TWEAK, APRIL, NGF, BDNF, NT-3, and EDA-A2.
23. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to claim 21 or 22, wherein the encoded cytokine is independently selected from TNF-C, OX40l, CD154, FasL, CD70, CD153, 4-1BB ligand, and EDA-A.
24. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to any one of claims 21 to 23, wherein the cytokine is independently selected from the group comprising IL-2, IFN-alpha, IFN-beta, IFN-gamma, Flt3 ligand, GM-CSF, IL-15, and IL-12.
25. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to any one of claims 10 to 24, wherein at least one further transgene encodes a chemokine.
26. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to claim 25, wherein the chemokine is independently selected from the group comprising MIP-1 alpha, RANTES, IL-8, CCL5, CCL17, CCL20, CCL22, CXCL9, CXCL10, CXCL11, CXCL13, CXCL12, CCL2, CCL19 and CCL21.
27. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to claim 26, wherein the chemokine encoded is MIP-1 alpha.
28. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to claim 27, wherein the virus comprises transgenes encoding a cytokine and chemokine combination selected from i) MIP-1 α and Flt3, and ii) MIP-1 α and IFN α .
29. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to any one of claims 1 to 28, wherein the anti-CD3 antibody or binding fragment has at least the binding domain comprising a VH and a VL regions from muromonab-CD3 (OKT3), oteelixumab, teplizumab or visilizumab.
30. A method of treating a cancer patient (for example by *in vivo* stimulation of T cells, for example T cells in the cancer cell environment, to focus on cancerous cells) comprising the step of:
administering a therapeutically effective amount of a replication deficient oncolytic viral vector or replication capable group B oncolytic adenovirus selected from the group consisting of Ad11 and enadenotucirev, wherein the virus encodes an antibody or a binding fragment thereof for expression on the surface of a cancer cell, wherein said antibody or binding fragment is specific to a CD3 protein of a T-cell receptor complex (TCR), wherein the virus does not encode a B7 protein or an active fragment thereof,
wherein the virus or viral vector selectively infects said cancerous cells and expresses on the surface of the cell the said encoded anti-CD3 antibody or binding fragment, as defined in any one of claims 1 to 26.

31. A replication deficient oncolytic viral vector or replication capable group B oncolytic adenovirus selected from the group consisting of Ad11 and enadenotucirev, wherein the virus encodes an antibody or a binding fragment thereof for expression on the surface of a cancer cell, wherein said antibody or binding fragment is specific to a CD3 protein of a T-cell receptor complex (TCR), wherein the virus does not encode a B7 protein or an active fragment thereof, as defined in any one of claims 1 to 29, for use in treatment.
32. A replication deficient oncolytic viral vector or replication capable group B oncolytic adenovirus according to claim 31, for use in the treatment of cancer.
33. A replication deficient oncolytic viral vector or replication capable group B oncolytic adenovirus according to claim 32, wherein the treatment is by *in vivo* stimulation of T cells, for example T cells in the cancer cell environment, to focus on cancerous cell.
34. A replication deficient oncolytic viral vector or replication capable group B oncolytic adenovirus selected from the group consisting of Ad11 and enadenotucirev, wherein the virus encodes an antibody or a binding fragment thereof for expression on the surface of a cancer cell, wherein said antibody or binding fragment is specific to a CD3 protein of a T-cell receptor complex (TCR), wherein the virus does not encode a B7 protein or an active fragment thereof, as defined in any one of claims 1 to 26, for use in the manufacture of a medicament.