Claims

1. A replication deficient oncolytic viral vector or replication capable oncolytic virus that can replicate in a host cell comprising: a first transgene encoding an anti-TCR antibody or a binding fragment thereof specific to CD3 and a transmembrane domain or a GPI anchor, for expression on the surface of a cancer cell for *in vivo* stimulation of T cells, and
at least one further transgene,
wherein a sequence encoding a 2A peptide links said genes,
wherein the transgenes are in a cassette encoded as a polycistronic mRNA, andwherein the virus is not selected from an adenovirus, a retrovirus and lentivirus.

2. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to claim 1 wherein the transmembrane domain is selected from a sequence shown in SEQ ID NO: 10 to 14.

3 A replication deficient oncolytic viral vector or replication competent oncolytic virus according to claims 1 or 2, wherein the oncolytic virus is selected from herpes simplex virus (such as HSV-1), vesicular stomatitis virus, reovirus, vaccina virus, Seneca valley virus, coxsackievirus, measles, Maraba virus and Newcastle disease virus.

4. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to any one of claims 1 to 3, 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.

5. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to claim 4, wherein the oncolytic virus encodes at least two further transgenes.

6. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to any one of claims 1 to 5, wherein the further transgene(s) encodes 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, and immunomodulator and combinations thereof.

7. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to claim 6, wherein at least one further transgene encodes an antibody molecule or a binding fragment thereof.

8. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to claim 7, wherein the antibody molecule or binding fragment is an inhibitor.

9. A replication deficient oncolytic viral vector or a replication competent oncolytic virus according to claims 6 or 7, wherein antibody molecule or binding fragment is an agonist, for example wherein the agonist is independently selected from the group comprising an antibody or binding fragment specific to CD40, GITR, OX40, CD27 and 4-1BB.

10. A replication deficient oncolytic viral vector or a replication competent oncolytic virus according to any one of claims 6 to 9, 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, 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-α2, 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.

11. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to any one of claims 1 to 10, wherein at least one further transgene encodes a cytokine (including secreted or cell membrane associated molecules).

12. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to any one of claims 1 to 11, wherein a second further transgene encodes a cytokine (including secreted or cell membrane associated molecules).

13. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to any one of claims 6 to 12, wherein the encoded cytokine is selected from TNF alpha super family (TNFRSF 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-8), IL-2 family, IL-10 family, IL-17 family, interferon family, for example 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.

14. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to claim 13, wherein the encoded cytokine is independently selected from TNF-C, OX40L, CD154, FasL, CD70, CD153, 4-1BB ligand, and EDA-A.

15. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to any one of claims 6 to 14, wherein the cytokine is selected from the group comprising IL-2, IFN-alpha, IFN-beta, IFN-gamma, Flt3 ligand, GM-CSF, IL-15, and IL-12.

16. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to any one of claims 1 to 15, wherein said at least one further transgene encodes a chemokine.

17. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to any one of claims 6 to 16, wherein the chemokine is selected from the group comprising MIP-1 alpha, RANTES, IL-8, CCL5, CCL17, CCL20, CCL22, CXCL9, CXCL10, CXCL11, CXCL13, CXCL12, CCL2, CCL19 and CCL21, for example wherein the chemokine encoded is MIP-1 alpha.

18. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to any one of claims 6 to 17, wherein the virus comprises transgenes encoding a cytokine and chemokine combination selected from i) MIP-1α and Flt3, and ii) MIP-1α and IFNα.

19. A replication deficient oncolytic viral vector or replication competent oncolytic virus according to any one of claims 1 to 18, 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), otelixizumab, teplizumab or visilizumab.

20. Use of a replication deficient oncolytic viral vector or oncolytic replication capable virus that can replicate in a host cell comprising: a first transgene encoding an anti-TCR antibody or a binding fragment thereof specific to CD3 and a transmembrane domain or a GPI anchor, for expression on the surface of a cancer cell for *in vivo* stimulation of T cells, and
at least one further transgene,
wherein a sequence encoding a 2A peptide linking the genes,
wherein the transgenes are in a cassette encoded as a polycistronic mRNA, and
wherein the virus is not selected from an adenovirus, a retrovirus and lentivirus, in the manufacture of a medicament for treating a cancer patient by *in vivo* stimulation of T cells.

21. Use according to claim 20, 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.

22. Use according to claims 20 or 21, wherein the virus is replication competent.

23. Use according to claims 20 or 21, wherein the virus is replication deficient.

24. Use according to any one of claims 20 to 23, wherein the oncolytic virus or viral vector is selected from herpes simplex virus (such as HSV-1), reovirus, vaccina virus, Seneca valley virus, coxsackie virus, measles virus, Maraba virus and Newcastle disease virus, for example wherein the virus or viral vector is selected from the group comprising Oncorine (H101), Talimogene laparepvec, Reolysin, Pexastimogene devacirepvec (JX-594), Cavatak, Seprehvir,CGTG-102, MV-NIS, PV701, CL-ONC1 and CG0070.

25. Use according to any one of claims 20 to 24, 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, for example wherein the antibody binding fragment is a single chain Fv.

26. Use according to any one of claims 20 to 25, wherein a further transgene encodes a protein independently selected from the group comprising a cytokine, a chemokine, an antagonistic antibody molecule or fragment thereof, an agonistic antibody molecule or fragment thereof and combinations thereof.

27. Use according to claim 26, wherein the cytokine is selected from the group comprising IL-2, IFN-alpha, IFN-beta, IFN-gamma, Flt3 ligand, GM-CSF, IL-15, IL-12 and combinations thereof.

28. Use according to claims 26 or 27, wherein the chemokine is selected from the group comprising MIP-1 alpha, RANTES, IL-8, CCL5, CCL17, CCL20, CCL22, CXCL9, CXCL10, CXCL11, CXCL13, CXCL12, CCL2, CCL19, CCL21 and combinations thereof.

29. Use according to any one of claims 26 to 28, wherein a cytokine and chemokine combination of MIP-1α and Flt3 or MIP-1α and IFNα is encoded in the virus.

30. Use according to any one of claims 20 to 29, 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), otelixizumab, teplizumab or visilizumab.

31. Use according any one of claims 20 to 30, wherein the anti-CD3 antibody or binding fragment thereof comprises a transmembrane domain or a GPI anchor.

32. Use according to any one of claims 20 to 31, where a linker sequence is employed between the transmembrane domain and the antibody or binding antibody fragment, such as ScFv.