Claims

1. A replication competent oncolytic adenovirus with selectivity for cancer cells, wherein the adenovirus comprises a transgene under the control of a promoter endogenous to the virus, wherein the transgene comprises a DNA sequence encoding a B7 protein or an active fragment thereof, and
said transgene is located between the stop codon-polyA recognition site of the adenovirus L5 gene and the stop codon-polyA recognition site of the adenovirus E4 gene,
wherein said transgene is under the control of the endogenous major late promoter.
2. A replication competent oncolytic virus according to claim 1, wherein the B7 protein or active fragment thereof is independently selected from the group comprising B7-1, B7-2, B7-DC, B7-H1, B7-H2, B7-H3, B7-H4, B7-H5 and B7-H6.
3. A replication competent oncolytic virus according to claim 2, wherein the B7 protein or B7-1 or an active fragment of B7-1.
4. A replication competent oncolytic virus according to claim 1, wherein the virus is a group B adenovirus.
5. A replication competent oncolytic virus according to any one of claims 1 to 4, wherein the virus is a chimeric virus.
6. A replication competent oncolytic virus according to claim 5, wherein the virus backbone is enadenotucirev.
7 A replication competent oncolytic virus according to claim 6, wherein the virus has a formula (I):

$$5'\text{ITR-}B_1\text{-}B_A\text{-}B_2\text{-}B_X\text{-}B_B\text{-}B_Y\text{-}B_3\text{-}3'\text{ITR} \qquad (I)$$

B_1 comprises: E1A, E1B or E1A-E1B;

B_A is E2B-L1-L2-L3-E2A-L4;

B_2 is a bond or comprises E3 or a transgene, for example under an endogenous or exogenous promoter;

B_X is a bond or a DNA sequence comprising: a restriction site, one or more transgenes or both;

B_B comprises L5;

B_Y comprises a transgene encoding a B7 protein or an active fragment thereof; and

B_3 is a bond or comprises E4.

8. A replication competent oncolytic virus according to any one of claims 1 to 7, wherein the B7 protein or active fragment thereof comprises a transmembrane sequence.
9. A replication competent oncolytic virus according to claim 8, wherein the transmembrane sequence encodes a transmembrane domain from a PDGF receptor, or GPI anchor suitable for anchoring the protein or fragment in a cell membrane.

10. A replication competent oncolytic virus according to any one of claims 1 to 9, which further comprises a second transgene.
11. A replication competent oncolytic virus according to claim 10, wherein the second transgene encodes a polypeptide selected from the group comprising a cytokine, a chemokine, an antagonistic antibody molecule or fragment thereof, and an agonistic antibody molecule or fragment thereof.
12. A replication competent oncolytic virus according to any one of claims 1 to 11, which comprises a second and a third transgene.
13. A replication competent oncolytic virus according to claim 12, wherein the second and third transgenes encode two different polypeptides selected from the group comprising a cytokine, a chemokine, an antagonistic antibody molecule or fragment thereof, and an agonistic antibody molecule or fragment thereof.
14. A replication competent oncolytic virus according to any one of claims 10 to 13, wherein the second or third transgene encodes a cytokine, selected from the group comprising IL-2, IFN-alpha, IFN-beta, IFN-gamma, Flt3 ligand, GM-CSF, IL-15, and IL-12.
15. A replication competent oncolytic virus according to any one of claims 10 to 13, wherein the second or third transgene encodes a chemokine, selected from the group comprising MIP-1 alpha, IL-8, CCL5, CCL17, CCL20, CCL22, CXCL9, CXCL10, CXCL11, CXCL13, CXCL12, CCL2, CCL19 and CCL21.
16. A replication competent oncolytic virus according to any one of claims 10 to 13, where a cytokine and a chemokine combination is encoded by the virus selected from the group comprising Mip1α and Flt3 ligand, and Mip1α and IFNα.
17. A replication competent oncolytic virus according to any one of claims 1 to 16, wherein the virus encodes an antibody molecule or fragment thereof.
18. A replication competent oncolytic virus according to claim 17, wherein the antibody molecule or fragment thereof comprises a transmembrane sequence or GPI anchor such that it is a cell membrane-anchored form, or a transmembrane domain.
19. A replication competent oncolytic virus according to claim 18, wherein the transmembrane domain is from a PDGF receptor.
20. A replication competent oncolytic virus according to claim 17 or 18, wherein the antibody molecule or fragment thereof comprises an anti-human CD3 antigen binding domain.
21. A replication competent oncolytic virus according to any one of claims 17 to 20, wherein the antibody molecule is an inhibitor.
22. A replication competent oncolytic virus according to claim 21, wherein the inhibitor is selected from the group comprising an inhibitor of an angiogenesis factor and an inhibitor of T cell deactivation factors.
23. A replication competent oncolytic virus according to claim 22, wherein the inhibitor of an angiogenesis factor is an anti-VEGF antibody molecule.
24. A replication competent oncolytic virus according to claim 22, wherein the inhibitor of T cell deactivation factors is an anti-CTLA-4 antibody molecule.

25. A replication competent oncolytic virus according to claim 17 to 24, wherein the antibody molecule is an agonist.
26. A replication competent oncolytic virus according to claim 25, wherein the agonist is selected from the group comprising CD40, GITR, OX40, CD27 and 4-1BB.
27. A pharmaceutical composition comprising a replication comprising a replication competent oncolytic adenovirus according to any one of claims 1 to 26, and a diluent or carrier.
28. A replication competent adenovirus according to claim 1 to 26 or a composition according to claim 27 for use in treatment.
29. Use of a replication competent adenovirus according to claim 1 to 26 or a composition according to claim 27 for use in the manufacture of a medicament for the treatment of cancer.
30. A method of generating a replication competent adenovirus according to claim 1 to 26, comprising the step of replicating the adenovirus in a host cell.