Claims

1. A replication competent oncolytic group B adenovirus EnAd comprising:

   two or more transgenes,

   a first transgene comprising a DNA sequence encoding B7-1 protein, and

   an additional transgene encoding an anti-CD3 antibody or binding fragment thereof

   wherein said transgenes are in the same location between the stop codon and poly recognition site of the adenoviral gene L5 and the stop codon and polyA recognition site of gene E4,

   under the control of a major later promoter endogenous to this virus.

2. A replication competent oncolytic virus according to claim 1, wherein the virus has a formula (I):

$$5'ITR\text{-}B_1\text{-}B_A\text{-}B2\text{-}B_X\text{-}B_B\text{-}B_Y\text{-}B_3\text{-}3'ITR \quad (I)$$

   B_1 is a bond or 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;
   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 said a transgene cassette comprising a transgene encoding said B7-1 protein and a regulatory element or a combination of regulatory elements; and
   B_3 is a bond or comprises E4.

3. A replication competent oncolytic virus according to claim 2, wherein the regulatory element is a high efficiency self-cleavable peptide.

4. A replication competent oncolytic virus according to claim 3, wherein the sequence is selected from P2A, T2A, F2A and E2A.

5. A replication competent oncolytic virus according to any one of claims 1 to 4, wherein one ore more proteins encoded by the virus are suitable for expression on the surface of an infected cancer cell and said proteins are not fusions proteins.

6. A replication competent oncolytic virus according to any one of claims 1 to 5, where the virus encodes multiple proteins for surface expression on an infected cancer cell.

7. A replication competent virus according to claim 5 or 6, wherein the proteins are independently processed and expressed in physically separate locations on the cancer cell membrane.

8. A replication competent oncolytic virus according to any one of claims 1 to 7, wherein the antibody or binding fragment further comprises a transmembrane domain or GPI anchor such that it is a cell membrane-anchored form.

9. A replication competent oncolytic virus according to any one of claims 1 to 8, wherein the anti-CD3 is a scFv antibody fragment.

10. A replication competent oncolytic virus according to any one of claims 1 to 9, wherein the B7-1 protein is full-length protein.

11. A replication competent oncolytic virus according to any one of claims 1 to 10, wherein the B7-1 protein comprises a transmembrane domain or GPI anchor.

12. A replication competent oncolytic virus according to any one of claims 1 to 10, wherein the B7-1 protein comprises a transmembrane domain from a B7 protein.

13. A replication competent virus according to any one of claims 1 to 12, wherein the virus comprises a third transgene encoding a polypeptide selected from the group comprising a cytokine, a chemokine, a ligand, an antagonistic antibody molecule, and an agonistic antibody molecule.

14. A replication competent virus according to any one of claims 1 to 13, wherein the B7-1 protein is human.

15. A replication competent virus according to claim 14, wherein the B7-1 protein has the sequence shown in SEQ ID NO: 11 or a sequence at least 95% identical thereto.

16. A replication competent virus according to any one of claims 1 to 15, wherein the antibody molecule or binding fragment thereof comprises an anti-human CD3 antigen binding domain.

17. A replication competent virus according to claim 16, wherein the binding fragment has a sequence shown in SEQ ID NO: 15 or 99.

18. A replication competent oncolytic adenovirus according to claim 1 comprising SEQ ID NO: 96.

19. A pharmaceutical composition comprising a replication competent virus according to any one of claims 1 to 18 and a pharmaceutically acceptable excipient.

20. A replication competent virus according to any one of claims 1 to 18, or a pharmaceutical composition according to claim 19, for use in treatment.

21. A replication competent virus according to any one of claims 1 to 18, or a pharmaceutical composition according to claim 19, for use in the manufacture of a medicament for the treatment of cancer.

18. A replication competent virus or pharmaceutical composition for use according to claim 21, wherein the cancer is selected from colorectal, lung, bladder, renal, pancreatic, hepatic, head and neck, breast and ovarian cancer.