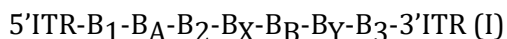


CLAIMS:

1. An oncolytic adenovirus comprising a sequence of formula **(I)**:



wherein:

B_1 is bond or comprises: E1A, E1B or E1A-E1B;

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

B_2 is a bond or comprises: E3;

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

B_3 is a bond or comprises: E4;

wherein the adenovirus encodes a Bispecific T cell Engager (BiTE™) in position B_Y comprising at least two binding domains wherein:

one of the said domains is specific to a component of the T-cell receptor complex (TCR); and

one the binding domains of the BiTE™ is specific to a tumour stromal antigen expressed on fibroblasts, tumour-associated macrophages, dendritic cells, NK cells and/or T-cells which have infiltrated the stroma;

wherein the adenovirus is Enadenotucirev (EnAd) or serotype 11 adenovirus (Ad11); and

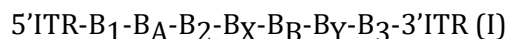
wherein the tumour stromal antigen is selected from: fibroblast activation protein (FAP), TREM1, IGFBP7, FSP-1, platelet-derived growth factor- α receptor (PDGFR- α), platelet-derived growth factor- β receptor (PDGFR- β) and vimentin.

2. An oncolytic adenovirus according to claim 1, wherein the adenovirus is EnAd.
3. An oncolytic adenovirus according to claims 1 or 2, wherein the component of the TCR is CD3.
4. An oncolytic adenovirus according to any one of claims 1 to 3, wherein the surface antigen is selected from the group consisting of CD3 ϵ , CD3 γ and CD3 δ .
5. An oncolytic adenovirus according to any one of claims 1 to 4, wherein the tumour stromal antigen is FAP.
6. An oncolytic adenovirus according to any one of claims 1 to 5, wherein the adenovirus is replication competent.
7. An oncolytic adenovirus according to any one of claims 1 to 6, wherein B_X comprises one or more transgenes or a transgene cassette.

8. An oncolytic adenovirus according to any one of claims 1 to 7, wherein the BiTE encoded in position B_Y is under the control of the major late promoter.
9. An oncolytic adenovirus according to any one of claims 1 to 8, wherein the adenovirus further encodes a second BiTE.
10. An oncolytic adenovirus according to claim 9, wherein both BiTEs are encoded in position B_Y.
11. An oncolytic adenovirus according to claim 10, wherein a BiTE is encoded in position B_X.
12. An oncolytic adenovirus according to claim 11, wherein the encoded BiTE is under the control of an exogenous promoter.
13. An oncolytic adenovirus according to any one of the claims 1 to 12, wherein the encoded BiTE binds to CD3 and comprises a VH domain comprising an amino acid sequence as set forth in SEQ ID NO: 8, or an amino acid sequence that is at least 95% identical thereto and a VL comprising an amino acid sequence as set forth in SEQ ID NO: 9 or a sequence at least 95% identical thereto.
14. An oncolytic adenovirus according to claim 13, wherein the encoded BiTE comprises an scFv comprising an amino acid sequence as set forth in SEQ ID NO: 7 or a sequence at least 95% identical thereto.
15. An oncolytic adenovirus according to any one of claims 1 to 13, wherein the encoded BiTE binds to FAP and comprises a VH domain comprising an amino acid sequence as set forth in SEQ ID NOs: 13, or an amino acid sequence that is at least 95% identical thereto and a VL comprising an amino acid sequence as set forth in SEQ ID NO: 12 or a sequence at least 95% identical thereto.
16. An oncolytic adenovirus according to claim 15, wherein the encoded BiTE comprises a scFv comprising an amino acid sequence as set forth in SEQ ID NO: 11 or 75 or a sequence at least 95% identical to any one of the same.
17. An oncolytic adenovirus according to claims 1 or 16, wherein the adenovirus comprises a sequence shown in SEQ ID NO: 36, 37, 81, 82, 97, 98, 99 or 100.

18. An oncolytic adenovirus according to any one of claims 1 to 17, wherein the adenovirus encodes 2, 3 or 4 further transgenes.
19. An oncolytic adenovirus according to claim 18, wherein a different cleavage peptide is encoded between each of the transgenes.
20. An oncolytic adenovirus according to any one of claims 18 to 19, wherein all the further transgenes are in position B_y.
21. An oncolytic adenovirus according to any one of claims 18 to 20, wherein at least one further transgene encodes a cytokine.
22. An oncolytic adenovirus according to claim 21, wherein the cytokine is selected from the group consisting of MIP1 α , IL-1 α , IL-1 β , IL-6, IL-9, IL-12, IL-13, IL-17, IL-18, IL-22, IL-23, IL-24, IL-25, IL-26, IL-27, IL-33, IL-35, IL-2, IL-4, IL-5, IL-7, IL-10, IL-15, IL-21, IL-25, IL-1RA, IFN α , IFN β , IFN γ , TNF α , lymphotoxin α (LTA), Flt3L, GM-CSF and IL-8.
23. An oncolytic adenovirus according to any one of claims 18 to 22, wherein at least one further transgene encodes a chemokine.
24. An oncolytic adenovirus according to claim 23, wherein the chemokine is selected from the group consisting of CCL2, CCL3, CCL5, CCL17, CCL20, CCL22, CXCL9, CXCL10, CXCL11, CXCL13, CXCL12, CCL2, CCL19 and CCL21.
25. A composition comprising an adenovirus according to any one of claims 1 to 24 and a diluent or carrier.
26. A composition according to claim 25, wherein the composition comprises a second oncolytic virus.
27. A composition according to claim 26, wherein the second oncolytic virus is Ad11 or a derivative thereof, or Enadenotucirev (EnAd).
28. An oncolytic adenovirus of any one of claims 1 to 24 or a composition according to any one of claims 25 to 27 for use in therapy.
29. Use of an oncolytic adenovirus of any one of claims 1 to 24 or a composition according to any one of claims 25 to 27 in the manufacture of a medicament for the treatment of a cancer that expresses a tumour stromal antigen.

30. Use of an oncolytic adenovirus in the manufacture of a medicament for targeting tumour stromal cells, wherein the adenovirus comprises a sequence of formula **(I)**:



wherein:

B_1 is bond or comprises: E1A, E1B or E1A-E1B;

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

B_2 is a bond or comprises: E3;

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

B_3 is a bond or comprises: E4;

wherein the adenovirus encodes a Bispecific T cell Engager (BiTE™) in position B_Y comprising at least two binding domains wherein:

one of the said domains is specific to a component of the T-cell receptor complex (TCR); and

one the binding domains of the BiTE™ is specific to a tumour stromal antigen expressed on fibroblasts, tumour-associated macrophages, dendritic cells, NK cells and/or T-cells which have infiltrated the stroma; and

the adenovirus is Enadenotucirev (EnAd) or serotype 11 adenovirus (Ad11).