

CLAIMS

1. An oncolytic virus (for example a replication competent virus) comprising a transgene cassette encoding an anti-CD40 antibody or binding fragment thereof, wherein the transgene cassette comprises an amino acid sequence given in SEQ ID NO: 12 or a sequence at least 95% identical thereto (such as 96, 97, 98 or 99% identical thereto), in particular a cassette of SEQ ID NO: 12.
2. An oncolytic virus according to claim 1, wherein the virus is selected from an adenovirus, herpes simplex virus, reovirus, measles virus, Newcastle disease virus, Seneca Valley virus, Vesicular stomatitis virus, polio virus, ECHO enterovirus, Cocksackie virus, and vaccinia virus, in particular an adenovirus.
3. An oncolytic virus according to claims 1 or 2, wherein the virus is selected from the group consisting of Enadenotucirev, talimogene laherparepvec, RIGVIR, Ad5-yCD/mutTKSR39rep-hIL12, Cavatak™, CG0070, DNX-2401, G207, HF10, Imlygic®, JX-594, MG1-MA3, MV-NIS, OBP-301, Reolysin®, Toca 511, in particular Enadenotucirev.
4. An oncolytic virus according to any one of claims 1 to 3, wherein the virus comprises SEQ ID NO: 1 or a sequence a sequence at least 95% identical thereto (such as a 96, 97, 98 or 99% identical thereto), such as comprising SEQ ID NO: 1.
5. An oncolytic virus according to claim 4, which consists of SEQ ID NO: 1.
6. A pharmaceutical composition comprising a virus according to any one of claims 1 to 5, and a pharmaceutically acceptable excipient, diluent or carrier.
7. An oncolytic virus according to any one of claims 1 to 5 or a pharmaceutical composition according to claim 6, for use in treatment.
8. Use of an oncolytic virus according to any one of claims 1 to 5 or a pharmaceutical composition according to claim 6 in the manufacture of a medicament for the treatment of cancer, insulin resistance, obesity and/or immune deficiency.
9. A use according to claim 8, wherein the virus or composition is for use in the treatment of cancer, for example for the treatment of cancer expressing CD40 (such as cancer with upregulated expression of CD40)
10. A combination therapy (for example for use in the treatment of cancer) comprising a virus according to any one of claims 1 to 5 or a composition according to claim 6 and a further anti-cancer therapy.
11. A combination therapy according to claim 10, wherein the further anti-cancer therapy is chemotherapy.
12. A combination therapy according to claim 10 or 11, wherein the further anti-cancer therapy is a check point inhibitor.

13. A combination therapy according to claim 12, wherein the anti-cancer therapy is selected from the group comprising a PD-1 inhibitor, a PD-L1 inhibitor, a CTLA-4 inhibitor, a TIM-3 inhibitor, a LAG-3 inhibitor, a TIGIT inhibitor, a B7-H3 (CD276) inhibitor, a B7-H4 (B7S1) inhibitor, a B7H7 (HHLA2) inhibitor, a CD96 inhibitor, a VISTA inhibitor and a combination of two or more of the same.
14. A combination therapy according to claim 13, wherein the inhibitor is an antibody or binding fragment thereof.
15. A combination therapy according to any one of claims 10 to 14, wherein the further anti-cancer therapy is a costimulatory pathway agonist.
16. A combination therapy according to claim 15, wherein the further anti-cancer therapy is selected from the group comprising a CD27 agonist, a CD28 agonist, an ICOS agonist, a TMIGD2 (IGPR-1/CD28H) agonist, a CD226 agonist, an OX40 agonist, a 4-1BB agonist, and a combination of two or more of the same.
17. A combination therapy according to claim 16, wherein the therapy is an antibody or binding fragment thereof.
18. A combination therapy according to any one of claims 10 to 17, wherein the further anti-cancer therapy activates immune responses or reverse suppression of immune responses, for example selected from IL-10, TGF β , IDO inhibitors, and a combination of two or more of the same.
19. A combination therapy according to any one of claims 10 to 18, wherein the further cancer therapy is an oncolytic virus, for example a replication competent oncolytic virus, such as an adenovirus, in particular a group B adenovirus.
20. A combination therapy according to claim 19, wherein the oncolytic virus encodes therapeutic gene encoding material selected from the group consisting of an RNAi sequence, an antibody or binding fragment thereof, chemokines, cytokines, immunomodulator and enzymes.