In relation to the data presented here, it is show that the insertion of DogTag into the hexon capsid protein performs well, and is capable of a good yield (Figure 12).

In relation to the data presented here, the insertion of the following first peptide partners into pIX have been demonstrated as viable: SpyCatcher, SnoopCatcher, DogCatcher, SpyTag and SnoopTagJr. In Figure 12 it is demonstrated that SpyCatcher fusions into pIX may be genetically less stable under certain circumstances, whilst SnoopCatcher and DogCatcher inserted into the same capsid protein may be more genetically stable, and therefore preferable under certain circumstances. However, SpyCatcher fusions are operable, see Figure 11 where various entities are attached, whilst the virus retains infectivity. In Figure 14 it is demonstrated that SnoopTagJr and SpyTag insertions into pIX do not adversely affect infectious yield, even when entities such as antigens are attached to these first peptide partners using the second peptide partner. It should be noted that the entire spike protein from Sars-CoV2 is over 500KDa and is therefore a large attachment which has been successfully attached. Thus, SpyCatcher, SnoopCatcher, DogCatcher, SpyTag and SnoopTagJr may be inserted into pIX as the first peptide partner, most preferably SnoopCatcher, DogCatcher, SpyTag and SnoopTagJr may be inserted into pIX as the first peptide partner.

Examples of the peptide:peptide binding pair described herein includes but are not limited to SpyTag and SpyCatcher, DogTag and DogCatcher, SnoopTag/SnoopTagJr and SnoopCatcher; RrgATag/RrgATag2/DogTag and RrgACatcher, IsopepTag/ IsopepTag-N and Pilin-C or Pilin-N, PsCsTag and PsCsCatcher; SnoopTagJr/SnoopTag and DogTag (mediated by SnoopLigase), and variants, derivatives and modifications of all these systems. Suitable peptide tag/binding partner pairs are described in detail in WO2011/098772, WO2016/193746, WO2018/189517 and WO2018/197854, herein incorporated by reference.

Accordingly, the second peptide partner may be linked or fused to an entity. This entity may be anything which it is desired to be attached to an adenoviral vector and is capable of being produced as a fusion to the second peptide partner. The type of entity will depend upon the prophylactic or therapeutic use to which the adenoviral vector will be put. The entity can be a targeting moiety, such as part of a ligand binding pair, an antibody or fragment thereof, or any other entity specifically recognised by a cell surface receptor. Such targeting moieties may be useful for oncolytic viruses and gene therapy applications. However, the entity may also simply have the

Claims

1. An adenoviral vector for preparation of a prophylactic or therapeutic composition, comprising at least one modification in a capsid protein, wherein said modification comprises the inclusion of a first peptide partner in a capsid protein, said first peptide partner is capable of forming or forms an isopeptide bond with a second peptide partner; and wherein said second peptide partner is attached to an entity.

2. The adenoviral vector according to claim 1 wherein the entity comprises an antigen, a targeting moiety or a shielding entity.

3. The adenoviral vector according to claim 2, wherein said shielding entity blocks the binding of host antibodies to the adenoviral vector.

4. The adenoviral vector according to any preceding claim wherein the at least one modification in a capsid protein is in a major capsid protein or in a minor capsid protein.

5. The adenoviral vector according to any one of claims 1 to 4 wherein the at least one modification in a major capsid protein is in the hexon protein, optionally in an HVR loop.

6. The adenoviral vector according to any one of claims 1 to 4 wherein the at least one modification in a minor capsid protein is in the pIX protein.

7. The adenoviral vector according to any one of claims 1 to 6 wherein the at least one modification in a capsid protein is the insertion or fusion of said first peptide partner to the capsid protein.

8. The adenoviral vector according to any preceding claim wherein the first peptide partner is selected from a DogTag, a DogCatcher, a SpyTag, a SpyTag002, a SpyCatcher, a SpyCatcher002, a SnoopCatcher, a SnoopTagJr, a SnoopTag or variants, derivatives and modifications of these, and wherein the second peptide partner is selected from a DogCatcher, a SpyCatcher, a SpyCatcher002, a SnoopCatcher, a DogTag, a SpyTag, a SpyTag002, a SnoopTagJr, a SnoopTag, or variants, derivatives and modifications of these.

9. The adenoviral vector according to any preceding claim wherein

    a) the first peptide partner is a SpyCatcher, optionally wherein the second peptide partner is a SpyTag;

b) the first peptide partner is a SnoopCatcher, optionally wherein the second peptide partner is a SnoopTagJr or a SnoopTag;

c) the first peptide partner is a DogCatcher, optionally wherein the second peptide partner is a DogTag;

d) the first peptide partner is a SnoopTagJr or a SnoopTag, optionally wherein the second peptide partner is a SnoopCatcher;

e) the first peptide partner is a SpyTag, optionally wherein the second peptide partner is a SpyCatcher; or

f) the first peptide partner is a DogTag, optionally wherein the second peptide partner is a DogCatcher, a SnoopTag or a SnoopTagJr.

10. The adenoviral vector according to any one of claims 2 to claim 9 wherein the second peptide partner is attached to an antigen via genetic fusion or is chemically attached to an antigen.

11. The adenoviral vector according to any one of claim 2 to claim 10 wherein said antigen is a tumour-associated antigen, such as a neoepitope or neoantigen, a self-antigen, or an antigen from a pathogen, such as a virus, bacterium, parasite or fungus, optionally wherein the virus is SARS-CoV-2.

12. The adenoviral vector according to any preceding claim wherein the size of said second peptide partner attached to an entity is over 15 kDa, 20 kDa, 30 kDa, 40 kDa, 50 kDa, 60 kDa, 70 kDa, 80 kDa, 90 kDa or 100 kDa.

13. The adenoviral vector according to claim 12 wherein said second peptide partner attached to an entity shields the adenovirus from antibody binding to the capsid.

14. The adenoviral vector according to any preceding claim for use in the manufacture of a vaccine comprising the addition of a second peptide partner attached to an antigen to said adenoviral vector.

15. A vaccine comprising the adenoviral vector of any preceding claim, wherein an antigen is attached to the adenoviral vector via the second peptide partner.

16. The vaccine as claimed in claim 15 wherein said antigen comprises at least one tumour-associated antigen, or virus antigen.

17. The adenoviral vector according to claim 11, or the vaccine according to claim 16, wherein the tumour-associated antigen is selected from adipophilin, AIM-2, ALDH1A1, alpha-actinin-4, alpha-fetoprotein ("AFP"), ARTC1, B-RAF, BAGE-1, BCLX (L), BCR-ABL fusion protein b3a2, beta-catenin, BING-4, CA-125, CALCA, carcinoembryonic antigen (CEA), CAGE 1 to 8, CASP-5, CASP-8, CD274, CD45, Cdc27, CDK12, CDK4, CDKN2A, CEA, CLPP, COA-1, CPSF, CSNK1A1, CTAG1, CTAG2, cyclin Dl, Cyclin-Al, dek-can fusion protein, DKK1, EFTUD2, Elongation factor 2, ENAH (hMena), Ep-CAM, EpCAM, EphA3, epithelial tumor antigen (ETA), ETV6-AML1 fusion protein, EZH2, ErbB receptors, E6, E7, FGF5, FLT3-ITD, FN1, G250/MN/CAIX, GAGE-1,2,8, GAGE-3,4,5,6,7, GAS7, glypican-3, GnTV, gp100/Pmel 17, GPNMB, HAUS3, Hepsin, HER-2/neu, HERV-K-MEL, HLA-A11, HLA-A2, HLA-DOB, hsp70-2, , HPV E2, HPV E6, HPV E7 antigen, IDO1, IGF2B3, IL13Ralpha2, Intestinal carboxyl esterase, K-ras, Kallikrein 4, KIF20A, KK-LC-1, KKLC1, KM-HN-1, KMHN1 also known as CCDC110, LAGE-1, LDLR-fucosyltransferase fusion protein, Lengsin, M-CSF, MAGE-A1, MAGE- A 10, MAGE-A12, MAGE-A2, MAGE- A3, MAGE-A4, MAGE-A6, MAGE-A9, MAGE-C1, MAGE-C2, malic enzyme, mammaglobin-A, MART2, MATN, MC1R, MCSP, mdm-2, ME1, Melan-A/MART- 1 , Meloe, Midkine, MMP-2, MMP-7, MUC1, MUC5AC, mucin, MUM-1, MUM-2, MUM-3, Myosin, Myosin class I, N-raw, NA88-A, neo-PAP, NFYC, NY-BR-1, NY-ESO-l/LAGE-2, OA1, OGT, OS-9, P polypeptide, p53, PAP, PAX5, PBF, pml-RARalpha fusion protein, polymorphic epithelial mucin (PEM), PPP1R3B, PRAME, PRDX5, PSA, PSMA, PTPRK, RAB 38/N Y-MEL- 1 , RAGE-1, RBAF600, RGS5, RhoC, R F43, RU2AS, SAGE, secernin 1, SIRT2, SNRPD1, SOX10, Spl7, SPA17, SSX-2, SSX-4, STEAP1, survivin, SYT-SSX1 or -SSX2 fusion protein, TAG-1, TAG-2, Telomerase, TGF-betaRII, TPBG, TRAG-3, Triosephosphate isomerase, TRP-l/gp75, TRP-2, TRP2-INT2, tyrosinase (TYR), VEGF, WT1 or XAGE-1b/GAGED2a.

18. The adenoviral vector according to claim 11, or the vaccine according to claim 16, wherein the virus is selected from Human Papilloma Viruses (HPV), Human Immunodeficiency virus (HIV), Herpes Simplex Virus (HSV2/HSV1), Influenza virus (types A, B and C), Polio virus, Respiratory Syncitial Virus (RSV), Rhinoviruses, Rotaviruses, Hepatitis A virus, Norwalk Virus Group, Enteroviruses, Astroviruses, Measles virus, Parainfluenza virus, Mumps virus, Varicella-Zoster virus, Human Cytomegalovirus (HCMV), Epstein-Barr virus, Adenoviruses, Rubella virus, Human T-cell Lymphoma type I virus (HTLV-I), Hepatitis B virus (HBV), Hepatitis C virus (HCV), Hepatitis D virus, Poxviruses, Marburg virus, Ebola virus or SARS-CoV-2, optionally SARS-CoV-2.

19. A method of producing an adenoviral vector as claimed in any one of claims 1 to 14 comprising:

    - introducing a nucleic acid which encodes a first peptide partner into a nucleic acid encoding a capsid protein;
    - inserting the modified capsid gene into the genome of an appropriate adenovirus; and
    - infecting a cell with said adenovirus and collecting the released progeny virus.

20. The vaccine comprising an adenoviral vector as claimed in claim 15 or claim 16 and an attached antigen for use in the treatment or prevention of a disease, preferably wherein the disease is an infectious disease or cancer.

21. The vaccine according to claim 20 wherein the cancer is selected from urogenital cancers (such as prostate cancer, renal cell cancers, bladder cancers), gynaecological cancers (such as ovarian cancers, cervical cancers, endometrial cancers), lung cancer, gastrointestinal cancers (such as non-metastatic or metastatic colorectal cancers, pancreatic cancer, gastric cancer, oesophageal cancers, hepatocellular cancers, cholangiocellular cancers), head and neck cancer (e.g. head and neck squamous cell cancer), malignant glioblastoma, malignant mesothelioma, non-metastatic or metastatic breast cancer (e.g. hormone refractory metastatic breast cancer), malignant melanoma, Merkel Cell Carcinoma or bone and soft tissue sarcomas, and haematologic neoplasias, such as multiple myeloma, acute myelogenous leukaemia, chronic myelogenous leukaemia, myelodysplastic syndrome and acute lymphoblastic leukaemia, preferably non-small cell lung cancer (NSCLC), breast cancer (e.g. hormone refractory metastatic breast cancer), head and neck cancer (e.g. head and neck squamous cell cancer), hormone sensitive or hormone refractory prostate cancer, colorectal cancer, ovarian cancer, hepatocellular cancer, renal cell cancer, soft tissue sarcoma, or small cell lung cancer.

22. A kit comprising an adenoviral vector as claimed in any one of claims 1 to 14.

23. A vaccine comprising an adenoviral vector as claimed in claim 1, wherein

a. said first peptide partner is a SpyCatcher which is fused to a pIX capsid protein, and said second peptide partner is a SpyTag, which is attached to an antigen, and wherein the SpyCatcher and the SpyTag are bound covalently through an isopeptide bond;

b. said first peptide partner is a SnoopCatcher which is fused to a pIX capsid protein, and said second peptide partner is a SnoopTagJr or a SnoopTag, which is attached to an antigen, and wherein the SnoopCatcher and the SnoopTagJr or the SnoopTag are bound covalently through an isopeptide bond;

c. said first peptide partner is a DogCatcher which is fused to a pIX capsid protein, and said second peptide partner is a DogTag which is attached to an antigen, and wherein the DogCatcher and the DogTag are bound covalently through an isopeptide bond;

d. said first peptide partner is a SnoopTagJr or a SnoopTag which is fused to a pIX capsid protein, and said second peptide partner is a SnoopCatcher, which is attached to an antigen, and wherein the SnoopTagJr or SnoopTag and the SnoopCatcher are bound covalently through an isopeptide bond;

e. said first peptide partner is a SpyTag which is fused to a pIX capsid protein, and said second peptide partner is a SpyCatcher, which is attached to an antigen, and wherein the SpyTag and the SpyCatcher are bound covalently through an isopeptide bond; or

f. said first peptide partner is a DogTag which is fused to the pIX capsid protein, and said second peptide partner is a DogCatcher, a SnoopTag or a SnoopTagJr, which is attached to an antigen, and wherein the DogTag and the DogCatcher, the SnoopTag or the SnoopTagJr are bound covalently through an isopeptide bond.

24. A vaccine comprising the adenoviral vector as claimed in claim 1, wherein said first peptide partner is a DogTag which is inserted into an HVR loop of a hexon protein, and said second peptide partner is a DogCatcher or a SnoopTagJr or a SnoopTag, said second peptide partner being attached to an antigen, and wherein the DogTag and the DogCatcher/SnoopTagJr/SnoopTag are bound covalently through an isopeptide bond.

25. An oncolytic virus preparation comprising the adenoviral vector as claimed in claim 1, wherein said second peptide partner is attached to a shielding entity or a targeting moiety.

26. The adenoviral vector as claimed in any one of claim 1 to claim 14 wherein said adenovirus is a human adenovirus.

27. The adenoviral vector as claimed in any one of claim 1 to claim 14, wherein said adenovirus is replication-competent, optionally modified to replicate only in selective cells.

28. The adenoviral vector as claimed in any one of claim 1 to claim 14, wherein said adenovirus is replication-incompetent.

29. The adenoviral vector as claimed in any one of claim 1 to claim 14, wherein said adenovirus is genetically modified to encode a transgene, and surface decorated via an isopeptide linkage.

30. An adenoviral vector capable of surface decoration via an isopeptide linkage via a modified capsid protein.