In relation to adenovirus, the present inventors found that the inclusion of the peptide pairs within the adenoviral capsid proteins were not as routine or straightforward as postulated, particularly in relation to the provision of an attachment means for antigens. Indeed, work by the inventors has shown that the most commonly utilised peptide pair, in this case insertion of SpyTag into the hexon capsid protein did not allow for the formation of a functional adenoviral vector (a vector allowing for effective coupling of SpyCatcher and capable of infecting cells). Indeed, the data showing that SpyTag was poorly reactive after insertion is included in the Examples, together with data on the lack of infectivity of the modified adenovirus. Thus, significant work has been expended in developing a system that works in relation to a modified adenoviral vector that is ready to accept peptide pairing and attachment of an entity to the modified capsid protein via the peptide partner inserted into the capsid protein.

Summary

In an aspect of the present disclosure, there is provided 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 forms an isopeptide bond with a second peptide partner; and wherein said second peptide partner is attached to an entity.

In another aspect of the present disclosure, there is provided an adenoviral vector disclosed herein for use in the manufacture of a vaccine comprising the addition of a second peptide partner attached to an antigen to said adenoviral vector.

In a further aspect of the present disclosure, there is provided a vaccine comprising the adenoviral vector as disclosed herein, wherein an antigen is attached to the adenoviral vector via the second peptide partner.

In another aspect of the present disclosure, there is provided a method of producing an adenoviral vector as disclosed herein, comprising:

- introducing a nucleic acid which encodes a first peptide partner into the 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.

In a further aspect of the present disclosure, there is provided a use of the vaccine comprising an adenoviral vector as disclosed herein and an attached antigen in the manufacture of a medicament for the treatment or prevention of an infectious disease or cancer.

In another aspect of the present disclosure, there is provided a kit comprising an adenoviral vector as disclosed herein.

In a further aspect of the present disclosure, there is provided a vaccine comprising an adenoviral vector as disclosed herein, wherein

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

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

In another aspect of the present disclosure, there is provided a vaccine comprising an adenoviral vector as disclosed herein, wherein said first peptide partner is DogTag which is inserted into HVR loops of the hexon protein, and said second peptide partner is DogCatcher or SnoopTagJr, said second peptide partner being attached to an antigen, and wherein DogTag and DogCatcher/SnoopTagJr are bound covalently through an isopeptide bond.

In a further aspect of the present disclosure, there is provided an oncolytic virus preparation comprising an adenoviral vector as disclosed herein, wherein said second peptide partner is attached to a shielding entity or a targeting moiety.

In another aspect of the present disclosure, there is provided an adenoviral vector capable of surface decoration via an isopeptide linkage via a modified capsid protein.

In another aspect of the present disclosure, there is provided the vaccine comprising an adenoviral vector of the disclosure and an attached antigen for use in the treatment or prevention of a disease, preferably wherein the disease is an infectious disease or cancer.

In accordance with a first example of the present disclosure, there is provided an adenoviral vector for preparation of a prophylactic or therapeutic adenoviral composition, comprising at least one modification in the capsid protein, wherein said modification comprises the inclusion of a first peptide partner in a capsid protein, wherein said first peptide is capable of forming a covalent bond with a second peptide partner, which can be attached to an entity.

The modification may be a fusion with the first peptide partner or an insertion of the first peptide partner into the capsid protein.

The capsid protein may be any capsid protein, but is preferably a hexon protein or a pIX protein.

The first peptide partner and the second peptide partner form a peptide partner pair, which may be covalently linked by an isopeptide or ester bond, preferably an isopeptide bond.

In one example, the first peptide partner is the “tag” partner, which may be covalently linked by an isopeptide or ester bond to a second peptide partner which is a “catcher”. In this example, the capsid protein is preferably a hexon protein. Thus, the first peptide partner or “tag” which modifies the hexon is preferably a DogTag, Isopeptag, Isopeptag-N, SdyTag, PsCsTag or Jo. It is preferred that the first peptide partner or tag is not SpyTag. In this example, SpyTag is unmodified during its insertion into the hexon protein.

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 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, wherein variants, derivatives and modifications involve amino acid additions, substitutions, alterations or deletions, and retain the same function in relation to the ability to form an isopeptide bond with the relevant binding partner.

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 claims 2 or claims 4-10 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.

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. Use of the vaccine comprising an adenoviral vector as claimed in claim 15 or claim 16 and an attached antigen in the manufacture of a medicament for the treatment or prevention of an infectious disease or cancer.

21. The use 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.

31. 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.