Claims

1. A composition for use in the prophylaxis and/or treatment of a disease wherein the composition comprises:
    i. a first polynucleotide encoding a protein fused to a first peptide tag; and
    ii. a second polynucleotide encoding an antigen fused to a second peptide tag,

    wherein the antigen and the protein upon expression in a cell are linked via an isopeptide bond between the first peptide tag and the second peptide tag, whereby i - ii form a particle displaying said antigen.

2. The composition for the use according to claim 1, wherein the particle is selected from the group consisting of: a virus-like particle; and a nanoparticle.

3. The composition for the use according to any one of the preceding claims, wherein the first and/or second polynucleotide is DNA or RNA, optionally, wherein the RNA is formulated in a lipid particle formulation.

4. The composition for the use according to any one of the preceding claims, wherein the protein is a particle-forming protein, optionally wherein the protein is a viral capsid protein or a viral envelope protein such as a glycoprotein, optionally wherein the protein is a viral capsid protein or a viral envelope protein from a mammalian virus such as a human virus , optionally wherein the protein is a protein from a hepatitis virus such as hepatitis B or E, for example a core protein from hepatitis B virus; a protein from a norovirus such as NoV; a protein from a papilloma virus such as Human Papilloma Virus (HPV), preferably HPV16 or HPV18, such as HPV L1; a protein from a polyomavirus such as polyomavirus vp1 (PyV); a protein from a calicivirus such as feline calicivirus (FCV), preferably FCV VP1; a protein from a circovirus such as a porcine circovirus (PCV), preferably PCV2 ORF2; a protein from a nervous necrosis virus (NNV), such as NNV coat protein; a protein from a parvovirus such as canine parvovirus (CVP), preferably CPV VP2, goose parvovirus (GPV) or porcine parvovirus (PPV), preferably structural proteins from GPV or PPV, or parvovirus B19; a protein from a protoparvovirus such as an enteritis virus, for example mink enteritis virus (MEV), preferably MEV VP2, or duck plague virus (DPV),

preferably a DPV structural protein, or optionally wherein the protein is a protein from a plant virus, such as a cowpea virus, a tobacco virus, a tomato virus, a cucumber virus or a potato virus, optionally wherein the plant virus is a mosaic virus, preferably Cowpea mosaic virus (CPMV); tobacco mosaic virus (TMV); tomato spotted wilt virus (TSWV); tomato yellow leaf curl virus (TYLCV); cucumber mosaic virus (CMV); or from potato virus Y (PVY), or optionally wherein the protein is a bacteriophage protein, such as a protein from *Salmonella* virus P22, from MS2, from QBeta, PRR1, PP7, bacteriophage R17, bacteriophage fr, bacteriophage GA, bacteriophage SP, bacteriophage M11, bacteriophage MX1, bacteriophage NL95, bacteriophage f2 or Cb5 , or optionally wherein the protein is a particle forming protein, such as ferritin as set forth in SEQ ID NO: 69, i301 as set forth in SEQ ID NO: 72, replicase polyprotein 1a (pp1a), a lumazine synthase as set forth in SEQ ID NO: 70, Hbc as set forth in SEQ ID NO: 92, tandemHBc as set forth in SEQ ID NO: 93, the 2-oxo acid dehydrogenase subunit E2 as set forth in SEQ ID NO: 97, or the norovirus capsid protein as set forth in SEQ ID NO: 98.

5. The composition for the use according to any one of the preceding claims, wherein the first or second peptide tag comprises a tag selected from the group consisting of a SpyTag as set forth in SEQ ID NO: 1, a SdyTag as set forth in SEQ ID NO: 2, a SnoopTag as set forth in SEQ ID NO: 3, a PhoTag as set forth in SEQ ID NO: 4, an EntTag as set forth in SEQ ID NO: 5, a KTag, a BacTag as set forth in SEQ ID NO: 15, a Bac2Tag as set forth in SEQ ID NO: 16, a Bac3Tag as set forth in SEQ ID NO: 17, a Bac4Tag as set forth in SEQ ID NO: 18, a RumTrunk D9N tag as set forth in SEQ ID NO: 13 or SEQ ID NO: 14, a Rum7Tag as set forth in SEQ ID NO: 12, a RumTag as set forth in SEQ ID NO: 6, a Rum2Tag as set forth in SEQ ID NO: 7, a Rum3Tag as set forth in SEQ ID NO: 8, a Rum4Tag as set forth in SEQ ID NO: 9, a Rum5Tag as set forth in SEQ ID NO: 10, a Rum6Tag as set forth in SEQ ID NO: 11, a Bac5Tag as set forth in SEQ ID NO: 19, a SpyCatcher as set forth in SEQ ID NO: 21, a SdyCatcher as set forth in SEQ ID NO: 22, and a SnoopCatcher as set forth in SEQ ID NO: 23, optionally wherein:

a) one of the first and second peptide tags is an SdyTag as set forth in SEQ ID NO: 2 and the other of the first and second peptide tags is an SdyCatcher as set forth in SEQ ID NO: 22;

b) one of the first and second peptide tags is a SpyTag as set forth in SEQ ID NO: 1, and the other of the first and second peptide tags is a SpyCatcher as set forth in SEQ ID NO: 21; or

c) one of the first and second peptide tags is a SnoopTag as set forth in SEQ ID NO: 3 and the other of the first and second peptide tags is a SnoopCatcher as set forth in SEQ ID NO: 23.

6. The composition for the use according to any one of the preceding claims, wherein one or more first peptide tags are fused to the N-terminal end, to the C-terminal end of the protein and/or inserted in-frame into the coding sequence of the protein, optionally by a linker, and/or wherein one or more second peptide tags are fused to the N-terminal end, to the C-terminal end of the antigen and/or inserted in-frame into the coding sequence of the antigen, optionally by a linker.

7. The composition for the use according to any one of the preceding claims, wherein the disease is cancer, a lipid disorder, a cardiovascular disease, an immune-inflammatory disease, a chronic disease, a neurological disease, an infectious disease and/or an allergic reaction/disease, optionally wherein the cancer is selected from the group consisting of breast cancer, gastric cancer, ovarian cancer, glioblastoma, bone cancer, skin cancer and uterine serous carcinoma, optionally wherein the lipid disorder is selected from the group consisting of a lipid disorder such as hyperlipidemia, type I, type II, type III, type IV, or type V hyperlipidemia, secondary hypertriglyceridemia, hypercholesterolemia, familial hypercholesterolemia, xanthomatosis and cholesterol acetyltransferase deficiency, optionally wherein the cardiovascular disease is selected from the group consisting of dyslipidemia, atherosclerosis, a coronary artery disease and/or hypercholesterolemia, optionally wherein the chronic or immune-inflammatory disease is selected from the group consisting of eosinophilic asthma, allergy, nasal polyposis, atopic dermatitis, eosinophilic esophagitis, hypereosinophilic syndrome, contact allergy and Churg-Strauss syndrome, optionally wherein the neurological disease is Alzheimer's disease, optionally wherein the infectious disease is selected from the group consisting of malaria, tuberculosis, and a disease caused by a virus,

such as a coronavirus, for example SARS-CoV-2, malaria, tuberculosis, HIV, HCV, Dengue fever, Chikungunya, Yellow fever, HBV or influenza.

8. The composition for the use according to any one of the preceding claims, wherein the antigen is a polypeptide, peptide and/or an antigenic fragment of a polypeptide associated with or specific for an abnormal physiological response, optionally wherein the abnormal physiological response is an autoimmune disease, an allergic reaction and/or a cancer.

9. The composition for the use according to any one of the preceding claims, wherein said antigen is a protein, peptide and/or an antigenic fragment of Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

10. The composition for the use according to any one of the preceding claims, wherein the antigen is selected from the group consisting of: hemagglutinin, GD2, EGF-R, CEA, CD52, CD21, neuraminidase, human melanoma protein gp100, human melanoma protein melan-A/MART1, HIV envelope protein, M2e, VAR2CSA, ICAM1, CSP, Dengue virus NS1, Dengue virus envelope protein, Chikungunya virus envelope protein, tyrosinase, HCV E2, NA17-A nt, MAGE-3, HPV 16 E7, HPV L2, PD1, PD-L1, CTLA-4, p53, hCG, Fel d1, EGRFvIII, endoglin, ANGPTL-3, CSPG4, CTLA-4, HER2, IgE, IL-1 beta, IL-5, IL-13, IL-17, IL-22, IL-31, IL-33, TSLP, NGF, (IHNV) G-protein, a lymphotoxin such as lymphotoxin α or β, a lymphotoxin receptor, a receptor activator of nuclear factor kB ligand, vascular endothelial growth factor VEGF, a VEGF receptor, IL-23 p19, ghrelin, CCL21, CXCL12, SDF-1, M-CSF, MCP-1, endoglin, GnRH, TRH, eotaxin, bradykinin, BLC, TNF-α, amyloid β peptide A, angiotensin, gastrin, progastrin, CETP, CCR5, C5a, CXCR4, Des-Arg-bradykinin, GnRH peptide, angiotensin peptide, TNF peptide, a SARS-CoV-2 envelope protein, a SARS-CoV-2 spike protein, a SARS-CoV-2 nucleocapsid protein and a SARS-CoV-2 envelope protein, IL-13, IL-31, IL-17A, PCSK9, an HIV trimer and an influenza virus trimer, eGFP as set forth in SEQ ID NO: 94, Pfs25 as set forth in SEQ ID NO: 96, and the His purification tag as set forth in SEQ ID NO: 95, or an antigenic fragment or antigenic variant thereof.

11. The composition for the use according to any one of the preceding claims for use in treatment of an infectious disease, wherein the antigen is a protein or a peptide specific to the pathogenic organism which causes the infectious disease, or a fragment thereof.

12. A composition comprising:

    i. a first polynucleotide encoding a protein fused to a first peptide tag; and

    ii. a second polynucleotide encoding an antigen fused to a second peptide tag,

wherein the antigen and the protein upon expression in a cell are linked via an isopeptide bond between the first peptide tag and the second peptide tag, whereby i - ii form a particle displaying said antigen, wherein the protein is selected from the group consisting of i301 as set forth in SEQ ID NO: 72 or a homologue thereof having at least 90% sequence identity thereto, Hbc as set forth in SEQ ID NO: 92 or a homologue thereof having at least 90% sequence identity thereto, tandemHBc as set forth in SEQ ID NO: 93 or a homologue thereof having at least 90% sequence identity thereto, human ferritin as set forth in SEQ ID NO: 69 or a homologue thereof having at least 90% sequence identity thereto, the 2-oxo acid dehydrogenase subunit E2 as set forth in SEQ ID NO: 97 or a homologue thereof having at least 90% sequence identity thereto, lumazine synthase as set forth in SEQ ID NO: 70 or a homologue thereof having at least 90% sequence identity thereto, and the norovirus capsid protein as set forth in SEQ ID NO: 98 or a homologue thereof having at least 90% sequence identity thereto.

13. The composition according to claim 12, wherein the first polynucleotide, the protein, the first peptide tag, the second polynucleotide, the antigen, the second peptide tag are as defined in any one of claims 1-11, optionally wherein the first and the second peptide tags are selected from the group consisting of SpyTag as set forth in SEQ ID NO: 1 or a homologue thereof having at least 90% sequence identity thereto, and SpyCatcher as set forth in SEQ ID NO: 21 or a homologue thereof having at least 90% sequence identity thereto, further optionally, wherein the antigen is selected from the group consisting of eGFP as set forth in SEQ ID NO: 94 or a homologue thereof having at least 90% sequence identity thereto, Pfs25 as set forth in SEQ ID NO: 96 or a homologue thereof having at least 90% sequence identity thereto, and

the His purification tag as set forth in SEQ ID NO: 95 or a homologue thereof having at least 90% sequence identity thereto.

14. An expression system comprising:
    i. a first polynucleotide encoding a protein fused to a first peptide tag; and
    ii. a second polynucleotide encoding an antigen fused to a second peptide tag,

    wherein upon expression of the first and second polynucleotides in a cell, the antigen and the protein are linked via an isopeptide bond between the first peptide tag and the second peptide tag, whereby i - ii form a particle displaying said antigen,
    wherein:
    i. the first polynucleotide further comprises a secretion or excretion signal, whereby the protein fused to the first peptide tag is secreted or excreted from the endoplasmic reticulum of the cell; and/or
    ii. the second polynucleotide further comprises a secretion or excretion signal, whereby the antigen fused to the second peptide tag is secreted or excreted from the endoplasmic reticulum of the cell.

15. The expression system according to claim 14, wherein the first peptide tag, the second peptide tag, the protein and/or the antigen are as defined in any one of claims 1 to 11, optionally wherein the first polynucleotide and the second polynucleotide are both DNA polynucleotides or RNA polynucleotides, optionally wherein the first and second polynucleotides are comprised within one vector such as a viral vector or a plasmid, or wherein the first and second polynucleotides are comprised within two vectors such as two viral vectors; two plasmids; or one viral vector and one plasmid, such as wherein the viral vector is an adenoviral vector, such as a modified adenoviral vector, e.g. a modified vaccinia Ankara (MVA) vector, optionally wherein the expression system comprises or consists of a plasmid, and/or of an mRNA.

16. The expression system according to any one of claims 14 to 15, wherein the first polynucleotide comprises or consists of a first polynucleotide encoding a protein comprising a first peptide tag, and the second polynucleotide comprises or consists of a second polynucleotide encoding an antigen comprising a second peptide tag.

17. The expression system according to any one of claims 14 to 16, wherein the secretion or excretion signal comprises or consists of SEQ ID NO: 79, SEQ ID NO: 80, SEQ ID NO: 81, SEQ ID NO: 82, SEQ ID NO: 83 or SEQ ID NO: 84.

18. The composition for the use according to any one of claims 1 to 11, the expression system according to any one of claims 14 to 17 for use in a method for inducing an immune response in a subject, the method comprising the step of administering said composition, polynucleotide or expression system to said subject at least once.

19. A method of administering a composition for use in the prophylaxis and/or treatment of a disease in a subject in need thereof comprising the step of
    i. administering at least one composition as defined in any one of claims 1 to 11 to a subject at least once for prophylaxis and/or treatment of a disease as defined in any one of the preceding claims.

20. The method of administering a composition for the use according to claim 19, wherein the composition is boosted by administration in a form or body part different from the previous administration, optionally wherein the composition is administered to the area most likely to be the receptacle of a given disease, optionally, wherein the subject is an animal, such as a mammal, such as a cow, pig, horse, sheep, goat, llama, mouse, rat, monkey, most preferably such as a human being; or a bird, such as a chicken or a fish, such as a salmon, optionally wherein the composition is administered in combination with any other vaccine, such as wherein the composition forms a part of a vaccine cocktail.

21. A kit of parts comprising
    i. a composition comprising:
        a) a first polynucleotide encoding a protein fused to a first peptide tag; and
        b) a second polynucleotide encoding an antigen fused to a second peptide tag,

    wherein upon expression of the first and second polynucleotides in a cell, the antigen and the protein are linked via an isopeptide bond, or an ester bond, between the first peptide tag and the second peptide tag, whereby

i - ii form a particle displaying said antigen, or an expression system according to any one of claims 14 to 17, and

ii. optionally, a medical instrument or other means for administering the composition, and

iii. instructions for use.

22. The kit of parts according to claim 21, optionally wherein the first polynucleotide, the protein, the first peptide tag, the second polynucleotide, the antigen, and/or the second peptide tag are as defined in any one of claims 1-11, optionally comprising a second active ingredient.