Claims

1. A pharmaceutical composition comprising:

(A) a polymeric carrier cargo complex, comprising:

a) a polymeric carrier comprising disulfide-crosslinked cationic components, preferably formed by disulfide-crosslinked cationic components, as a carrier, wherein the cationic components of the polymeric carrier comprised in said polymeric carrier cargo complex are cationic peptides; and

b) at least one nucleic acid molecule as a cargo, wherein said nucleic acid molecule

cargo is an immunostimulatory RNA,

and

(B) at least one protein or peptide antigen that is selected from the group consisting of:

(i) an antigen from a pathogen associated with infectious disease;

(ii) an antigen associated with allergy or allergic disease;

(iii) an antigen associated with autoimmune disease; and

(iv) an antigen associated with a cancer or tumour disease ~~or a fragment, variant and/or derivative of said protein or peptide antigen.~~

or an antigenic fragment, variant and/or derivative of said protein or peptide antigen, wherein the at least one protein or peptide antigen is a separate component and wherein the at least one protein or peptide antigen is not ovalbumin or ovalbumin-derived peptide SIINFEKL.

2. The pharmaceutical composition of claim 1, wherein component (B) is not covalently linked to component (A).

3. The pharmaceutical composition of claim 1 or 2, wherein said protein or peptide antigen is from a pathogen selected from the list consisting of: Rabies virus, Hepatitis B virus, human Papilloma virus (hPV), Bacillus anthracis, Respiratory syncytial virus (RSV), Herpes simplex virus (HSV), Influenza virus and Mycobacterium tuberculosis.

~~(RSV), Herpes simplex virus (HSV), Influenza virus and Mycobacterium tuberculosis.~~

4. The pharmaceutical composition of any one of claims 1~~-~~ to 3, wherein said protein or peptide antigen is selected from the list consisting of:

The Hemagglutinin (HA), the Neuraminidase (NA), the Nucleoprotein (NP), the M1 protein, the M2 protein, the NS1 protein, the NS2 protein (the NEP protein: nuclear export protein), the PA protein, the PB1 protein (polymerase basic 1 protein), the PB1-F2 protein and the PB2 protein of Influenza virus;

- The nucleoprotein (N), the phosphoprotein (P), the matrix protein (M), the glycoprotein (G), and the viral RNA polymerase (L), in each case of Rabies virus;
- the Hepatitis B surface antigen (HBsAg), the Hepatitis B core antigen (HbcAg), the Hepatitis B virus DNA polymerase, the HBx protein, the preS2 middle surface protein, the large S protein, the virus

protein VP1, the virus protein VP2, the virus protein VP3, and the virus protein VP4, in each case of Hepatitis B virus;

- the E1 protein, the E2 protein, the E3 protein, the E4 protein, the E5 protein, the E6 protein, the E7 protein, the E8 protein, the L1 protein, and the L2 protein, in each case of human Papilloma virus (hPV);

- the protective antigen (PA), the edema factor (EF), the lethal factor (LF), and the Slayer homology proteins (SLH), in each case of Bacillus anthracis;

- the Fusion (F) protein, the nucleocapsid (N) protein, the phosphoprotein (P), the matrix (M) protein, the glycoprotein (G), the large protein (L; RNA polymerase), the non-structural protein 1 (NS1), the non-structural protein 2 (NS2), the small hydrophobic (SH) protein, the elongation factor M2-1, and the transcription regulation protein M2-2, in each case of respiratory syncytial virus (RSV);

- the Glycoprotein L (UL1), the Uracil-DNA glycosylase UL2, the UL3 protein, the UL4 protein, the DNA replication protein UL5, the Portal protein UL6, the Virion maturation protein UL7, the DNA helicase UL8, the Replication origin-binding protein UL9, the Glycoprotein M (UL10), the UL11 protein, the Alkaline exonuclease UL12, the Serine-threonine protein kinase UL13, the Tegument protein UL14, the Terminase (UL15), the Tegument protein UL16, the UL17 protein , the Capsid protein VP23 (UL18), the Major capsid protein VP5 (UL19), the Membrane protein UL20, the Tegument protein UL21, the Glycoprotein H (UL22), the Thymidine Kinase UL23, the UL24 protein, the UL25 protein, the Capsid protein P40 (UL26, VP24, VP22A), the Glycoprotein B (UL27), the ICP18.5 protein (UL28), the Major DNA-binding protein ICP8 (UL29), the DNA polymerase UL30, the Nuclear matrix protein UL31, the Envelope glycoprotein UL32, the UL33 protein, the Inner nuclear membrane protein UL34, the Capsid protein VP26 (UL35), the Large tegument protein UL36, the Capsid assembly protein UL37, the VP19C protein (UL38), the Ribonucleotide reductase (Large subunit) UL39, the Ribonucleotide reductase (Small subunit) UL40, the Tegument protein/Virion host shutoff VHS protein (UL41), the DNA polymerase processivity factor UL42, the Membrane protein UL43, the Glycoprotein C (UL44), the Membrane protein UL45, the Tegument proteins VP11/12 (UL46), the Tegument protein VP13/14 (UL47), the Virion maturation protein VP16 (UL48, Alpha-TIF), the Envelope protein UL49, the dUTP diphosphatase UL50, the Tegument protein UL51, the DNA helicase/primase complex protein UL52, the Glycoprotein K (UL53), the Transcriptional regulation protein IE63 (ICP27, UL54), the UL55 protein, the UL56 protein, the Viral replication protein ICP22 (IE68, US1), the US2 protein, the Serine/threonine-protein kinase US3, the Glycoprotein G (US4), the Glycoprotein J (US5), the Glycoprotein D (US6), the Glycoprotein I (US7), the Glycoprotein E (US8), the Tegument protein US9, the Capsid/Tegument protein US10, the Vmw21 protein (US11), the ICP47 protein (IE12, US12), the Major transcriptional activator ICP4 (IE175, RS1), the E3 ubiquitin ligase ICP0 (IE110), the Latency-related protein 1 (LRP1), the Latency-related protein 2 (LRP2), the Neurovirulence factor RL1 (ICP34.5), and the Latency-associated transcript (LAT), in each case of Herpes simplex virus (HSV); or
- the ESAT-6 protein, the ESX-1 protein, the CFP10 protein, the TB10.4 protein, the MPT63 protein, the MPT64 protein, the MPT83 protein, the MTB12 protein, the MTB8 protein, the AG85A protein, the AG85B protein, the Rpf-like proteins, the KATG protein, the PPE18 protein, the MTB32 protein, the MTB39 protein, the Crystallin, the HSP65 protein, the PST-S protein, and the HBHA protein, the 10 kDa filtrate antigen EsxB, the serine protease PepA, the fibronectin-binding protein D FbpD, the secreted protein MPT51, the periplasmic phosphate-binding lipoprotein PSTS1 (PBP-1), the periplasmic phosphate-binding lipoprotein PSTS3 (PBP-3, Phos-1), the PPE family protein PPE14, the PPE family protein PPE68, the protein MTB72F, the molecular chaperone DnaK, the cell surface

lipoprotein MPT83, the lipoprotein P23, the Phosphate transport system permease protein PstA, the 14 kDa antigen, the fibronectin-binding protein C FbpC1, the Alanine dehydrogenase TB43, and the Glutamine synthetase 1, in each case of Mycobacterium tuberculosis.

5. The pharmaceutical composition of claim 1 or 2, wherein said protein or peptide antigen is associated with allergy or allergic disease and is derived from a source selected from the list consisting of: grass pollen, tree pollen, flower pollen, herb pollen, dust mite, mold, animals, food, and insect venom.

6. The pharmaceutical composition of claim 1 or 2, wherein said protein or peptide antigen is associated with autoimmune disease and is selected from the list consisting of:

- myelin basic protein (MBP), proteolipid protein (PLP), and myelin oligodendrocyte glycoprotein (MOG), in each case associated with multiple sclerosis (MS);
- CD44, preproinsulin, proinsulin, insulin, glutamic acid decaroxylase (GAD65), tyrosine phosphatase-like insulinoma antigen 2 (IA2), zinc transporter ((ZnT8), and heat shock protein 60 (HSP60), in each case associated with diabetes Typ I;
- interphotoreceptor retinoid-binding protein (IRBP) associated with autoimmune uveitis;
- acetylcholine receptor AchR, and insulin-like growth factor-1 receptor (IGF-1R), in each case associated with Myasthenia gravis;
- M-protein from beta-hemolytic streptocci (pseudo-autoantigen) associated with Rheumatic Fever;
- Macrophage migration inhibitory factor associated with Arthritis;
- Ro/La RNP complex, alpha- and beta-fodrin, islet cell autoantigen, poly(ADP)ribose polymerase (PARP), NuMA, NOR-90, Ro60 autoantigen, and p27 antigen, in each case associated with Sjögren's syndrome;
- Ro60 autoantigen, low-density lipoproteins, Sm antigens of the U-1 small nuclear ribonucleoprotein complex (B/B', D1, D2, D3, E, F, G), and RNP ribonucleoproteins, in each case associated with lupus erythematosus;
- oxLDL, beta(2)GPI, HSP60/65, and oxLDL/beta(2)GPI, in each case associated with Atherosclerosis;
- cardiac beta(1)-adrenergic receptor associated with idiopathic dilated cardiomyopathy (DCM);
- histidyl-tRNA synthetase (HisRS) associated with myositis;
- topoisomerase I associated with scleroderma;
- IL-17; or

heat shock proteins.

7. The pharmaceutical composition of claim 1 or 2, wherein said protein or peptide antigen is associated with a cancer or tumour disease and is selected from the list consisting of: p53, CA125, EGFR, Her2/neu, hTERT, PAP, MAGE-A1, MAGE-A3, Mesothelin, MUC-1, NY-ESO-1, GP100, MART-1, Tyrosinase, PSA, PSCA, PSMA VEGF, VEGFR1, VEGFR2, Ras, CEA and WT1.

8. The pharmaceutical composition of any one of claims 1 to 7, wherein said polymeric carrier cargo complex is for use as an adjuvant.

~~9.~~ The pharmaceutical composition of any one of claims 1 to 8~~, wherein said nucleic acid molecule cargo is an immunostimulatory nucleic acid.~~

~~10. The pharmaceutical composition of any one of claims 1 to 9, wherein said nucleic acid molecule cargo is RNA; preferably wherein said nucleic acid molecule cargo is an immunostimulatory RNA (isRNA).~~

9. ~~11. The pharmaceutical composition of any one of claims 1 to 10~~, wherein the cationic components of the polymeric carrier and the nucleic acid molecule cargo comprised in said polymeric carrier cargo complex are provided in an N/P ratio in the range of 0.1-20, or in the range of 0.1-5, or in the range of 0.1-1, or in the range of 0.5-0.9.

10. ~~12.~~ The pharmaceutical composition of any one of claims 1 to ~~11~~9, wherein ~~the~~said cationic

~~components of the polymeric carrier comprised in said polymeric carrier cargo complex are cationic~~ peptides~~.~~

~~13. The pharmaceutical composition of claim 12, wherein said cationic peptides are~~

are selected from peptides according to formula (I)

$$(Arg)_l;(Lys)_m;(His)_n;(Orn)_o;(Xaa)_x,$$

wherein

l + m + n +o + x = 3-100, and

l, m, n or o = independently of each other is any number selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21-30, 3140, 41-50, 51-60, 61-70, 71-80, 81-90 and 91-100, provided that the overall content of Arg, Lys, His and Orn represents at least 10% of all amino acids of the cationic peptide; and Xaa is any amino acid selected from native (= naturally occurring) or non-native amino acids except of Arg, Lys, His or Orn; and

x = any number selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21-30, 31-40, 41-50, 51-60, 61-70, 71-80, 81-90, provided, that the overall content of Xaa does not exceed 90% of all amino acids of the cationic peptide,

~~12, 13, 14, 15, 16, 17, 18, 19, 20, 21-30, 31-40, 41-50, 51-60, 61-70, 71-80, 81-90, provided, that the overall content of Xaa does not exceed 90 % of all amino acids of the cationic peptide,~~

~~or~~ said cationic peptides are selected from peptides according to subformula(IIIa) $\{(Arg)_l;(Lys)_m;(His)_n;(~~Orn~~Orn)_o;(~~Xaa'~~Xaa')_x\ (Cys)_y\}$

or said cationic peptides from peptides according to subformula (Ib)

$$Cys_1\ \{(Arg)_l;(Lys)_m;(His)_n;(Orn)_o;(Xaa)_x\}\ Cys_2$$

wherein $(Arg)_l$; $(Lys)_m$; $(His)_n$; $(Orn)_o$; and x are as defined above; Xaa' is any amino acid selected from native (= naturally occurring) or non-native amino acids except of Arg,

Lys, His, Orn; or Cys and y is any number selected from ~~0,~~ 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21-30, 31-40, 41-50, 51-60, 61-70, 71-80, and 81-90, provided that the overall content of Arg (Arginine), Lys (Lysine), His (Histidine) and Orn (Ornithine) represents at least 10% of all amino acids of the oligopeptide and wherein Cys1 and Cys2 are Cysteines proximal to, or terminal to $(Arg)_l;(Lys)_m;(His)_n;(Orn)_o;(Xaa)_x$.

~~14~~11. The pharmaceutical composition of any one of claims 1 to ~~13~~10, wherein said polymeric carrier cargo complex does not include said protein or peptide antigen.

~~15~~12. A kit or kit of parts comprising:

a) a polymeric carrier cargo complex as defined according to claim 1, 2, or any one of claims 8 to ~~14~~11; and

b) at least one protein or peptide antigen or antigenic fragment, variant and/or derivative thereof as defined according to any one of claims 1 to 7.

~~16.~~13. ~~The~~ A pharmaceutical composition of any one of claims 1 to ~~14~~11, or the kit or kit of parts of claim ~~15~~12, for use as a vaccine.

~~17.~~14. A polymeric carrier cargo complex as defined according to claim 1, 2, or any one of claims 8 to ~~14~~11 for use in ~~therapy~~improving an immune response in combination with at

least one protein or peptide antigen or antigenic fragment, variant and/or derivative thereof as defined according to any one of claims 1 to 7.

~~18.~~15. A protein or peptide antigen or antigenic fragment, variant and/or derivative thereof as defined according to any one of claims 1 to 7 ~~for use in therapy~~when used in combination with a polymeric carrier cargo complex as defined according to claim 1, 2, or any one of claims 8 to ~~14~~11 for use in improving an immune response.

~~19. The polymeric carrier cargo complex of claim 17 for use in the therapy of; or the protein or peptide antigen or fragment, variant and/or derivative thereof of claim 18 for use in the therapy of:~~

16. The pharmaceutical composition according to any one of claims 1 to 11 for use in the treatment of:

(i) an infectious disease;

(ii) an allergy or allergic disease;

(iii) an autoimmune disease; or

(iv) a cancer or tumour disease.

~~20. A pharmaceutical package, including:~~

~~a~~17. Use of the pharmaceutical composition according to any one of claims 1 to 11, in the manufacture of a medicament for treating:

(i) an infectious disease;

(ii) an allergy or allergic disease;

(iii) an autoimmune disease; or

(iv) a cancer or tumour disease.

~~(A)~~ 18. The polymeric carrier cargo complex as defined according to claim 1, 2, or any one of claims 8 to ~~14~~11; and

~~(B) instructions describing the use of said polymeric carrier cargo complex in therapy in combination with~~ at least one protein or peptide antigen or antigenic fragment, variant and/or derivative thereof as defined according to any one of claims 1 to 7~~.~~

~~21. A pharmaceutical package, including:~~

~~(A) at least one protein or peptide antigen or fragment, variant and/or derivative thereof as defined according to any one~~, for use in the treatment of ~~claims 1 to 7; and~~:

(i) ~~(B) instructions describing the use~~an infectious disease;

(ii) an allergy or allergic disease;

(iii) an autoimmune disease; or

(iv) a cancer or tumour disease.

19. Use of ~~said protein or peptide antigen or fragment, variant and/or derivative thereof in therapy in combination with a~~the polymeric carrier cargo complex as defined according to claim 1, 2, or any one of claims 8 ~~to14.~~

~~22. The pharmaceutical package~~to 11; and at least one protein or peptide antigen or antigenic fragment, variant and/or derivative thereof as defined according to any one of ~~claim 20 or 21, wherein said instructions further~~

~~describe~~ claims 1 to 7, in the ~~use in the therapy~~manufacture of a medicament for treating:

(i) an infectious disease;

(ii) an allergy or allergic disease;

(iii) an autoimmune disease; or

(iv) ~~(iv)~~a cancer or tumour disease.