Claims

1. Polymeric carrier molecule according to formula (I):

$$L\text{-}P^1\text{-}S\text{-}[S\text{-}P^2\text{-}S]_n\text{-}S\text{-}P^3\text{-}L$$

wherein,

P^1 and P^3 are different or identical to each other and represent a linear or branched hydrophilic polymer chain, each P^1 and P^3 exhibiting at least one –SH-moiety, capable to form a disulfide linkage upon condensation with component P^2, the linear or branched hydrophilic polymer chain selected independent from each other from polyethylene glycol (PEG), poly-*N*-(2-hydroxypropyl)methacrylamide, poly-2-(methacryloyloxy)ethyl phosphorylcholines, poly(hydroxyalkyl L-asparagine), poly(2-(methacryloyloxy)ethyl phosphorylcholine), hydroxyethylstarch or poly(hydroxyalkyl L-glutamine), wherein the hydrophilic polymer chain exhibits a molecular weight of about 1 kDa to about 100 kDa,

P^2 is a cationic or polycationic peptide or protein, having a length of about 3 to about 100 amino acids, or
is a cationic or polycationic polymer, having a molecular weight of about 0.5 kDa to about 30 kDa,
each P^2 exhibiting at least two –SH-moieties, capable to form a disulfide linkage upon condensation with further components P^2 or component(s) P^1 and/or P^3;

-S-S- is a (reversible) disulfide bond;

L is an optional ligand, which may be present or not, and may be selected independent from the other from RGD, Transferrin, Folate, a signal peptide or signal sequence, a localization signal or sequence, a nuclear localization signal or sequence (NLS), an antibody, a cell penetrating peptide, TAT, a ligand of a receptor, cytokines,

hormones, growth factors, small molecules, carbohydrates, mannose, galactose, synthetic ligands, small molecule agonists, inhibitors or antagonists of receptors, or RGD peptidomimetic analogues; and

n is an integer, selected from a range of about 1 to 50, preferably in a range of about 1, 2, 3, 4, or 5 to 10 , more preferably in a range of about 1, 2, 3, or 4 to 9.

2. The polymeric carrier molecule according to claim 1, wherein the polymeric carrier molecule additionally contains an amino acid component $(AA)_x$, wherein x is an integer selected from a range of about 1 to 100.

3. The polymeric carrier molecule according to claim 2, wherein the amino acid component $(AA)_x$ comprises an aromatic amino acid component, a hydrophilic amino acid component, a lipophilic amino acid component, a weak basic amino acid component, a signal peptide, localization signal or sequence, a nuclear localization signal or sequence, a cell penetrating peptide, a therapeutically active protein or peptide, an antigen or an antigenic epitope, a tumour antigen, a pathogenic antigen (an animal antigen, a viral antigen, a protozoal antigen, a bacterial antigen, an allergic antigen), an autoimmune antigen, or a further antigen, an allergen, an antibody, an immunostimulatory protein or peptide, an antigen-specific T-cell receptor, or another protein or peptide suitable for a specific (therapeutic) application.

4. The polymeric carrier molecule according to any of claims 2 or 3, wherein the amino acid component $(AA)_x$ occurs as a mixed repetitive amino acid component $[(AA)_x]_z$, wherein z is an integer selected from a range of about 1 to 30.

5. The polymeric carrier molecule according to any of claims 2 to 4, wherein formula (I) is modified according to formula (Ia)

$$L\text{-}P^1\text{-}S\text{-}\{[S\text{-}P^2\text{-}S]_a[S\text{-}(AA)_x\text{-}S]_b\}\text{-}S\text{-}P^3\text{-}L,$$

wherein x, z, S, L, AA, P^1, P^2 and P^3 are as defined before and

a + b = n, wherein

n is as defined before, preferably in a range of about 1, 2, 3, 4, or 5 to 10;

a is an integer, selected independent from integer b from a range of about 1 to 50, preferably in a range of about 1, 2, 3, 4, or 5 to 10, and

b is an integer, selected independent from integer a from a range of about 1 to 50, preferably in a range of about 1, 2, 3, 4, or 5 to 10,

and wherein the single components [S-P^2-S] and [S-$(AA)_x$-S] occur in any order in the subformula {[S-P^2-S]$_a$[S-$(AA)_x$-S]$_b$}.

6. The polymeric carrier molecule according to any of claims 1 to 5, wherein component P^2 is a cationic or polycationic peptide selected from protamine, nucleoline, spermine or spermidine, poly-L-lysine (PLL), basic polypeptides, poly-arginine, cell penetrating peptides (CPPs), chimeric CPPs, Transportan, or MPG peptides, HIV-binding peptides, Tat, HIV-1 Tat (HIV), Tat-derived peptides, oligoarginines, members of the penetratin family, Penetratin, Antennapedia-derived peptides (particularly from *Drosophila antennapedia*), pAntp, plsl, etc., antimicrobial-derived CPPs, Buforin-2, Bac715-24, SynB, SynB(1), pVEC, hCT-derived peptides, SAP, MAP, KALA, PpTG20, Proline-rich peptides, Loligomere, Arginine-rich peptides, Calcitonin-peptides, FGF, Lactoferrin, histones, VP22 derived or analog peptides, HSV, VP22 (Herpes simplex), MAP, KALA or protein transduction domains (PTDs, PpT620, prolin-rich peptides, lysine-rich peptides, Pep-1, L-oligomers, Calcitonin peptide(s).

7. The polymeric carrier molecule according to any of claims 1 to 6, wherein the –SH-moiety of component(s) P^2 is provided by a cysteine.

8. The polymeric carrier molecule according to any of claims 1 to 7, wherein component P^2 is selected from a peptide comprising a cationic peptide of formula (IIb):

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

wherein

l + m + n +o + x = 8-15, and l, m, n or o independently of each other may be any number selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 or 15, provided that the overall content of Arg, Lys, His and Orn represents at least 10% of all amino acids of the oligopeptide; and Xaa may be any amino acid selected from native or non-native amino acids except of Arg, Lys, His or Orn; and x may be any number selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or 14, provided, that the overall content of Xaa does not exceed 90 % of all amino acids of the oligopeptide.

9. Polymeric carrier cargo complex formed of a polymeric carrier molecule according to any of claims 1 to 8 and a nucleic acid.

10. The polymeric carrier cargo complex according to claim 9, wherein the nucleic acid is provided in a molar ratio of about 5 to 10000 of inventive polymeric carrier molecule : nucleic acid.

11. The polymeric carrier cargo complex according to claim 9 or 10, wherein the nucleic acid is a DNA or a RNA, a coding nucleic acid, a coding DNA, a coding RNA, a coding mRNA, an siRNA, an immunostimulatory nucleic acid, an immunostimulatory CpG nucleic acid, or an immunostimulatory RNA (isRNA),

12. The polymeric carrier cargo complex according to any of claims 9 to 11, wherein the nucleic acid encodes a therapeutically active protein or peptide, an antigen, including tumor antigens, pathogenic antigens, animal antigens, viral antigens, protozoal antigens, bacterial antigens, allergic antigens, autoimmune antigens, allergens, antibodies, immunostimulatory proteins or peptides, or antigen-specific T-cell receptors.

13. Method of preparing a polymeric carrier molecule as defined in any of claims 1 to 8 comprising following steps

a) providing at least one cationic or polycationic protein or peptide as component P^2 as defined herein and/or at least one cationic or polycationic

polymer as component P^2 as defined according to one of claims 1 to 8, and optionally at least one further component $(AA)_x$, mixing these components, preferably in a basic milieu, preferably in the presence of oxygen or a further starter which leads to mild oxidation conditions, and thereby condensing and thus polymerizing these components with each other via disulfide bonds in a polymerization condensation or polycondensation to obtain a repetitive component $H\text{-}[S\text{-}P^2\text{-}S]_n\text{-}H$ or $H\{[S\text{-}P^2\text{-}S]_a[S\text{-}(AA)_x\text{-}S]_b\}H$;

b) providing a hydrophilic polymer P^1 and/or P^3 as defined according to any of claims 1 to 8, optionally modified with a ligand L and/or an amino acid component $(AA)_x$ as defined according to any of claims 1 to 8;

c) mixing the hydrophilic polymer P^1 and/or P^3 according to step b) with the repetitive component $H\text{-}[S\text{-}P^2\text{-}S]_n\text{-}H$ or $H\{[S\text{-}P^2\text{-}S]_a[S\text{-}(AA)_x\text{-}S]_b\}H$ obtained according to step a) in a ratio of about 2 : 1, and thereby typically terminating the polymerization condensation or polycondensation reaction and obtaining the inventive polmeric carrier molecule according to formula (I) or (Ia);

d) optionally purifying the polymeric carrier molecule obtained according to step c);

e) optionally adding a nucleic acid as defined herein to the polymeric carrier obtained according to step c) or d) and complexing the nucleic acid with the polymeric carrier obtained according to step c) or d) to obtain a polymeric carrier cargo complex as defined according to any of claims 9 to 12.

14. Pharmaceutical composition or vaccine, comprising the polymeric carrier cargo complex according to any of claims 9 to 12 and optionally a pharmaceutically acceptable carrier and/or vehicle.

15. Polymeric carrier molecule according to any of claims 1 to 8, or a polymeric carrier cargo complex according to any of claims 9 to 12 for use as a medicament.

16. Polymeric carrier molecule according to any of claims 1 to 8 with a nucleic acid as defined according to any of claims 9 to 12, or polymeric carrier cargo complex according to any of claims 9 to 12, for use in the prophylaxis, treatment and/or

amelioration of diseases selected from cancer or tumour diseases, infectious diseases, preferably (viral, bacterial or protozoological) infectious diseases, autoimmune diseases, allergies or allergic diseases, monogenetic diseases, i.e. (hereditary) diseases, or genetic diseases in general, diseases which have a genetic inherited background and which are typically caused by a defined gene defect and are inherited according to Mendel's laws, cardiovascular diseases, neuronal diseases, diseases of the respiratory system, diseases of the digestive system, diseases of the skin, musculoskeletal disorders, disorders of the connective tissue, neoplasms, immune deficiencies, endocrine, nutritional and metabolic diseases, eye diseases and ear diseases.

Claims

1. Polymeric carrier molecule according to formula (I):

$$L\text{-}P^1\text{-}S\text{-}[S\text{-}P^2\text{-}S]_n\text{-}S\text{-}P^3\text{-}L$$

wherein,

P^1 and P^3 are different or identical to each other and represent a linear or branched hydrophilic polymer chain, each P^1 and P^3 exhibiting at least one –SH-moiety, capable to form a disulfide linkage upon condensation with component P^2, the linear or branched hydrophilic polymer chain selected independent from each other from polyethylene glycol (PEG), poly-*N*-(2-hydroxypropyl)methacrylamide, poly-2-(methacryloyloxy)ethyl phosphorylcholines, poly(hydroxyalkyl L-asparagine), poly(2-(methacryloyloxy)ethyl phosphorylcholine), hydroxyethylstarch or poly(hydroxyalkyl L-glutamine), wherein the hydrophilic polymer chain exhibits a molecular weight of 1 kDa to 100 kDa,

P^2 is a cationic or polycationic peptide or protein, having a length of 3 to 100 amino acids, or
is a cationic or polycationic polymer, having a molecular weight of 0.5 kDa to 30 kDa,
each P^2 exhibiting at least two –SH-moieties, capable to form a disulfide linkage upon condensation with further components P^2 or component(s) P^1 and/or P^3;

-S-S- is a disulfide bond;

L is an optional ligand, which may be present or not, and may be selected independent from the other from RGD, Transferrin, Folate, a signal peptide or signal sequence, a localization signal or sequence, a nuclear localization signal or sequence (NLS), an antibody, a cell penetrating peptide, TAT, a ligand of a receptor, cytokines, hormones, growth factors, small molecules, carbohydrates, mannose, galactose, synthetic ligands, small molecule agonists, inhibitors or antagonists of receptors, or RGD peptidomimetic analogues; and

n is an integer, selected from a range of 1 to 50, preferably in a range of 1, 2, 3, 4, or 5 to 10 , more preferably in a range of 1, 2, 3, or 4 to 9, and

wherein any of components P^2 may be the same or different from each other, and

wherein at least one additional amino acid component $(AA)_x$ is present or absent in the polymeric carrier molecule, wherein AA is an amino acid and x is an integer selected from a range of 1 to 100 and

wherein, if component $(AA)_x$ is present,

the at least one additional amino acid component $(AA)_x$ is a linker between components P^1 or P^3 and component L

or,

if component L is absent, the at least one additional amino acid component $(AA)_x$ is a part of components P^1 or P^3.

2. The polymeric carrier molecule according to claim 1, wherein the polymeric carrier molecule is represented by one of the following formulae:

L-$(AA)_x$-P^1-S-[S-P^2-S]$_n$-S-P^3-$(AA)_x$-L,
L-[$(AA)_x$]$_z$-P^1-S-[S-P^2-S]$_n$-S-P^3-[$(AA)_x$]$_z$-L,
L-$(AA)_x$-S-S-P^1-S-[S-P^2-S]$_n$-S-P^3-S-S-$(AA)_x$-S-S-L,
L-S-S-$(AA)_x$-S-S-P^1-S-[S-P^2-S]$_n$-S-P^3-S-S-$(AA)_x$-S-S-L,
L-S-[S-$(AA)_x$-S]$_z$-S-P^1-S-[S-P^2-S]$_n$-S-P^3-S-[S-$(AA)_x$-S]$_z$-S-L,
$(AA)_x$-P^1-S-[S-P^2-S]$_n$-S-P^3-$(AA)_x$,
[$(AA)_x$]$_z$-P^1-S-[S-P^2-S]$_n$-S-P^3-[$(AA)_x$]$_z$,
$(AA)_x$-S-S-P^1-S-[S-P^2-S]$_n$-S-P^3-S-S-$(AA)_x$, or
H-[S-$(AA)_x$-S]$_z$-S-P^1-S-[S-P^2-S]$_n$-S-S-P^3-S-[S-$(AA)_x$-S]$_z$-H,

wherein z is an integer selected from a range of 1 to 30.

3. Polymeric carrier molecule according to formula (Ia)

L-P^1-S-{[S-P^2-S]$_a$[S-$(AA)_x$-S]$_b$}-S-P^3-L,

wherein;

P^1 and P^3 are different or identical to each other and represent a linear or branched hydrophilic polymer chain, each P^1 and P^3 exhibiting at least one –SH-moiety, capable to form a disulfide linkage upon condensation with component P^2, the linear or branched hydrophilic polymer chain selected independent from each other from polyethylene glycol (PEG), poly-*N*-(2-hydroxypropyl)methacrylamide, poly-2-(methacryloyloxy)ethyl phosphorylcholines, poly(hydroxyalkyl L-asparagine), poly(2-

(methacryloyloxy)ethyl phosphorylcholine), hydroxyethylstarch or poly(hydroxyalkyl L-glutamine), wherein the hydrophilic polymer chain exhibits a molecular weight of 1 kDa to 100 kDa,

P^2 is a cationic or polycationic peptide or protein, having a length of 3 to 100 amino acids, or
is a cationic or polycationic polymer, having a molecular weight of 0.5 kDa to 30 kDa,
each P^2 exhibiting at least two –SH-moieties, capable to form a disulfide linkage upon condensation with further components P^2 or component(s) P^1 and/or P^3;

-S-S- is a disulfide bond;

L is an optional ligand, which may be present or not, and may be selected independent from the other from RGD, Transferrin, Folate, a signal peptide or signal sequence, a localization signal or sequence, a nuclear localization signal or sequence (NLS), an antibody, a cell penetrating peptide, TAT, a ligand of a receptor, cytokines, hormones, growth factors, small molecules, carbohydrates, mannose, galactose, synthetic ligands, small molecule agonists, inhibitors or antagonists of receptors, or RGD peptidomimetic analogues;

AA is an amino acid component,

x is an integer selected from a range of 1 to 100

a + b = n, wherein

- n is an integer, selected from a range of 1 to 50, preferably in a range of 1, 2, 3, 4, or 5 to 10;
- a is an integer, selected independent from integer b from a range of 1 to 50, preferably in a range of 1, 2, 3, 4, or 5 to 10, and
- b is an integer, selected independent from integer a from a range of 1 to 50, preferably in a range of 1, 2, 3, 4, or 5 to 10,

and wherein any of components P^2 may be the same or different from each other, and wherein the single components [S-P^2-S] and [S-$(AA)_x$-S] occur in any order in the subformula $\{[S\text{-}P^2\text{-}S]_a[S\text{-}(AA)_x\text{-}S]_b\}$.

4. The polymeric carrier molecule according to any of claims 1 to 3, wherein the amino acid component $(AA)_x$ comprises an aromatic amino acid component, a hydrophilic amino acid component, a lipophilic amino acid component, a weak basic amino acid component, a signal peptide, localization signal or sequence, a nuclear localization signal or sequence, a cell penetrating peptide, a therapeutically active protein or peptide, an antigen or an antigenic epitope, a tumour antigen, a pathogenic antigen, an animal antigen, a viral antigen, a protozoal antigen, a bacterial antigen, an allergic antigen, an autoimmune antigen, an allergen, an antibody, an immunostimulatory protein or peptide, or an antigen-specific T-cell receptor.

5. The polymeric carrier molecule according to any of claims 1 to 4, wherein the amino acid component $(AA)_x$ occurs as a mixed repetitive amino acid component $[(AA)_x]_z$, wherein z is an integer selected from a range of 1 to 30.

6. The polymeric carrier molecule according to any of claims 1 to 5, wherein component P^2 is a cationic or polycationic peptide selected from protamine, nucleoline, spermine or spermidine, poly-L-lysine (PLL), basic polypeptides, poly-arginine, cell penetrating peptides (CPPs), chimeric CPPs, Transportan, or MPG peptides, HIV-binding peptides, Tat, HIV-1 Tat (HIV), Tat-derived peptides, oligoarginines, members of the penetratin family, Penetratin, Antennapedia-derived peptides, particularly Antennapedia-derived peptides derived from *Drosophila antennapedia*, pAntp, pIsl, antimicrobial-derived CPPs, Buforin-2, Bac715-24, SynB, SynB(1), pVEC, hCT-derived peptides, SAP, MAP, KALA, PpTG20, Proline-rich peptides, Loligomere, Arginine-rich peptides, FGF, Lactoferrin, histones, VP22 derived or analog peptides, HSV, VP22 (Herpes simplex), MAP, KALA or protein transduction domains (PTDs), PpT620, prolin-rich peptides, lysine-rich peptides, Pep-1, L-oligomers, Calcitonin peptide(s).

7. The polymeric carrier molecule according to any of claims 1 to 6, wherein the –SH-moiety of component(s) P^2 is provided by a cysteine.

8. The polymeric carrier molecule according to any of claims 1 to 7, wherein component P^2 has the sequence $CysHis_6Arg_4His_6Cys$.

9. The polymeric carrier molecule according to any of claims 1 to 7, wherein component P^2 is selected from a peptide comprising a cationic peptide of formula (IIb):

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

wherein

l + m + n +o + x = 8-15, and l, m, n or o independently of each other may be any number selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 or 15, provided that the overall

content of Arg, Lys, His and Orn represents at least 10% of all amino acids of the oligopeptide; and Xaa may be any amino acid selected from native or non-native amino acids except of Arg, Lys, His or Orn; and x may be any number selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or 14, provided, that the overall content of Xaa does not exceed 90 % of all amino acids of the oligopeptide.

10. Polymeric carrier cargo complex formed of a polymeric carrier molecule according to any of claims 1 to 9 and a nucleic acid.

11. The polymeric carrier cargo complex according to claim 10, wherein the nucleic acid is provided in a molar ratio of 5 to 10000 of polymeric carrier molecule : nucleic acid.

12. The polymeric carrier cargo complex according to claim 10 or 11, wherein the nucleic acid is a DNA or a RNA, a coding nucleic acid, a coding DNA, a coding RNA, a coding mRNA, an siRNA, an immunostimulatory nucleic acid, an immunostimulatory CpG nucleic acid, or an immunostimulatory RNA (isRNA),

13. The polymeric carrier cargo complex according to any of claims 10 to 12, wherein the nucleic acid encodes a therapeutically active protein or peptide, an antigen, including tumor antigens, pathogenic antigens, animal antigens, viral antigens, protozoal antigens, bacterial antigens, allergic antigens, autoimmune antigens, allergens, antibodies, immunostimulatory proteins or peptides, or antigen-specific T-cell receptors.

14. Method of preparing a polymeric carrier molecule as defined in any of claims 1 to 9 comprising following steps

a) providing at least one cationic or polycationic protein or peptide as component P^2 and/or at least one cationic or polycationic polymer as component P^2 as defined according to one of claims 1 to 9, and optionally at least one further component $(AA)_x$, mixing these components, preferably in a basic milieu, preferably in the presence of oxygen or a further starter which leads to mild oxidation conditions, and thereby condensing and thus polymerizing these components with each other via disulfide bonds in a polymerization condensation or polycondensation to obtain a repetitive component H-[S-P^2-S]$_n$-H or H{[S-P^2-S]$_a$[S-$(AA)_x$-S]$_b$}H;

b) providing a hydrophilic polymer P^1 and/or P^3 as defined according to any of claims 1 to 9, optionally modified with a ligand L and/or an amino acid component $(AA)_x$ as defined according to any of claims 1 to 9;

c) mixing the hydrophilic polymer P^1 and/or P^3 according to step b) with the repetitive component H-[S-P^2-S]$_n$-H or H{[S-P^2-S]$_a$[S-$(AA)_x$-S]$_b$}H obtained according to step a) in a ratio of 2 : 1, and thereby typically terminating the polymerization

condensation or polycondensation reaction and obtaining the polmeric carrier molecule according to formula (I) or (Ia);

d) optionally purifying the polymeric carrier molecule obtained according to step c);

e) optionally adding a nucleic acid, preferably a nucleic acid as defined in any of claims 11 to 13, to the polymeric carrier obtained according to step c) or d) and complexing the nucleic acid with the polymeric carrier obtained according to step c) or d) to obtain a polymeric carrier cargo complex as defined according to any of claims 10 to 13.

15. Pharmaceutical composition or vaccine, comprising the polymeric carrier cargo complex according to any of claims 10 to 13 and optionally a pharmaceutically acceptable carrier and/or vehicle.

16. Polymeric carrier molecule according to any of claims 1 to 9, or a polymeric carrier cargo complex according to any of claims 10 to 13 for use as a medicament.

17. Polymeric carrier molecule according to any of claims 1 to 9 with a nucleic acid as defined according to any of claims 10 to 13, or polymeric carrier cargo complex according to any of claims 10 to 13, for use in the prophylaxis, treatment and/or amelioration of diseases selected from cancer or tumour diseases, infectious diseases, preferably viral, bacterial or protozoological infectious diseases, autoimmune diseases, allergies or allergic diseases, monogenetic diseases, i.e. hereditary diseases, or genetic diseases in general, diseases which have a genetic inherited background and which are typically caused by a defined gene defect and are inherited according to Mendel's laws, cardiovascular diseases, neuronal diseases, diseases of the respiratory system, diseases of the digestive system, diseases of the skin, musculoskeletal disorders, disorders of the connective tissue, neoplasms, immune deficiencies, endocrine, nutritional and metabolic diseases, eye diseases and ear diseases.