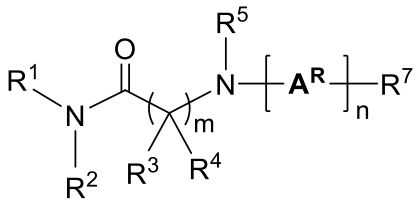
CLAIMS

1. A compound represented by general formula (1) for preparing lipid nanoparticles encapsulating a therapeutic, prophylactic and/or biological agent:



(1)

wherein

$\mathbf{A^R}$ comprises a unit from a poly(amino acid);

R^1 and R^2 are each independently a hydrophobic group;

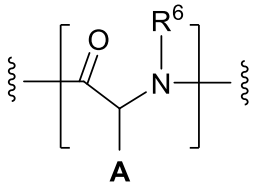
R^3, R^4, and R^5 are each independently H, optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

R^7 is –H or –C(=O)R^8, wherein R^8 is optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl or optionally substituted alkoxy;

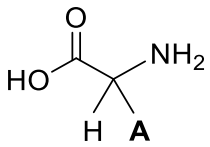
m ≥ 1; and

n ≥ 1.

2. The compound of claim 1, wherein $\mathbf{A^R}$ comprises a structure that is represented by general formula (2), and wherein **A** comprises a hydrophilic organic group that is part of an amino acid represented by general formula (3):



(2)



(3)

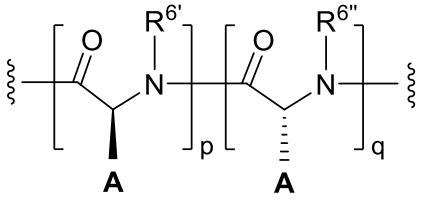
wherein

R^6 is H, optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

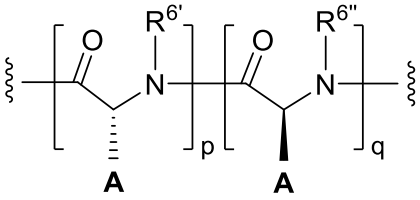
optionally wherein **A** is selected from the group consisting of $–CH_2OH$,$–CH_2CH_2C(=O)OH$, and combinations thereof; and

optionally wherein the poly(amino acid) is selected from the group consisting of polyserine, polyglutamic acid and combinations thereof.

3. The compound of any one of the preceding claims, wherein $\mathbf{A^R}$ comprises a structure that is represented by general formula (2A) and/or (2B):



(2A)



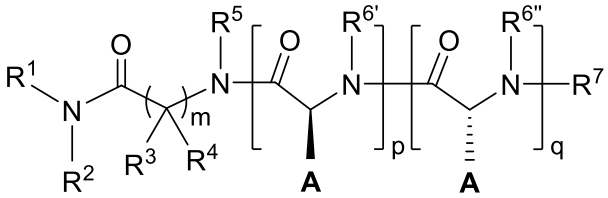
(2B)

wherein

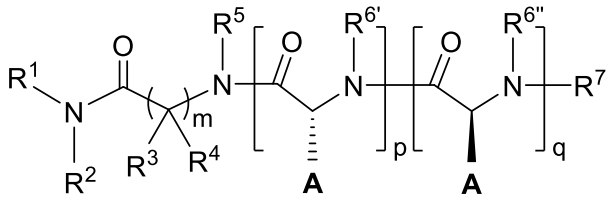
p + q = n; and

$R^{6'} = R^{6''} = R^6$.

4. The compound of any one of the preceding claims, wherein the compound represented by general formula (1) comprises a structure that is represented by general formula (1A) and/or (1B):



(1A)



(1B)

wherein

p + q = n; and

$R^{6'} = R^{6''} = R^6$.

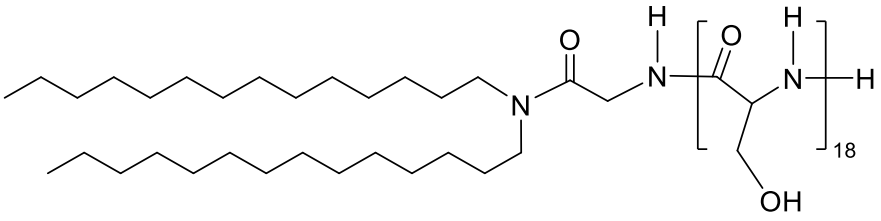
5. The compound of any one of the preceding claims, wherein n ≤ 60;

and/or the hydrophobic group at R^1 and R^2 each independently comprises optionally substituted alkyl having at least 8 carbon atoms;

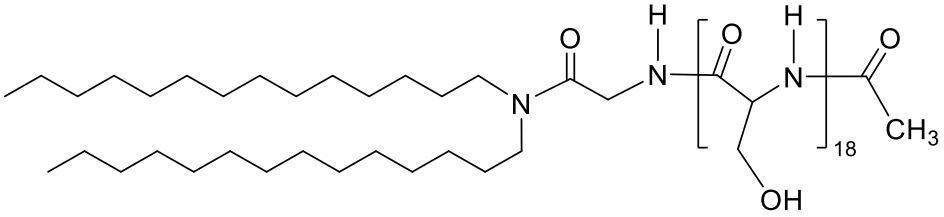
and/or the hydrophobic group at R^1 and R^2 each independently comprises optionally substituted alkyl having no more than 18 carbon atoms;

and/or R^3, R^4, R^5, and R^6 are all H.

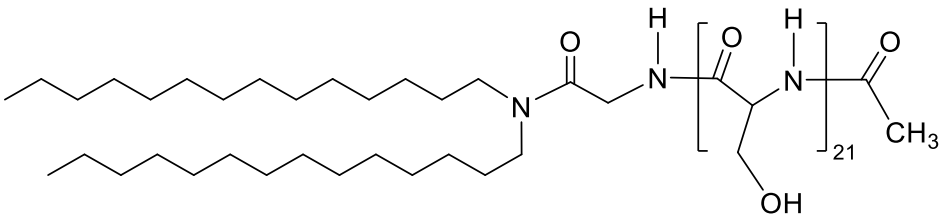
6. The compound of any one of the preceding claims, wherein the compound comprises a structure selected from one or more of the following:



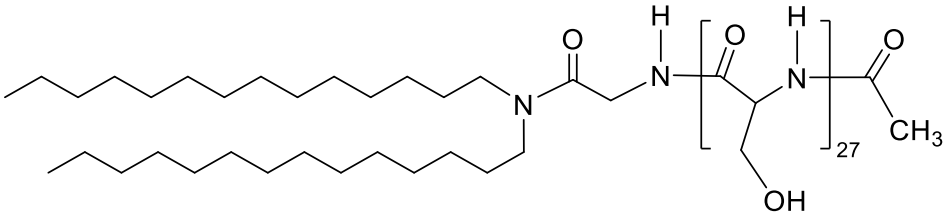
C14-pDLS1 (n = 18)



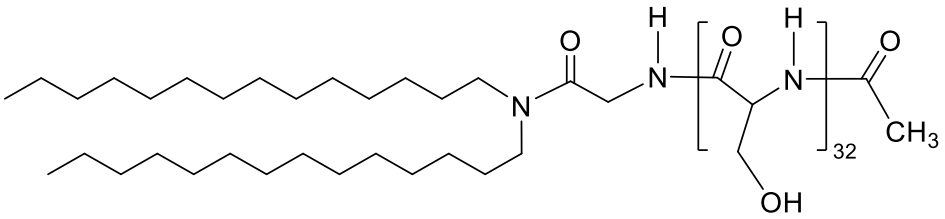
C14-pDLS2 (n = 18)



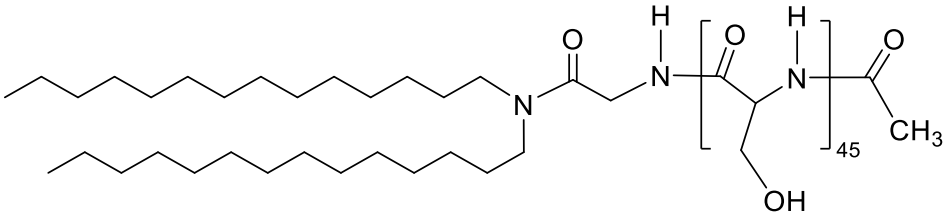
C14-pDLS3 (n = 21)



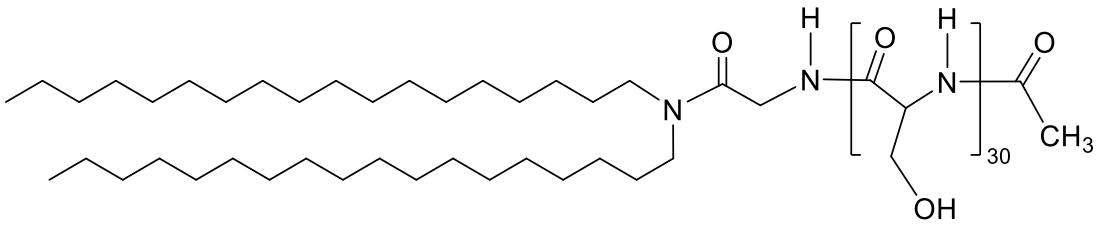
C14-pDLS4 (n = 27)



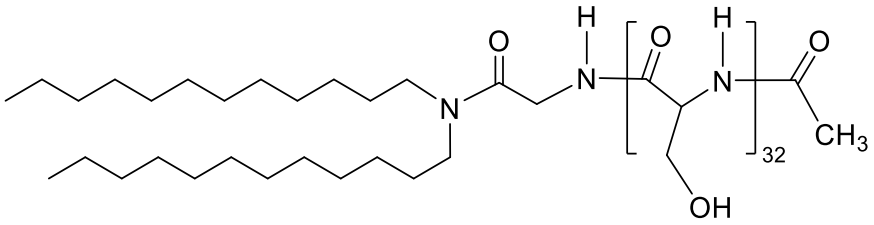
C14-pDLS5 (n = 32)



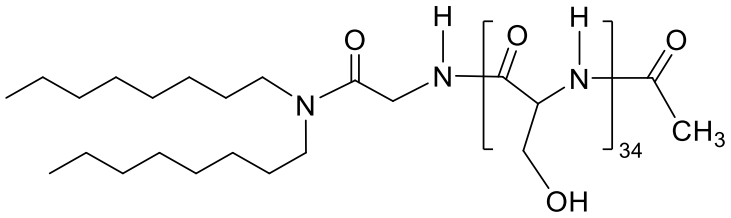
C14-pDLS6 (n = 45)



C18-pDLS (n = 30)



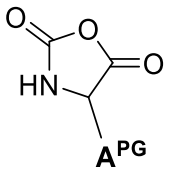
C12-pDLS (n = 32)



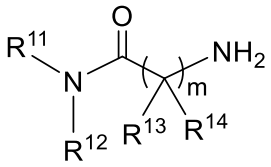
C8-pDLS (n = 34)

7. A method of preparing a compound as claimed in any one of the preceding claims, the method comprising:

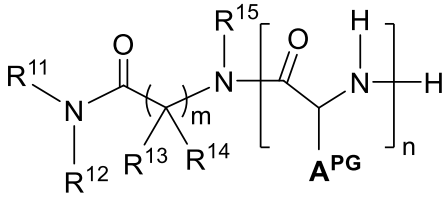
(i) polymerizing one or more N-carboxyanhydride (NCA) monomers represented by general formula (5) with a lipid initiator/molecule represented by general formula (6) to obtain a first intermediate compound represented by general formula (7):



(5)



(6)



(7)

wherein

$\mathbf{A}^{PG}$ represents **A** protected with one or more protecting groups, where **A** comprises a hydrophilic organic group that is part of an amino acid represented by general formula (3);

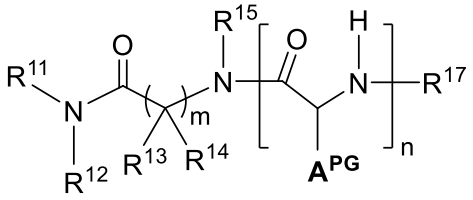
R^{11} and R^{12} are each independently a hydrophobic group;

R^{13}, R^{14}, and R^{15} are each independently H, optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

$m \geq 1$; and

$n \geq 1$;

(ii) optionally reacting the first intermediate compound represented by general formula (7) with an acylating agent to obtain a second intermediate compound represented by general formula (8):

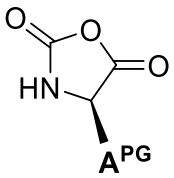


(8)

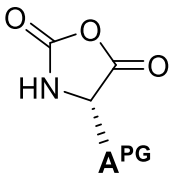
wherein R^{17} is –H or –C(=O)R^{18}, wherein R^{18} is optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl or optionally substituted alkoxy;

(iii) deprotecting the first intermediate compound represented by general formula (7) or the second intermediate compound represented by general formula (8) to obtain the compound represented by general formula (1);

optionally wherein the N-carboxyanhydride (NCA) monomer represented by general formula (5) comprises a structure represented by general formula (5A) and/or (5B):



(5A)

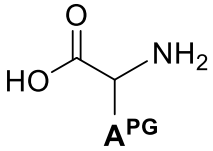


(5B) ; and

optionally wherein (i) comprises mixing the general formula (5A) with the general formula (5B) at a molar ratio of from 1:5 to 5:1.

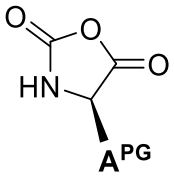
8. The method of claim 7, wherein the method further comprises, prior to (i):

(a-i) reacting a protected amino acid represented by general formula (10) with a carbonylating agent to obtain a N-carboxyanhydride (NCA) monomers represented by general formula (5):

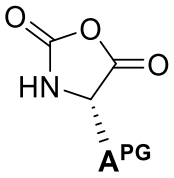


(10) ;

optionally wherein the N-carboxyanhydride (NCA) monomer represented by general formula (5) comprises a structure represented by general formula (5A) and/or (5B):



(5A)



(5B) ; and

optionally wherein (i) comprises mixing the general formula (5A) with the general formula (5B) at a molar ratio of from 1:5 to 5:1.

9. A nanoparticle composition for delivery of a therapeutic, prophylactic and/or biological agent, the nanoparticle composition comprising:

a compound as claimed in any one of claims 1 to 6; and

a therapeutic, prophylactic and/or biological agent.

10. The nanoparticle composition of claim 9, wherein the composition further comprises:

(a) ionizable lipid;

(b) helper lipid; and

(c) cholesterol and/or derivatives thereof.

11. The nanoparticle composition of claim 10, wherein the ionizable lipid, helper lipid, cholesterol and/or derivatives thereof, and compound represented by general formula (1) are mixed at a mole ratio of 5 – 65 : 4 – 20 : 10 – 60 : 0.1 – 20;

optionally wherein the ionizable lipid is selected from ALC-0315, SM-102, Lipid 5, DLinDMA, D-Lin-MC2-DMA, DLin-MC3-DMA, D-Lin-MC4-DMA, Dlin-KC2-DMA, YSK05, AA3-Dlin, SSPalmM, SSPalmO-Phe, Lipid A9, L319, DODMA, CL1, BP Lipid 310, ATX-001, ATX-100, Lipid 2, 80-O16B, BP Lipid 309, BP Lipid 307, 93-O17S, 93-O17O, NT1-O14B, 306-O12B-3, 306-O12B, 113-O16B, 306Oi10, 306Oi9-cis2, BAMEA-O16B, Al-28, 113-O12B, 98N12-5, Ckk-E12, OF-02, C12-200, BP Lipid 311, BP Lipid 308, BP Lipid 314, BP Lipid 312, LP01, TCL053, Lipid C24, BP Lipid 315, Lipid 29, 9A1P9, C13-112-tri-tail, C13-113-tri-tail, C13-112-tetra-tail, or C13-113-tetra-tail, C12-200 and combinations thereof;

optionally wherein the helper lipid is selected from the group consisting of 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), 1,2-dioleoyl-sn-glycero-3-phosphoethanolamine (DOPE), 1,2-dilinoleoyl-sn-glycero-3-phosphocholine (DLPC), 1,2-dimyristoyl-sn-glycero-phosphocholine (DMPC), 1,2-dioleoyl-sn-glycero-3-phosphocholine (DOPC), 1,2-dipalmitoyl-sn-glycero-3-phosphocholine (DPPC), 1,2-diundecanoyl-sn-glycero-phosphocholine (DUPC), 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC), 1,2-di-O-octadecenyl-sn-glycero-3-phosphocholine (18:0 Diether PC), 1-oleoyl-2-cholesterylhemisuccinoyl-sn-glycero-3-phosphocholine (OChemsPC), 1-hexadecyl-sn-glycero-3-phosphocholine (C16 Lyso PC), 1,2-dilinolenoyl-sn-glycero-3-phosphocholine, 1,2-diarachidonoyl-sn-glycero-3-phosphocholine, 1,2-

didocosahexaenoyl-sn-glycero-3-phosphocholine, 1,2-diphytanoyl-sn-glycero-3-phosphoethanolamine (ME 16.0 PE), 1,2-distearoyl-sn-glycero-3-phosphoethanolamine, 1,2-dilinoleoyl-sn-glycero-3-phosphoethanolamine, 1,2-dilinolenoyl-sn-glycero-3-phosphoethanolamine, 1,2-diarachidonoyl-sn-glycero-3-phosphoethanolamine, 1,2-didocosahexaenoyl-sn-glycero-3-phosphoethanolamine, 1,2-dioleoyl-sn-glycero-3-phospho-rac-(1-glycerol) sodium salt (DOPG), sphingomyelin and combinations thereof; and

optionally wherein the cholesterol and/or derivatives thereof is selected from cholesterol, fecosterol, sitosterol, ergosterol, campesterol, stigmasterol, brassicasterol, avenasterol and combinations thereof.

12. The nanoparticle composition of any one of claims 9 to 11, wherein the nanoparticle composition comprises nanoparticles having a N/P ratio from 1:1 to 50:1;

and/or the nanoparticle composition comprises nanoparticles having an average particle size of no more than 300 nm;

and/or the nanoparticle composition comprises nanoparticles having a zeta potential of from -20 mV to +20 mV.

13. The nanoparticle composition as claimed in any one of claims 9 to 12 for use in medicine.

14. The nanoparticle composition as claimed in any one of claims 9 to 12 for use in the treatment or prophylaxis of a disease, disorder or condition in a subject in need thereof,

optionally wherein an immune response in the subject is to be induced through the administration of the nanoparticle composition thereto;

optionally wherein the disease, disorder or condition is mediated by a coronavirus; and

optionally wherein the coronavirus is a SARS-CoV-2 coronavirus.

15. Use of a nanoparticle composition as claimed in any one of claims 9 to 12 in the manufacture of a medicament for inducing an immune response in a subject;

optionally wherein the immune response is against a coronavirus; and

optionally wherein the coronavirus is a SARS-CoV-2 coronavirus.