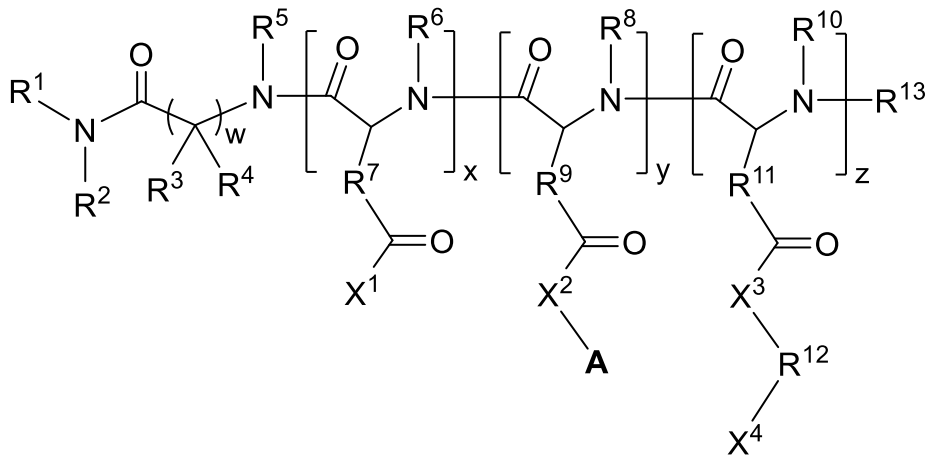
CLAIMS

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



(1)

wherein

A comprises a hydrophilic moiety selected from carbohydrate/sugar/saccharide and derivatives thereof;

X^1 is $–OR^a$ or $–NR^bR^c$;

X^4 is $–OR^y$, $–SR^z$ or a hydrophilic group, where R^y to R^z are independently selected from the group consisting of H, optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

X^2 and X^3 are each independently –O– or $–NR^d–$, where R^a to R^d are independently selected from the group consisting of H, optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

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

R^3, R^4, R^5, R^6, R^8 and R^{10} are each independently H, optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

R^7, R^9, R^{11} and R^{12} are each independently optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

R^{13} is H, optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl, or $–C(=O)R^{14}$, where R^{14} is optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl;

w ≥ 1;

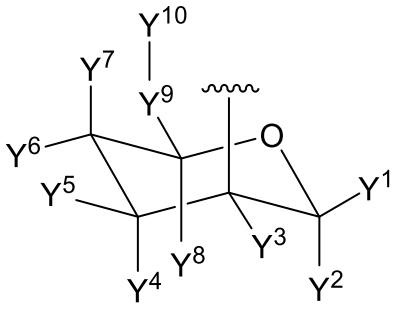
x is 0 or ≥ 1;

y is 0 or ≥ 1; and

z is 0 or ≥ 1.

2. The compound of claim 1, wherein the compound is capable of targeting carbohydrate receptors on a cell surface.

3. The compound of any one of the preceding claims, wherein **A** is a 5-membered ring or represented by general formula (2) having a 6-membered ring structure:



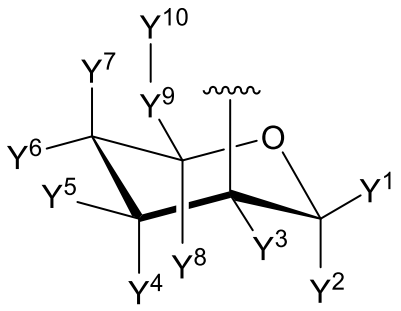
(2)

wherein

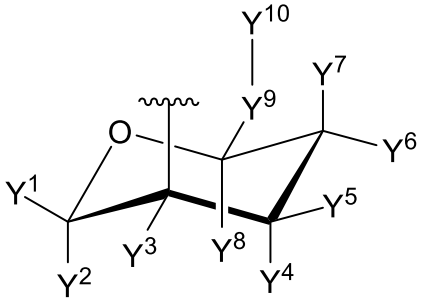
Y^1 to Y^8 and Y^{10} are each independently selected from –H or –OH; and

Y^9 is alkyl.

4. The compound of any one of the preceding claims, wherein **A** is represented by general formula (2A) and/or (2B) having a 6-membered ring structure:



(2A)



(2B)

wherein

Y^1 to Y^8 and Y^{10} are each independently selected from –H or –OH; and

Y^9 is alkyl.

5. The compound of any one of the preceding claims, wherein the total sum of x + y + z is from 1 to 300.

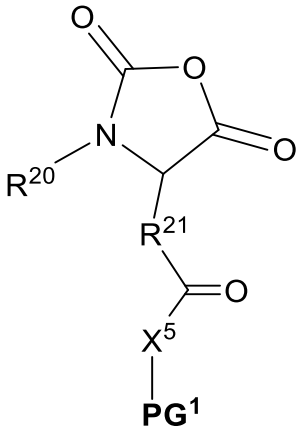
6. The compound of any one of the preceding claims, wherein the hydrophobic group at R^1 and R^2 each independently comprises optionally substituted alkyl.

7. The compound of any one of the preceding claims, wherein the compound is selected from the group consisting of LPP1, LPP2, LPP3, LPP4, LPP5, LPP6, LPP7, LPP8, LPP9, LPP10, LPP11, LPP12, LPP13, LPP14, LPP15 and combinations thereof.

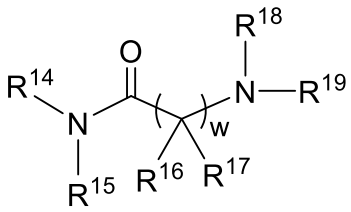
8. A method of preparing a compound as claimed in any one of the preceding claims, the method comprising:

(a-i) polymerizing one or more N-carboxyanhydride (NCA) monomers represented by general formula (3) with a lipid initiator represented

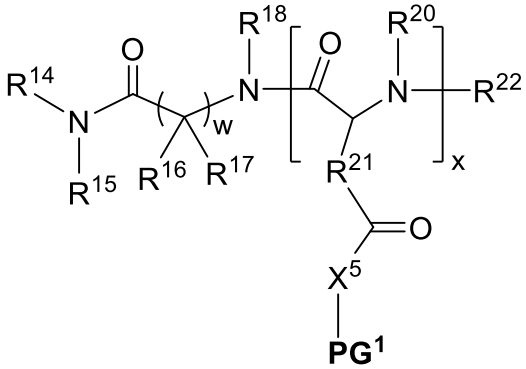
by general formula (4) to obtain a first intermediate compound represented by general formula (5):



(3)



(4)



(5)

wherein

X^5 is –O– or –NR^e–, where R^e is selected from the group consisting of H, optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

R^{14} and R^{15} are each independently a hydrophobic group;

R^{16}, R^{17}, R^{18}, R^{19}, R^{20} and R^{22} are each independently H, optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

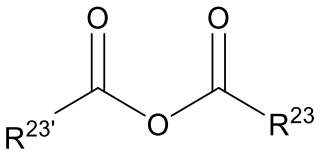
R^{21} is optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

$w \geq 1$;

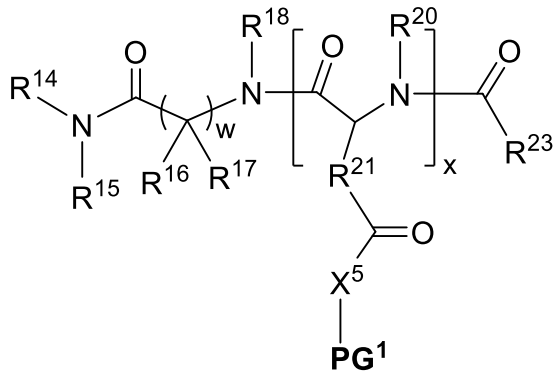
x is 0 or ≥ 1; and

PG^1 is a protecting group selected from benzyl, *tert*-butyl or combinations thereof;

(a-ii) optionally reacting the first intermediate compound represented by general formula (5) with an acylating agent represented by general formula (6) to obtain a second intermediate compound represented by general formula (7):



(6)

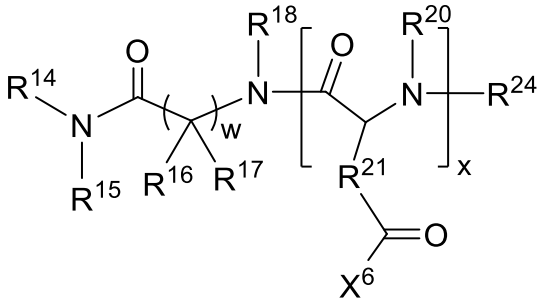


(7)

wherein

R^{23} and $R^{23'}$ are each independently optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

(a-iii) deprotecting the first intermediate compound represented by general formula (5) and/or the second intermediate compound represented by general formula (7) to obtain a compound represented by general formula (8);



(8)

wherein

X^6 is $–OR^a$ or $–NR^fR^g$, where R^a, R^f and R^g are independently selected from the group consisting of H, optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl; and

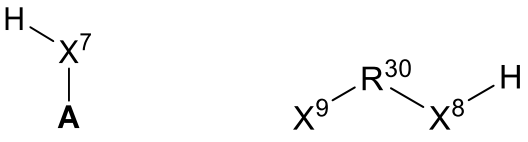
R^{24} is H, optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl, or $–C(=O)R^{25}$, where R^{25} is optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl;

(a-iv) reacting the compound represented by general formula (8) with at least one substrate selected from the following:

(i) an amidating agent comprising a hydrophilic moiety represented by general formula (9); and

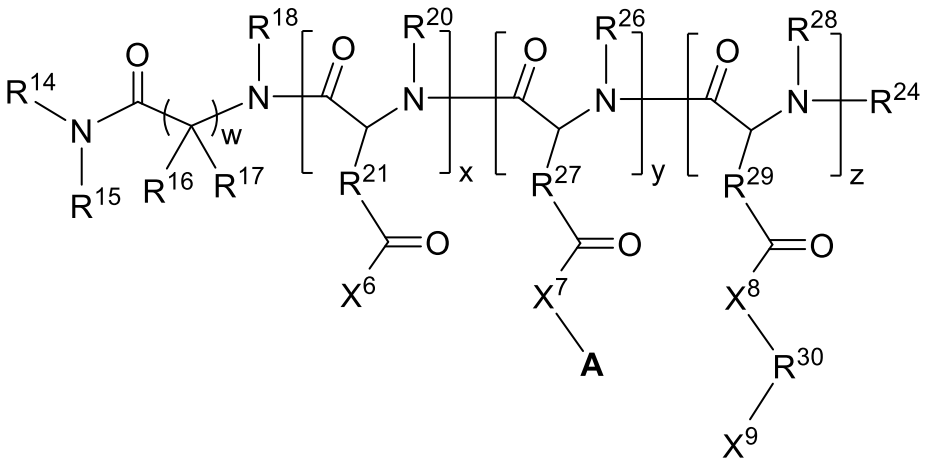
(ii) an alkanolamine represented by general formula (10)

to obtain a compound represented by general formula (11);



(9)

(10)



(11)

wherein

A comprises a hydrophilic moiety selected from carbohydrate/sugar/saccharide and derivatives thereof;

X^7 and X^8 are each independently –O– or $–NR^h–$,

X^9 is independently $–OR^i$ or $–NR^jR^k$, where R^h to R^k are independently selected from the group consisting of H, optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

R^{26} and R^{28} are each independently H, optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

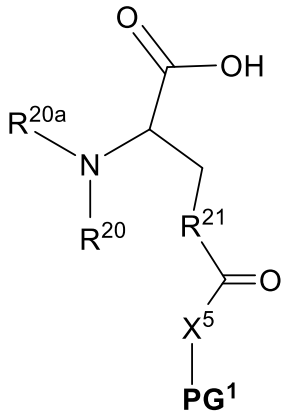
R^{27}, R^{29} and R^{30} are each independently optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

y is 0 or ≥ 1; and

z is 0 or ≥ 1;

optionally wherein the method further comprises, prior to (a-i):

(b-i) reacting a protected amino acid represented by general formula (12) with a carbonylating agent to obtain the N-carboxyanhydride (NCA) monomer represented by general formula (3):

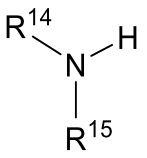


(12)

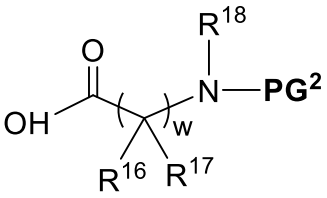
wherein R^{20a} is H, optionally substituted alkyl, optionally substituted alkenyl or optionally substituted alkynyl;

and optionally wherein the method further comprises, prior to (a-i):

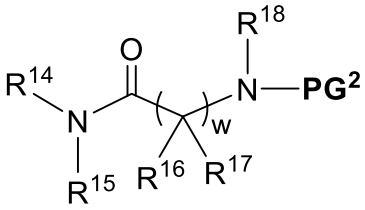
(c-i) reacting a lipid compound represented by general formula (13) with a protected amino acid represented by general formula (14) to obtain a protected lipid initiator represented by general formula (15):



(13)



(14)



(15)

wherein **PG²** is a protecting group selected from *tert*-butoxycarbonyl protecting group (BOC), *tert*-butyl or combinations thereof; and

(c-ii) deprotecting the protected lipid initiator represented by general formula (15) to obtain the lipid initiator represented by general formula (4).

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 7; and

a therapeutic, prophylactic and/or biological agent that is encapsulated in said composition.

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

(a) ionizable lipid;

(b) helper lipid; and

(c) sterol.

11. The nanoparticle composition of claim 10, wherein the ionizable lipid, helper lipid, sterol, and compound represented by general formula (1) are mixed at a mole ratio of 15 – 140 : 3 – 30 : 14 – 130 : 0.2 – 40;

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 sterol 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 2:1 to 40:1;

and/or the nanoparticle composition comprises nanoparticles having an average particle size of no more than 800 nm;

and/or the nanoparticle composition comprises nanoparticles having a zeta potential of from -40 mV to +40 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 to a subject;

optionally wherein the immune response is against a coronavirus; and

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