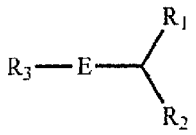
CLAIMS

1. A lipid having the structure

XXXIII



or salts or isomers thereof,

wherein:

R_1 and R_2 are each independently for each occurrence C_{10}-C_{30} alkyl, C_{10}-C_{30} alkenyl, or C_{10}-C_{30} alkynyl;

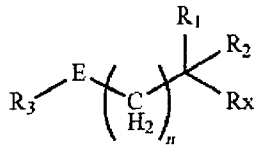
R_3 is ω-aminoalkyls or ω-(substituted)aminoalkyls;

E is O, N(Q)C(O), C(O)N(Q), (Q)N(CO)O, O(CO)N(Q), SS or O=N; and,

Q is H, or alkyl.

2. A lipid having the structure

XXXVIII



or salts or isomers thereof,

wherein,

E is O, N(Q)C(O), C(O)N(Q), (Q)N(CO)O, O(CO)N(Q), SS or O=N;

Q is H, or alkyl;

R_1 and R_2 and R_x are each independently for each occurrence H, C_{10}-C_{30} alkyl, C_{10}-C_{30} alkenyl, or optionally substituted C_{10}-C_{30} alkynyl provided that at least one of R_1, R_2 and R_x is not H;

R_3 is ω-aminoalkyls or ω-(substituted)aminoalkyls; and

n is 1, 2, or 3.

3. A lipid particle comprising a lipid of claim 1.

4. A lipid particle comprising a lipid of claim 2.

5. The lipid particle of claim 3, wherein the particle further comprises a neutral lipid and a lipid capable of reducing aggregation.

6. The lipid particle of claim 3, wherein the lipid particle consists essentially of

a. the lipid of claim 1;

b. a neutral lipid selected from DSPC, DPPC, POPC, DOPE and SM;

c. a sterol; and

d. PEG-DMG,

in a molar ratio of about 20-60% lipid of claim 1: 5-25% neutral lipid: 25-55% sterol: 0.5-15% PEG-DMG.

7. The lipid particle of claim 3, further comprising a therapeutic agent.

8. The lipid particle of claim 7, wherein the therapeutic agent is a nucleic acid.

9. The lipid particle of claim 8, wherein the nucleic acid is a plasmid.

10. The lipid particle of claim 8, wherein the nucleic acid is an immunostimulatory oligonucleotide.

11. The lipid particle of claim 8, wherein the nucleic acid is selected from the group consisting of an siRNA, an antisense oligonucleotide, a microRNA, an antagomir, an aptamer, and a ribozyme.

12. The lipid particle of claim 11, wherein the nucleic acid is an siRNA.

13. The lipid particle of claim 6, wherein the molar ratio is 52% lipid of claim 1: 5% neutral lipid: 30% sterol: 13% PEG-DMG.

14. A pharmaceutical composition comprising a lipid particle of claim 3 and a pharmaceutically acceptable excipient, carrier, or diluent.

15. The lipid particle of claim 7 for use in the modulation of the expression of a target gene in a cell.

16. The lipid particle of claim 7 wherein the therapeutic agent is selected from an siRNA, an antagomir, an antisense oligonucleotide, and a plasmid capable of expressing an siRNA, a ribozyme, an aptamer or an antisense oligonucleotide for use in the modulation of the expression of a target gene in a cell.

17. The lipid particle of claim 7 wherein the therapeutic agent is selected from an siRNA, an antagomir, an antisense oligonucleotide, and a plasmid capable of expressing an siRNA, a ribozyme, an aptamer or an antisense oligonucleotide for use in the modulation of the expression of a target gene in a cell wherein the target gene is selected from the group consisting of Factor VII, Eg5, PCSK9, TPX2, apoB, SAA, TTR, RSV, PDGF beta gene, Erb-B gene, Src gene, CRK gene, GRB2 gene, RAS gene, MEKK gene, JNK gene, RAF gene, Erk1/2 gene, PCNA(p21) gene, MYB gene, JUN gene, FOS gene, BCL-2 gene, Cyclin D gene, VEGF gene, EGFR gene, Cyclin A gene, Cyclin

E gene, WNT-1 gene, beta-catenin gene, c-MET gene, PKC gene, NFKB gene, STAT3 gene, survivin gene, Her2/Neu gene, SORT1 gene, XBP1 gene, topoisomerase I gene, topoisomerase II alpha gene, p73 gene, p21(WAF1/CIP1) gene, p27(KIP1) gene, PPM1D gene, RAS gene, caveolin I gene, MIB I gene, MTAI gene, M68 gene, tumor suppressor genes, and p53 tumor suppressor gene.

18. The lipid particle of claim **7** wherein the therapeutic agent is selected from an siRNA, an antagomir, an antisense oligonucleotide, and a plasmid capable of expressing an siRNA, a ribozyme, an aptamer or an antisense oligonucleotide and wherein the nucleic acid is a plasmid that encodes the polypeptide or a functional variant or fragment thereof, such that expression of the polypeptide or the functional variant or fragment thereof is increased for use in the modulation of the expression of a target gene in a cell.

19. The lipid particle of claim **7**, wherein the therapeutic agent is selected from an siRNA, a microRNA, an antisense oligonucleotide, and a plasmid capable of expressing an siRNA, a microRNA, or an antisense oligonucleotide, and wherein the siRNA, microRNA, or antisense RNA comprises a polynucleotide that specifically binds to a polynucleotide that encodes the polypeptide, or a complement thereof for use in the treatment of a disease or disorder characterized by overexpression of a polypeptide in a subject.

20. The lipid particle of claim **7**, wherein the therapeutic agent is a plasmid that encodes the polypeptide or a functional variant or fragment thereof for use in the treatment of a disease or disorder characterized by underexpression of a polypeptide in a subject.