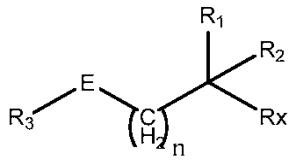
Claims

1. A lipid having the structure



XXXVIII or a salt or isomer thereof, wherein

E is C(O)O or OC(O);

R_1 and R_2 and R_x are each independently for each occurrence H, optionally substituted C_1-C_{10} alkyl, or optionally substituted C_{10}-C_{30} acyl, provided that at least one of R_1, R_2 and R_x is not H;

R_3 is optionally substituted C_2-C_{10} alkenyl, optionally substituted C_2-C_{10} alkynyl, alkylheterocycle, alkylphosphate, alkylphosphorothioate, alkylphosphorodithioate, alkylphosphonate, alkylamine, hydroxyalkyl, ω-aminoalkyl, ω-(substituted)aminoalkyl, ω-phosphoalkyl, ω-thiophosphoalkyl, heteroaryl, or heterocycle; and

n is 0, 1, 2, or 3.

2. A lipid particle comprising a lipid of claim 1, or a salt or isomer thereof.

3. The lipid particle of claim 2, wherein the particle further comprises a neutral lipid and a lipid capable of reducing aggregation.

4. The lipid particle of claim 3, wherein the lipid capable of reducing aggregation is a PEG-lipid.

5. The lipid particle of claim 2, further comprising a therapeutic agent.

6. The lipid particle of claim 5, wherein the therapeutic agent is a nucleic acid.

7. The lipid particle of claim 6, wherein the nucleic acid is selected from the group consisting of an siRNA and an antisense oligonucleotide.

8. The lipid particle of claim 6, wherein the nucleic acid is an siRNA.

9. The lipid particle of claim 6, wherein the nucleic acid is an mRNA.

10. A pharmaceutical composition comprising a lipid particle of claim 2 and a pharmaceutically acceptable excipient, carrier, or diluent.

11. Use of the lipid particle of claim 5 in the manufacture of a medicament for modulating the expression of a target gene in a cell, wherein said medicament is to be provided to the cell.

12. Use of the lipid particle of claim 8 in the manufacture of a medicament for modulating the expression of a target gene in a cell, wherein said medicament is to be provided to the cell.

13. Use of the lipid particle of claim 9 in the manufacture of a medicament for modulating the expression of a target gene in a cell, wherein said medicament is to be provided to the cell.

14. The lipid particle of claim 3, wherein the neutral lipid is a phospholipid.

15. The lipid particle of claim 3, wherein the particle further comprises a sterol.

16. The lipid particle of claim 15, wherein the sterol is cholesterol.