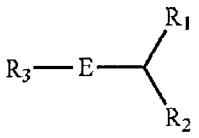
CLAIMS

1. A lipid having the structure

XXXIII



or a salt or isomer thereof, wherein:

R_1 and R_2 are each independently for each occurrence optionally substituted C_{10}-C_{20} alkenyl or optionally substituted C_{10}-C_{20} alkynyl;

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

E is C(O)O;

provided that when R_3 is 2-(dimethylamino)ethyl, R_1 and R_2 are not each linoleyl.

2. The lipid of claim **1** wherein R_3 is ω-aminoalkyl.

3. The lipid of claim **1** wherein R_3 is ω-(substituted)aminoalkyl.

4. The lipid of claim **1** wherein R_3 is 2-(dimethylamino) ethyl, 3-(diisopropylamino)propyl, or 3-(N-ethyl-n-isopropylamino)-1-methylpropyl.

5. The lipid of claim **1** wherein R_3 is alkylaminoalkyl, dialkylaminoalkyl, or alkylheterocycle.

6. The lipid of claim **1** wherein R_1 and R_2 are each optionally substituted C_{10}-C_{20} alkenyl.

7. The lipid of claim **1** wherein R_1 and R_2 are each linoleyl.

8. A lipid particle comprising a lipid of claim **1**.

9. The lipid particle of claim **8**, wherein the particle further comprises a neutral lipid and a lipid capable of reducing aggregation.

10. The lipid particle of claim **9** wherein the lipid capable of reducing aggregation is a PEG-lipid.

11. The lipid particle of claim **8**, further comprising a therapeutic agent.

12. The lipid particle of claim **11**, wherein the therapeutic agent is a nucleic acid.

13. The lipid particle of claim **12**, wherein the nucleic acid is selected from the group consisting of an siRNA and an antisense oligonucleotide.

14. The lipid particle of claim **13**, wherein the nucleic acid is an siRNA.

15. A pharmaceutical composition comprising a lipid particle of claim **11** and a pharmaceutically acceptable excipient, carrier, or diluent.

16. The lipid particle of claim **11** for use in the modulation of the expression of a target gene in a cell.

17. The lipid particle of claim **11**, wherein the therapeutic agent is selected from a siRNA and an antisense oligonucleotide for use in the modulation of the expression of a target gene in a cell.

18. The pharmaceutical composition of claim **15**, wherein the therapeutic agent is selected from an siRNA and an antisense oligonucleotide, and wherein the siRNA, or antisense oligonucleotide, 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.

19. The lipid particle of claim **8** comprising a lipid of claim **1**, a neutral lipid, cholesterol, and a PEG lipid, wherein the lipid of claim **1**, the neutral lipid, the cholesterol, and the PEG lipid are present in molar ratios of 20-70%:5-45%:20-55%: 0.5-15%, respectively.