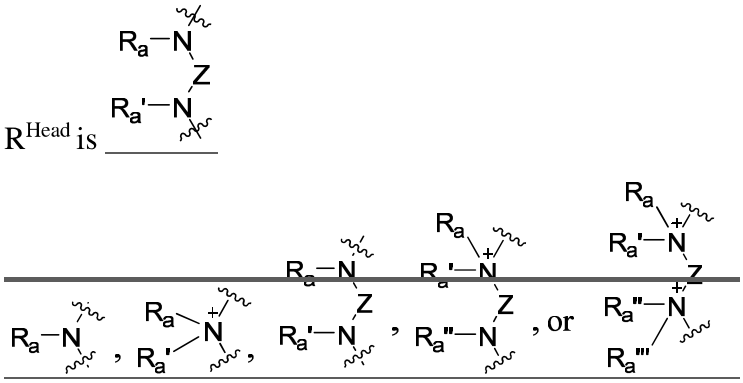
We claim:

1. Use of a lipidoid nanoparticle in the manufacture of a medicament for treating a lipoprotein metabolism disorder or a cardiovascular disease, wherein the lipidoid nanoparticle comprises A method of treating a human lipoprotein metabolism disorder or a cardiovascular disease, comprising administering to a subject in need thereof a lipidoid nanoparticle, which comprises a lipid, a CRISPR/Cas9 mRNA, and a single guide RNA (sgRNA), wherein the sgRNA is single guide Angiopoietin-like 3 (sgANGPTL3) or single guide proprotein convertase subtilisin/kexin type 9 (sgPCSK9);

wherein the lipid is represented by formula I:

$$R^{Head}—R^{Lipid} \quad (I),$$

or a pharmaceutically acceptable salt thereof, wherein

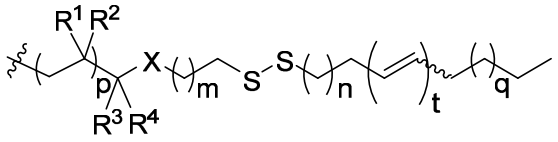
R^{Head} is 

R^a and, $R^{a'}$ are , $R^{a''}$, and $R^{a'''}$ each independently is R^{Lipid}, H, C_1-C_{20} alkyl, C_2-C_{20} alkenyl, C_2-C_{20} alkynyl, C_3-C_{20} cycloalkyl, C_1-C_{20} heteroalkyl, C_1-C_{20} heterocycloalkyl, aryl, or heteroaryl, wherein R^a and $R^{a'}$ or $R^{a''}$ and $R^{a'''}$ are not both R^{Lipid};

R^a, $R^{a'}$, $R^{a''}$, and $R^{a'''}$ each independently is R^{Lipid}, H, C_1-C_{20} alkyl, C_2-C_{20} alkenyl, C_2-C_{20} alkynyl, C_3-C_{20} cycloalkyl, C_1-C_{20} heteroalkyl, C_1-C_{20} heterocycloalkyl, aryl, or heteroaryl, wherein R^a and $R^{a'}$ or $R^{a''}$ and $R^{a'''}$ are not both R^{Lipid};

Z is a C_1-C_{20} bivalent aliphatic radical, a C_1-C_{20} bivalent heteroaliphatic radical, a bivalent aryl radical, or a bivalent heteroaryl radical; and

R^{Lipid} each independently is



,

wherein:

R^1 and R^2 are H, OH, NHR^{30}, or SH;

~~R^3 and R^4 are both H; or~~ R^3 and R^4 are taken together to form an oxo (=O) group;

X is CH_2, O, NR^{30}, or S;

R^{30} is H, C_{1-6} alkyl, C_{1-6} alkenyl, or C_{1-6} alkynyl;

m is an integer selected from 1-3;

n is an integer selected from 1-14;

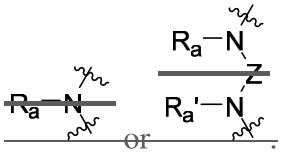
p is 0 or 1;

q is an integer selected from 1-10; and~~and~~

t is 0, 1, or 2.

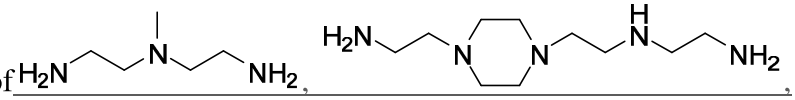
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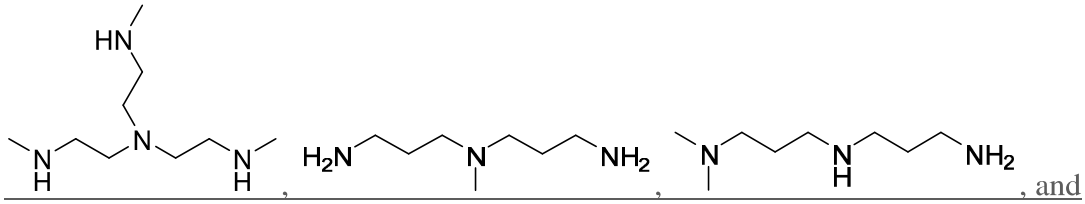
~~2. The method of claim 1, wherein R^{Head} is~~



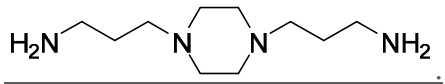
~~or~~ .

~~3. The method of claim 2, wherein R^a and $R^{a'}$ are R^{Lipid}, H, or C_1-C_{20} alkyl.~~

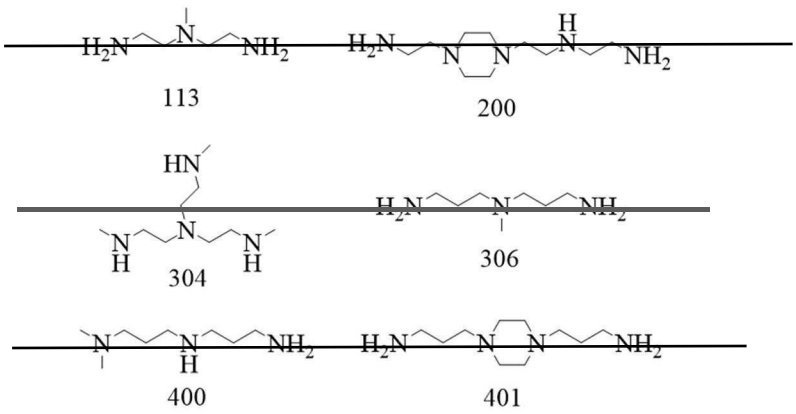
42. The ~~method~~ use of claim ~~2~~1, wherein R^{Head} is derived from a compound selected from the group consisting of ,



, and



.



53. The use method of any one of claims 1-4claim 1 or 2, wherein R^1 and R^2 are H.

64. The use method of claim 1 or 2any one of claims 1-4, wherein R^1 is H; and R^2 is OH.

7. The method of any one of claims 1-6, wherein R^3 and R^4 are H.

8. The method of any one of claims 1-6, wherein R^3 and R^4 are taken together to form an oxo (=O) group.

95. The use method of any one of claims 1-84, wherein Z is CH_2, O, or NR^{30}.

106. The use method of any one of claims 1-84, wherein Z is CH_2.

117. The use method of any one of claims 1-84, wherein Z is O.

128. The use method of any one of claims 1-84, wherein Z is NR^{30}.

139. The use method of any one of claims 1-128, wherein m is 1 or 2.

1410. The use method of any one of claims 1-139, wherein n is an integer selected from 4-12.

1511. The use method of any one of claims 1-139, wherein n is an integer selected from 6-10.

~~16~~12. The use ~~method~~ of any one of claims 1-~~15~~11, wherein p is 0.

~~17~~13. The use ~~method~~ of any one of claims 1-~~15~~11, wherein p is 1.

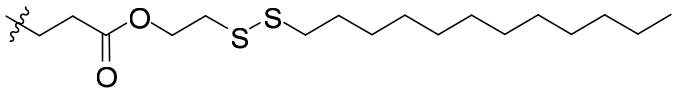
~~18~~14. The use ~~method~~ of any one of claims 1-~~17~~13, wherein q is an integer selected from 2-8.

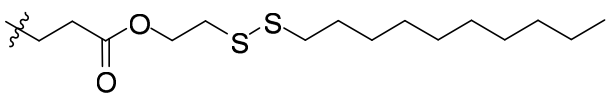
~~19~~15. The use ~~method~~ of any one of claims 1-~~17~~13, wherein q is an integer selected from 4-8.

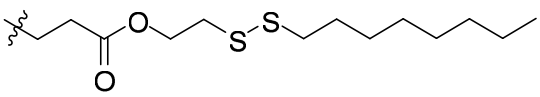
~~20~~16. The use ~~method~~ of any one of claims 1-~~19~~15, wherein t is 0.

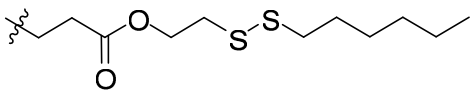
~~21~~17. The use ~~method~~ of any one of claims 1-~~19~~15, wherein t is 1.

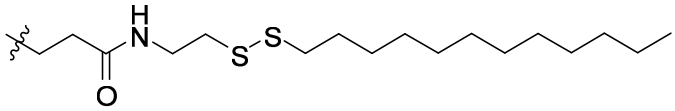
~~22~~18. The use ~~method~~ of any one of claims 1-~~21~~17, wherein R^{Lipid} each independently is selected from the group consisting of

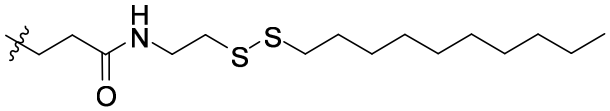

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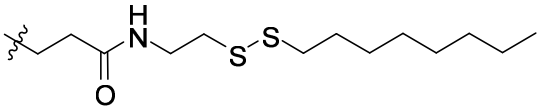

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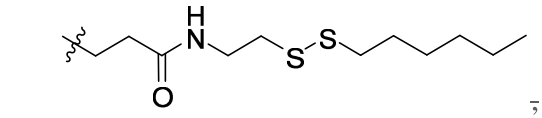

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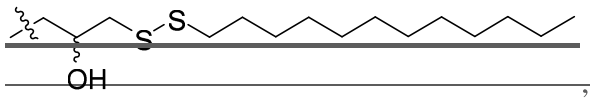

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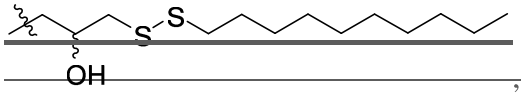

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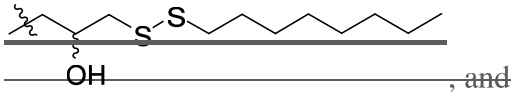

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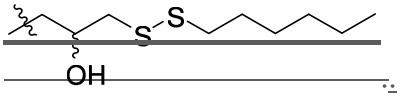

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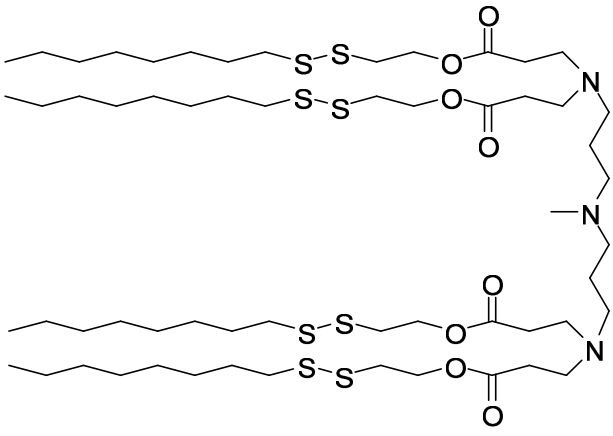




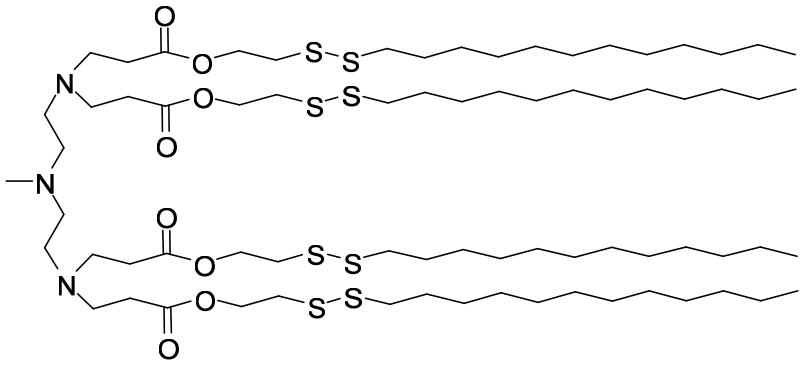




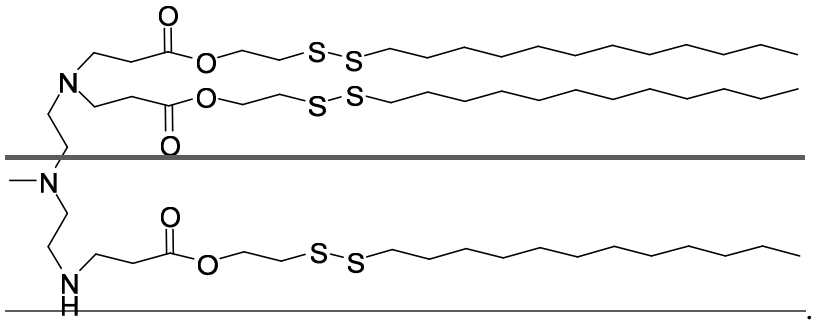
~~23~~19. The use ~~method~~ of ~~any one of claims 1-22~~claim 1, wherein the lipid is selected from the group consisting of



, and



~~, and~~



.

~~24~~20. The use ~~method~~ of any one of claims 1-~~23~~19, wherein the ratio of the lipid to the CRISPR/Cas9 mRNA is about 3:1 to about 15:1.

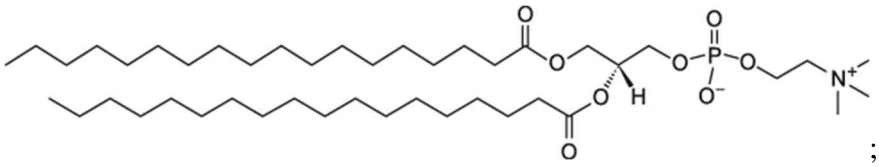
~~25~~21. The use ~~method~~ of any one of claims 1-~~23~~19, wherein the ratio of the lipid to the CRISPR/Cas9 mRNA is about 7.5:1.

~~26~~22. The use ~~method~~ of any one of claims 1-~~25~~21, wherein the lipidoid nanoparticle further comprises cholesterol.

~~27~~23. The use ~~method~~ of claim ~~26~~22, wherein the ratio of the lipid to the cholesterol is about 1:1 to about 2:1.

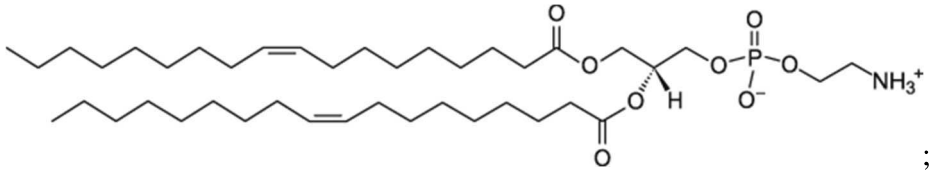
~~28~~24. The use ~~method~~ of any one of claims 1-~~27~~23, wherein the lipidoid nanoparticle further comprises DOPE, DSPC, or DOPC; and DMG-PEG2K; wherein

DSPC has the structure:



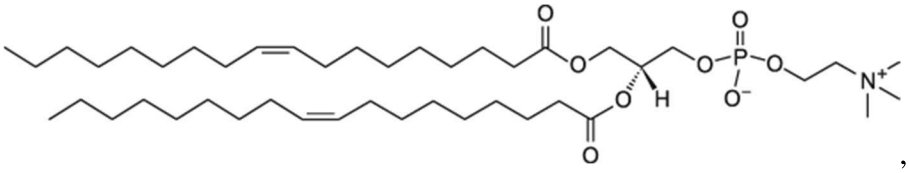
;

DOPE has the structure:



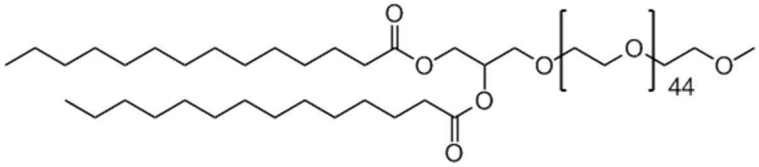
;

DOPC has the structure:



, and

DMG-PEG2K has the structure:



.

~~29~~25. The use ~~method~~ of claim ~~28~~24, wherein the lipidoid nanoparticle comprises DOPC and DMG-PEG2K.

~~30~~26. The use ~~method~~ of claim ~~29~~25, wherein the ratio of the lipid to the DOPC is about 4:1 to about 6:1; and the ratio of the lipid to the DMG-PEG2K is about 4:1 to about 100:1 to about 4:1 to about 20:1.

~~31~~27. The use ~~method~~ of any one of claims 1-~~30~~26, wherein the lipidoid nanoparticle has a particle size of about 25 nm to about 1000 nm.

~~32~~28. The use ~~method~~ of any one of claims 1-~~30~~26, wherein the lipidoid nanoparticle has a particle size of about 50 nm to about 500 nm.

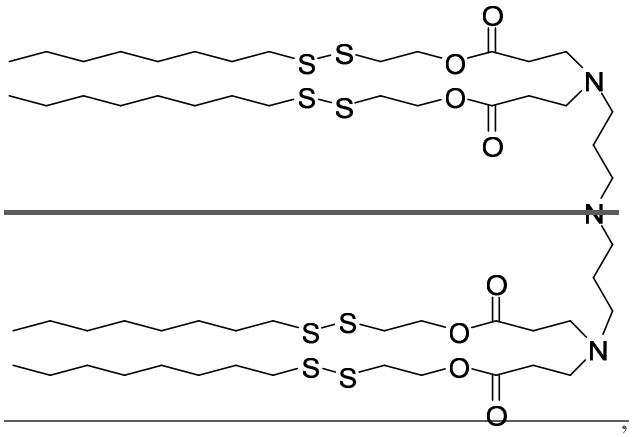
~~33~~29. The use ~~method~~ of any one of claims 1-~~32~~28, wherein the human lipoprotein metabolism disorder is associated with loss-of-function mutations in ANGPTL3 gene.

~~34~~30. The use ~~method~~ of any one of claims 1-~~32~~28, wherein the cardiovascular disease is associated with proprotein convertase subtilisin/kexin type 9 gene (PCSK9).

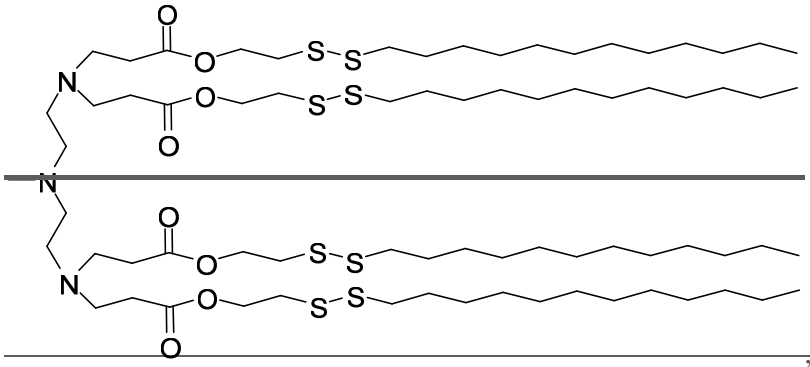
~~35~~31. The use ~~method~~ of any one of claims 1-~~32~~28, wherein the human lipoprotein metabolism disorder is associated with low levels of plasma high density lipoprotein cholesterol, high levels of serum low density lipoprotein cholesterol, or high levels of triglycerides.

~~36~~32. The use ~~method~~ of any one of claims 1-~~32~~28, wherein the cardiovascular disease is selected from the group consisting of ~~-~~homozygous familial hypercholesterolemia, and hypercholesterolemia.

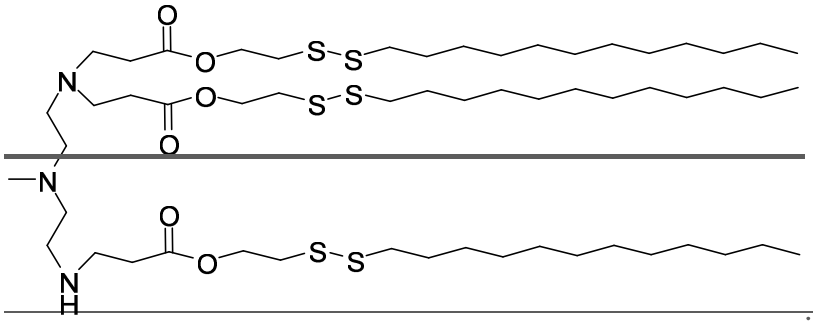
~~37. A lipid selected from the group consisting of~~



,



~~, and~~



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