FIGURE 1

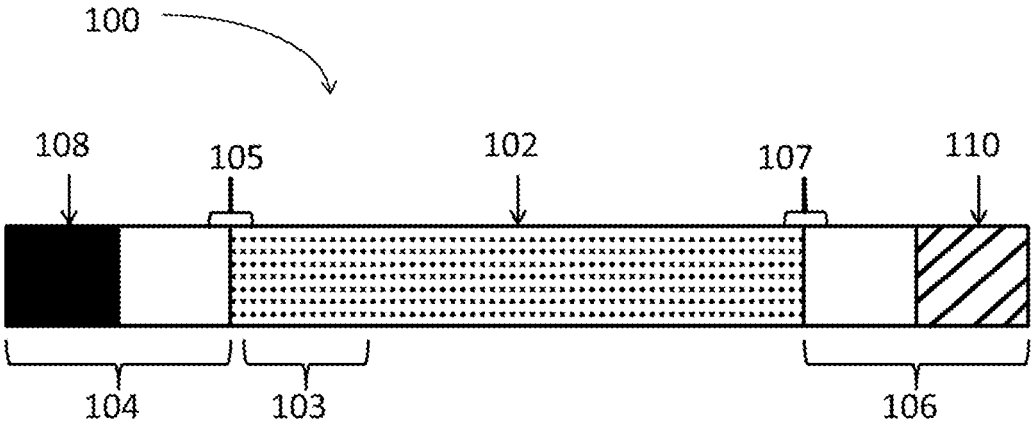


FIGURE 2

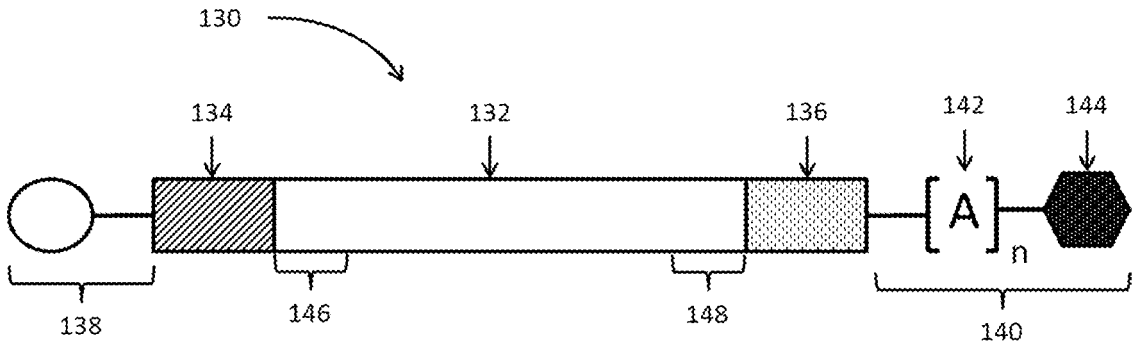


FIGURE 3

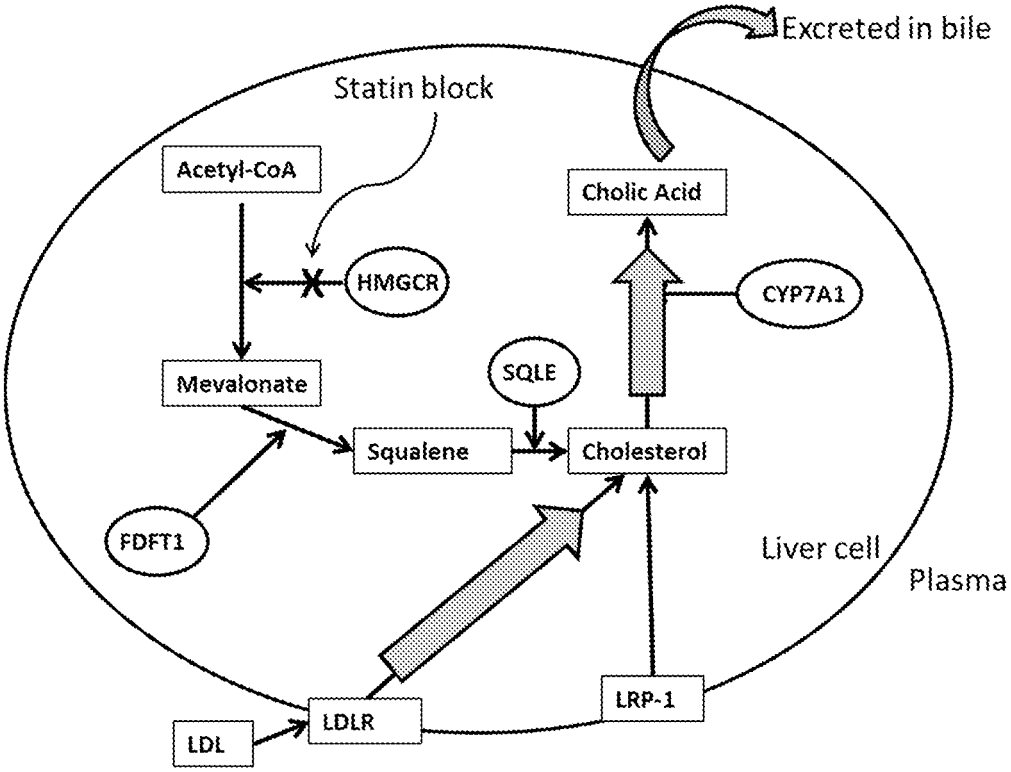

Excreted in bile
Statin block
Acetyl-CoA
Cholic Acid
HMGCR
CYP7A1
SQLE
Mevalonate
Squalene
Cholesterol
FDFT1
Liver cell
Plasma
LRP-1
LDLR
LDL

FIGURE 4

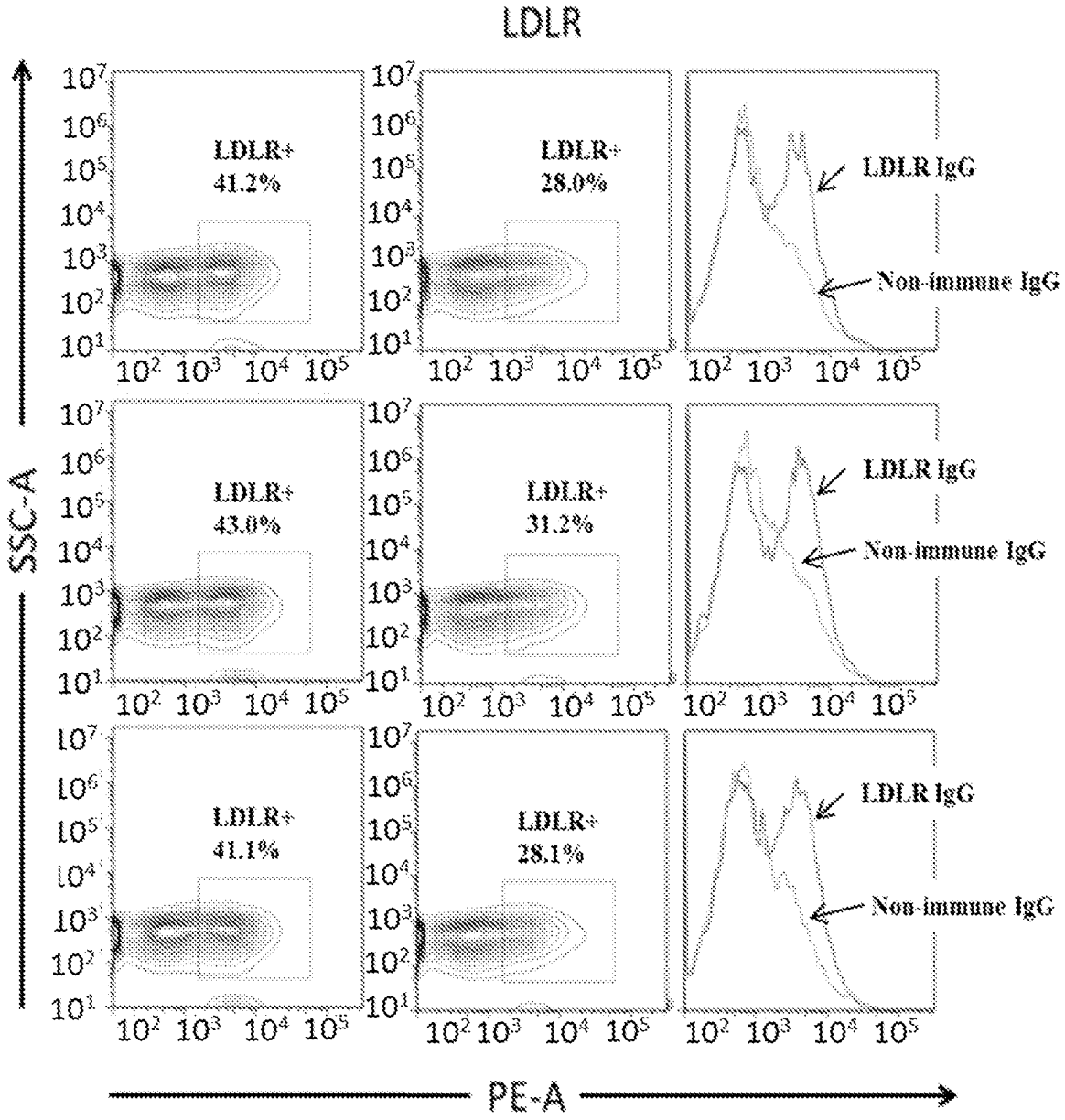

LDLR
SSC-A
PE-A
LDLR+
41.2%
LDLR+
28.0%
LDLR IgG
Non-immune IgG
LDLR+
43.0%
LDLR+
31.2%
LDLR IgG
Non-immune IgG
LDLR+
41.1%
LDLR+
28.1%
LDLR IgG
Non-immune IgG

FIGURE 5

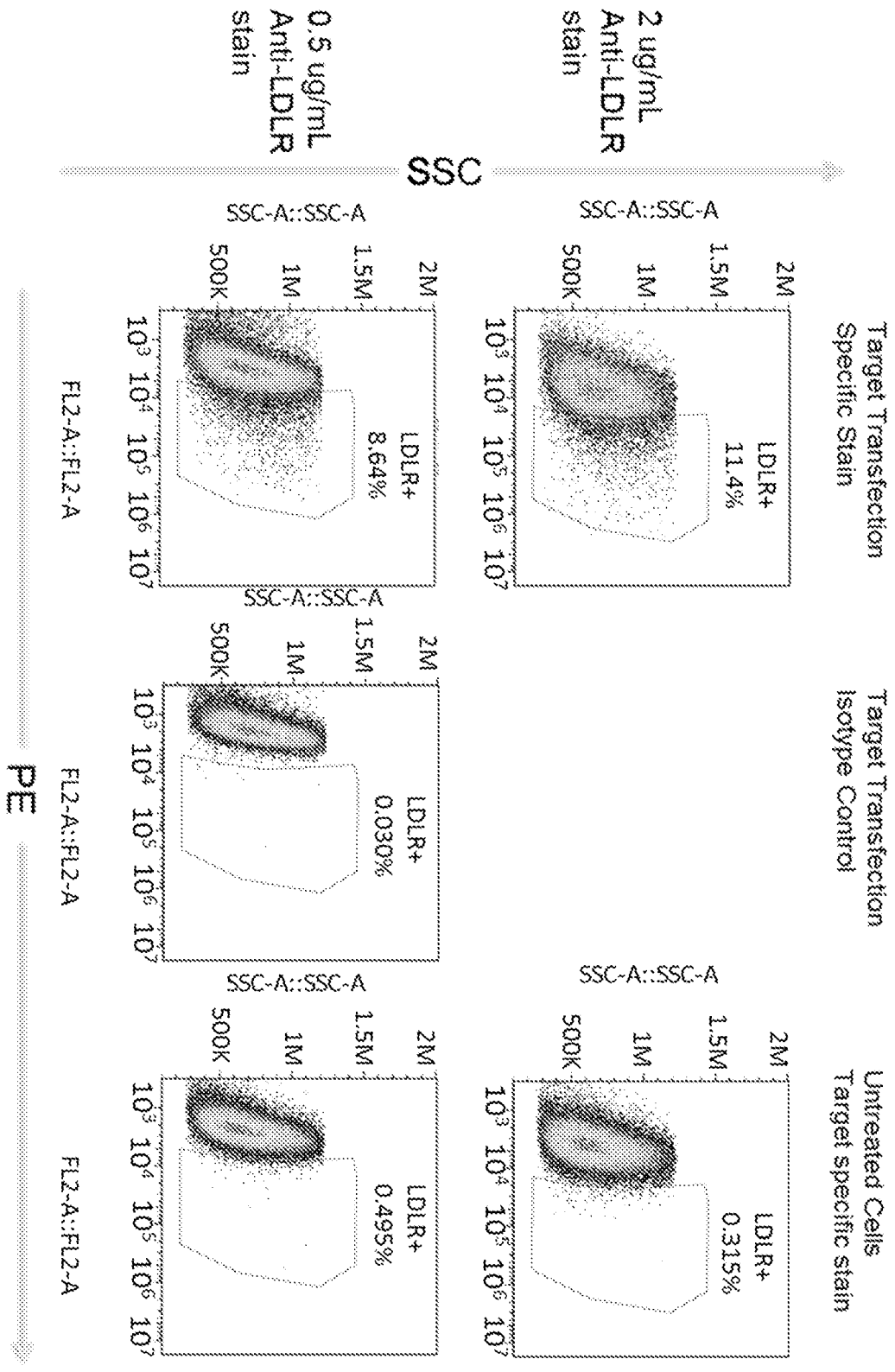
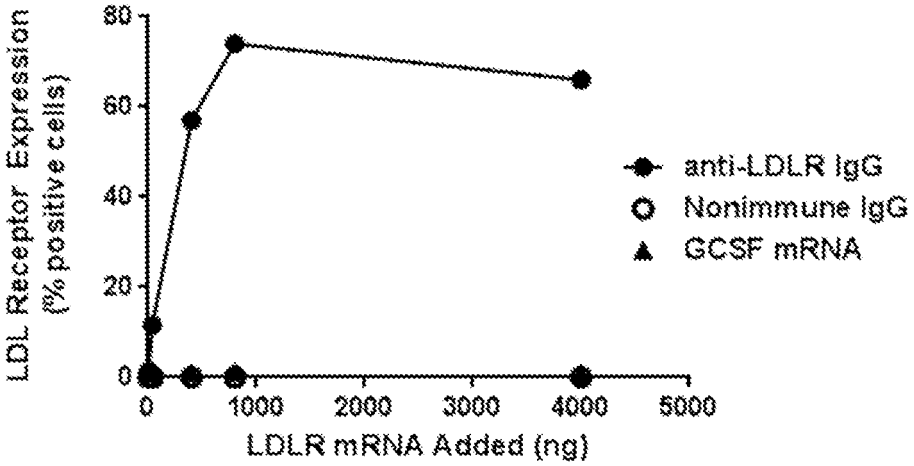

2 ug/mL Anti-LDLR stain
0.5 ug/mL Anti-LDLR stain
SSC
Target Transfection Specific Stain
Target Transfection Isotype Control
Untreated Cells Target specific stain
SSC-A::SSC-A
2M
1.5M
1M
500K
LDLR+
11.4%
8.64%
0.030%
0.315%
0.495%
10^3 10^4 10^5 10^6 10^7
FL2-A::FL2-A
PE

FIGURE 6

A.


LDL Receptor Expression
(% positive cells)
80
60
40
20
0
0
1000
2000
3000
4000
5000
LDLR mRNA Added (ng)
anti-LDLR IgG
Nonimmune IgG
GCSF mRNA

B.

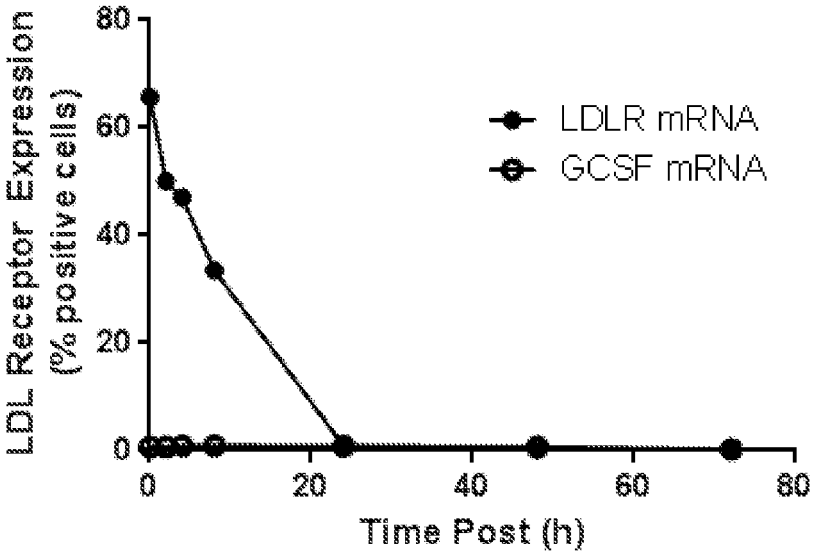
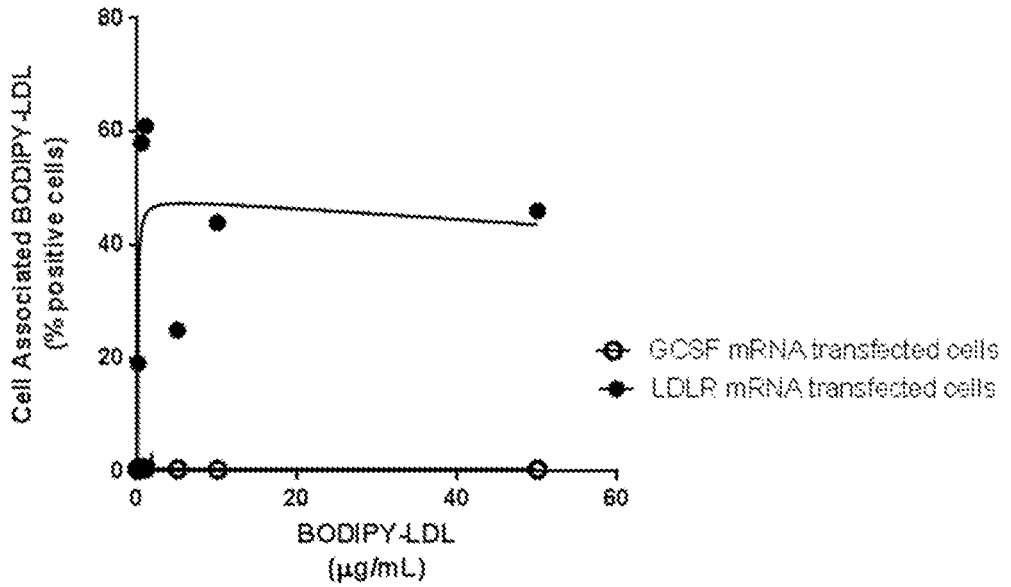

LDL Receptor Expression
(% positive cells)
80
60
40
20
0
0
20
40
60
80
Time Post (h)
LDLR mRNA
GCSF mRNA

FIGURE 6 CONT.

C.



D.

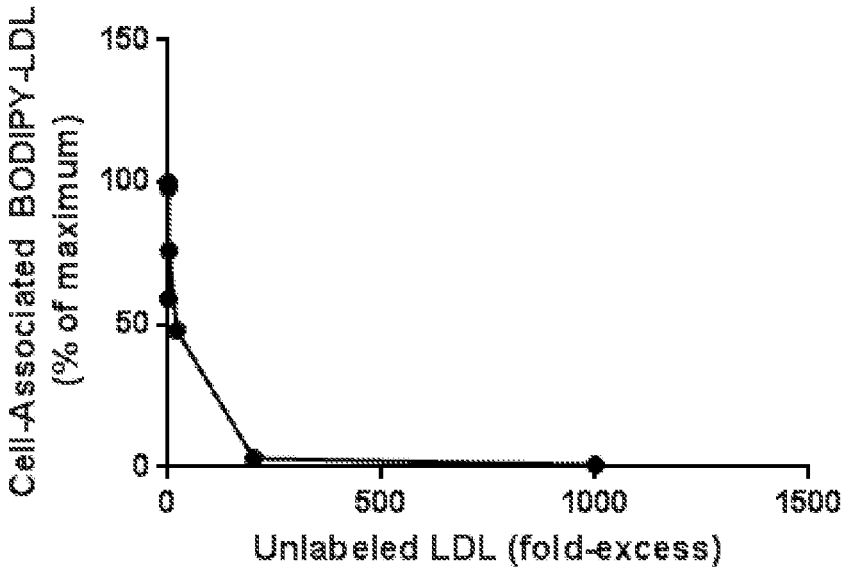


FIGURE 6 CONT.

E.

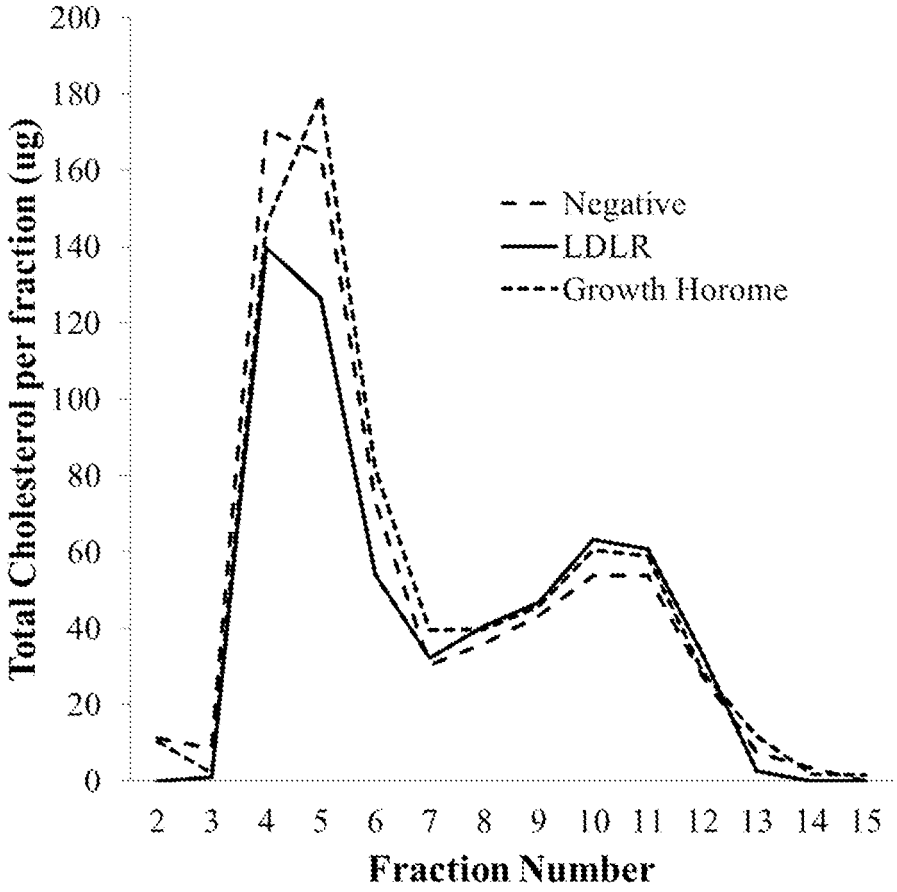


FIGURE 7

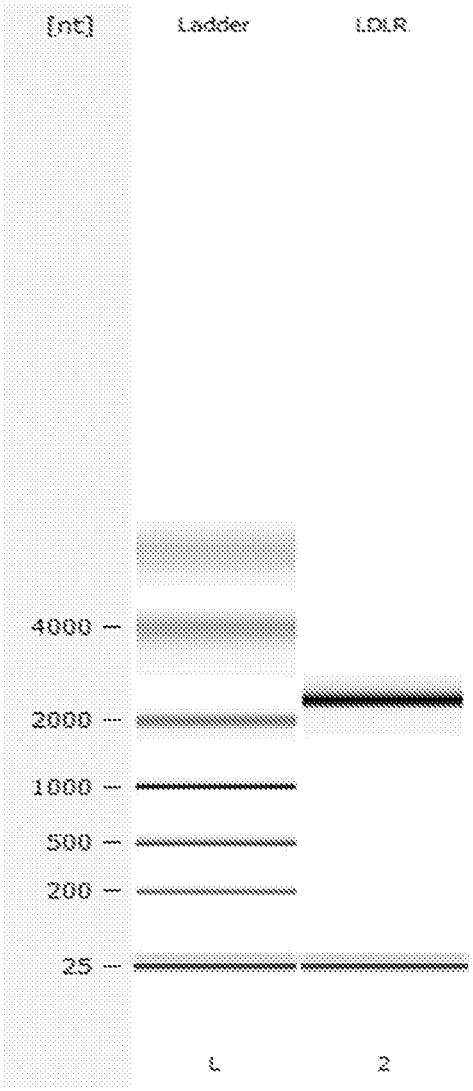


FIGURE 8

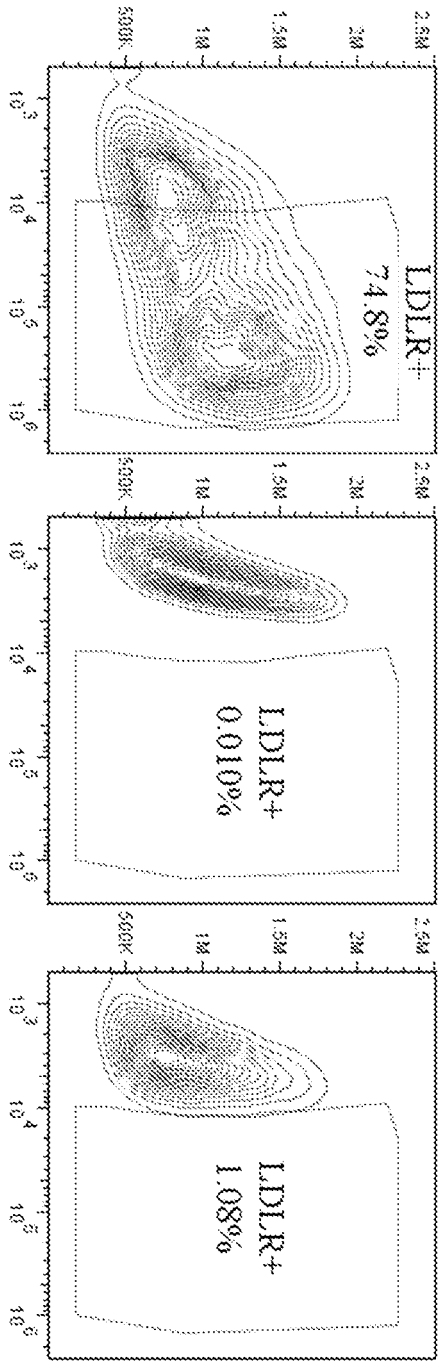


FIGURE 9

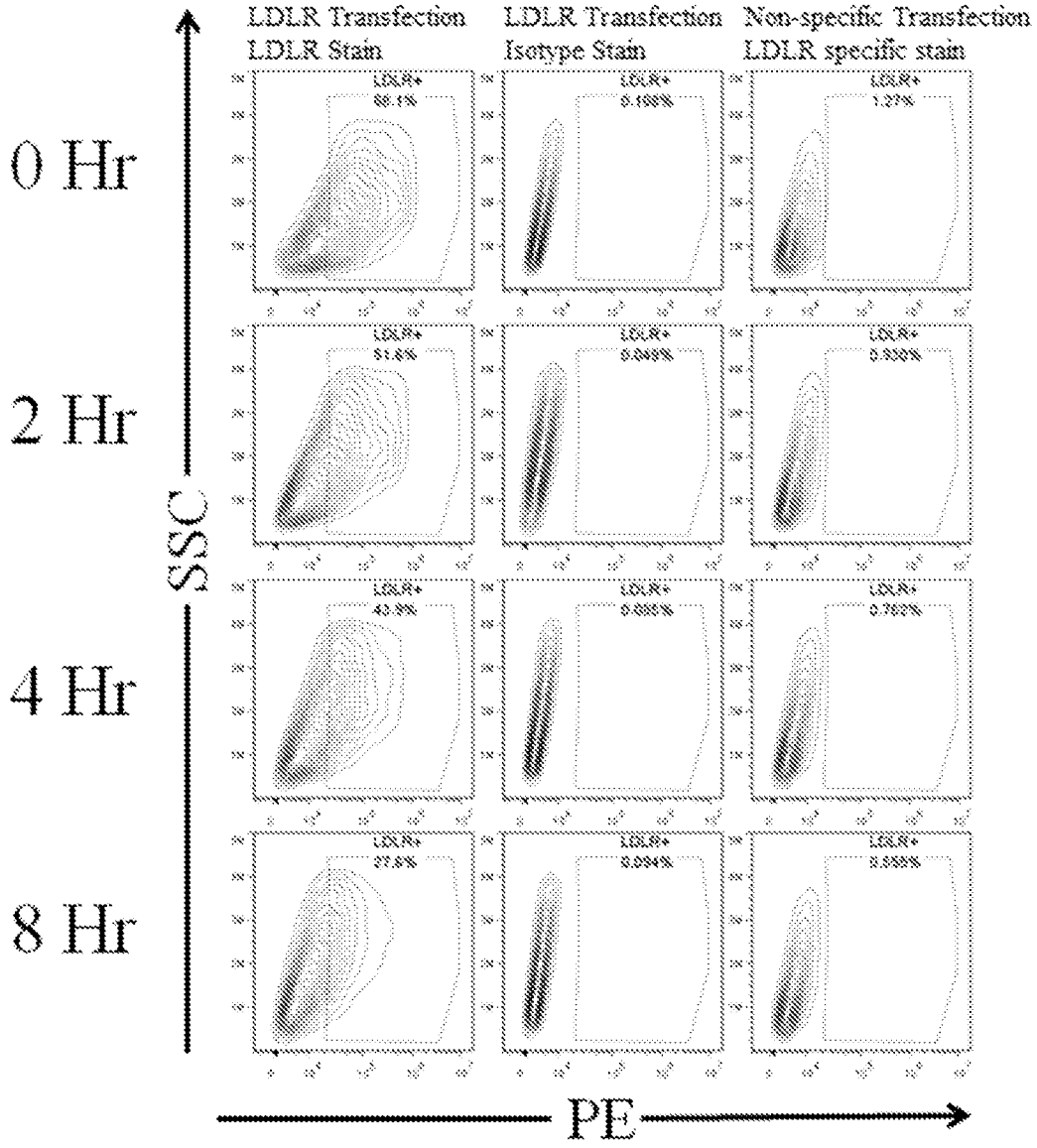

LDLR Transfection
LDLR Stain
LDLR Transfection
Isotype Stain
Non-specific Transfection
LDLR specific stain
0 Hr
2 Hr
4 Hr
8 Hr
SSC
PE

FIGURE 10

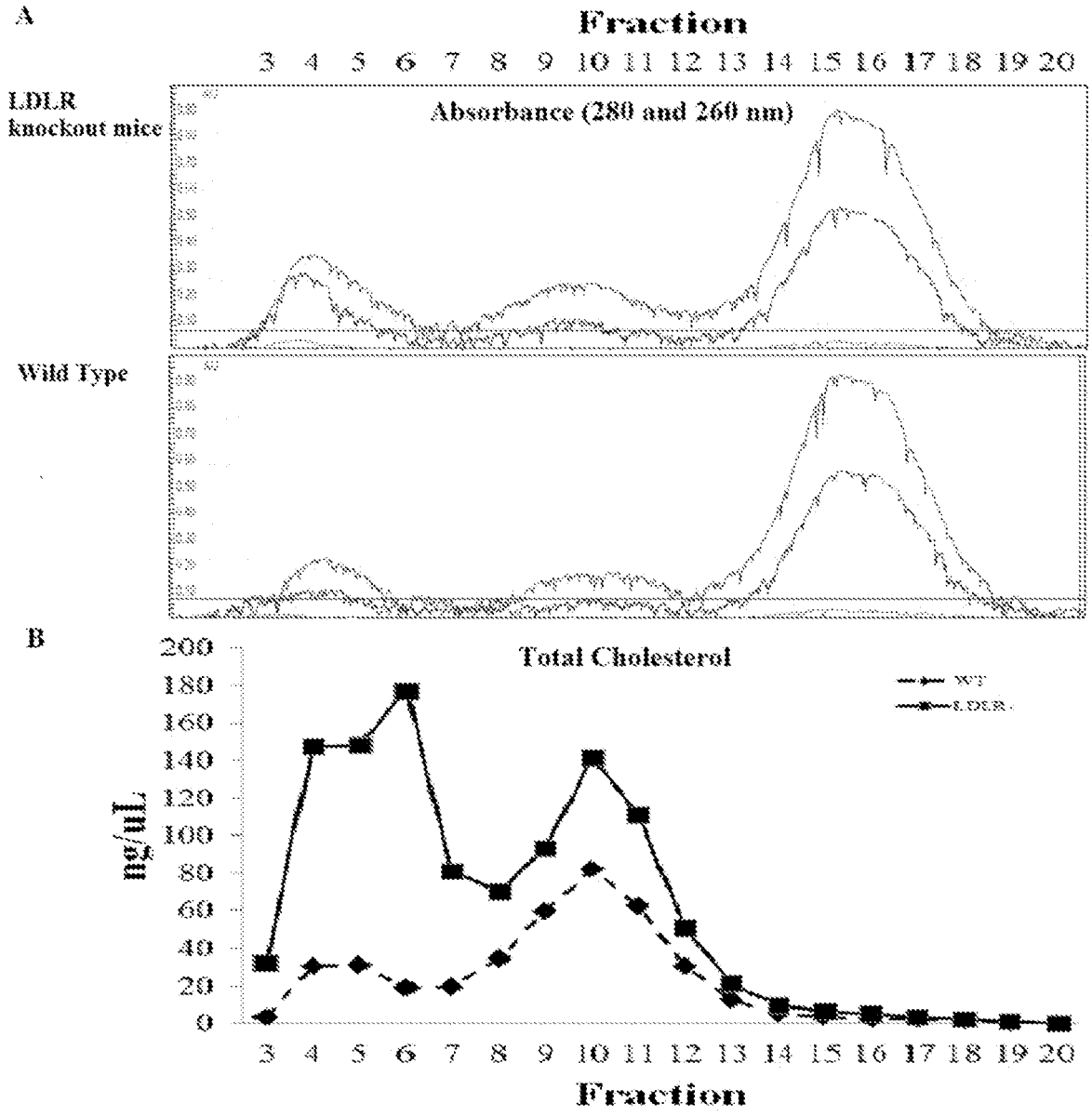

A
Fraction
3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
LDLR knockout mice
Absorbance (280 and 260 nm)
Wild Type
B
Total Cholesterol
WT
LDLR-
mg/mL
200
180
160
140
120
100
80
60
40
20
0
3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Fraction

FIGURE 11

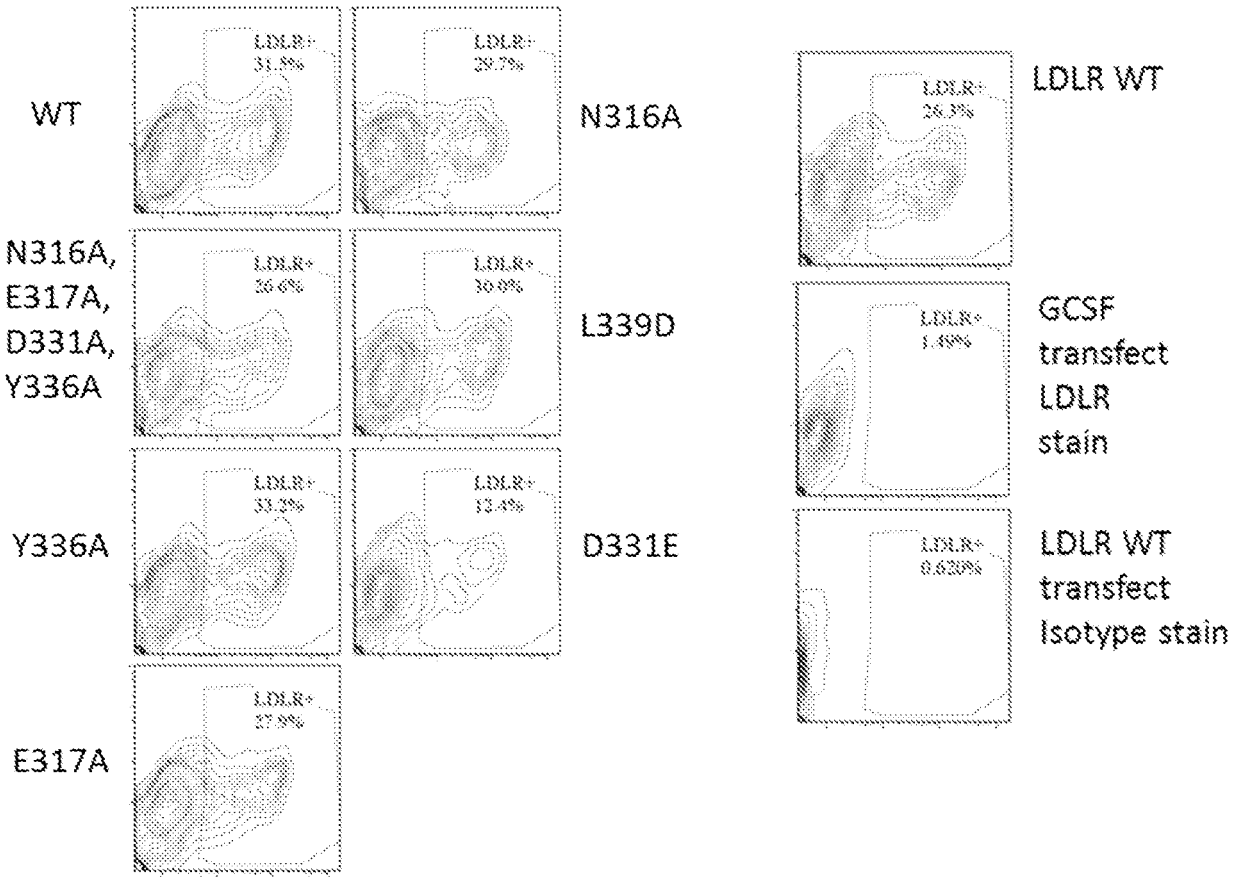

WT
N316A
N316A, E317A, D331A, Y336A
L339D
Y336A
D331E
E317A
LDLR WT
GCSF transfect LDLR stain
LDLR WT transfect Isotype stain

FIGURE 12

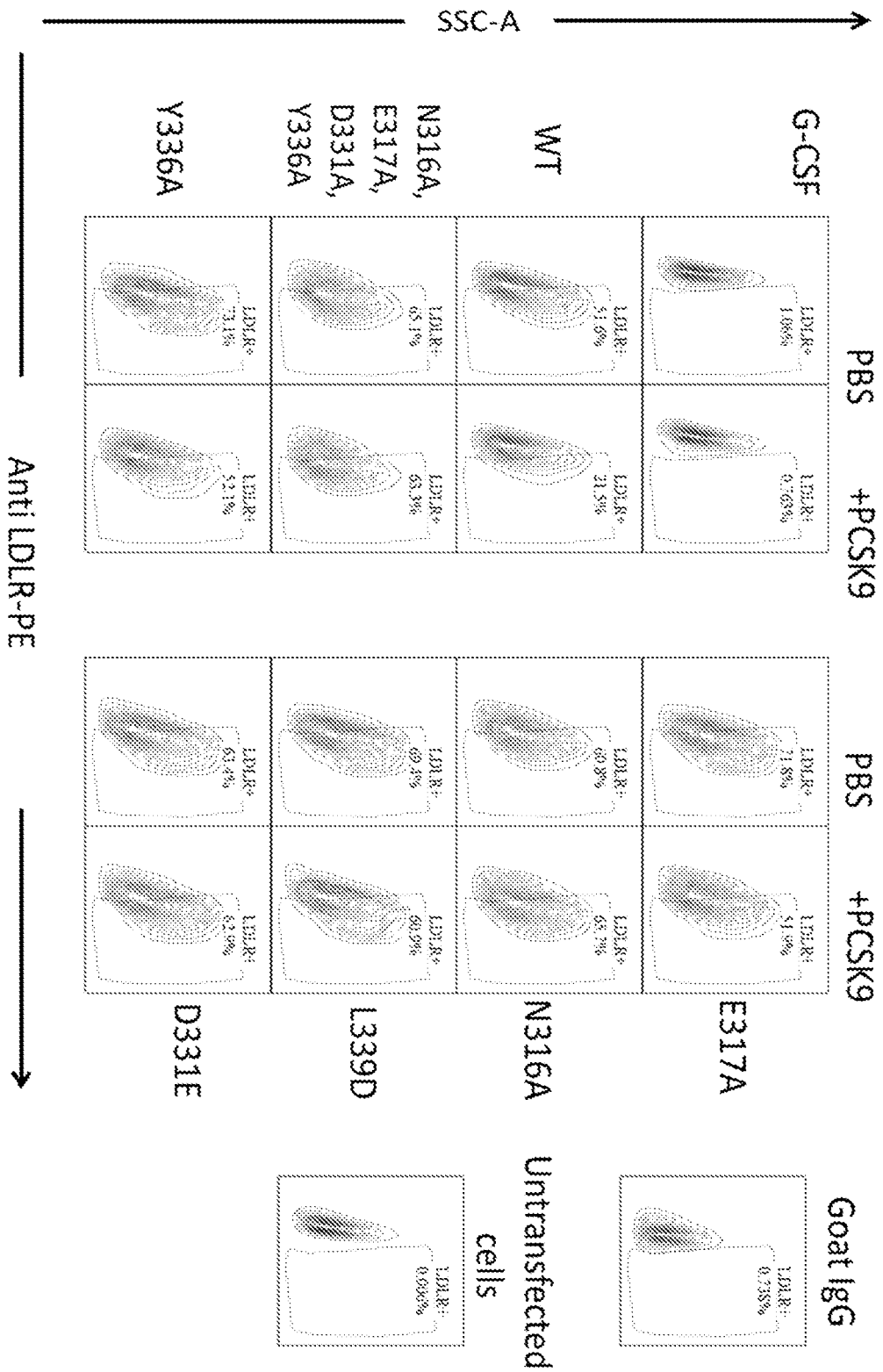

SSC-A
Anti LDLR-PE
G-CSF
WT
N316A, E317A, D331A, Y336A
Y336A
PBS
+PCSK9
PBS
+PCSK9
E317A
N316A
L339D
D331E
Goat IgG
Untransfected cells

FIGURE 13

A.

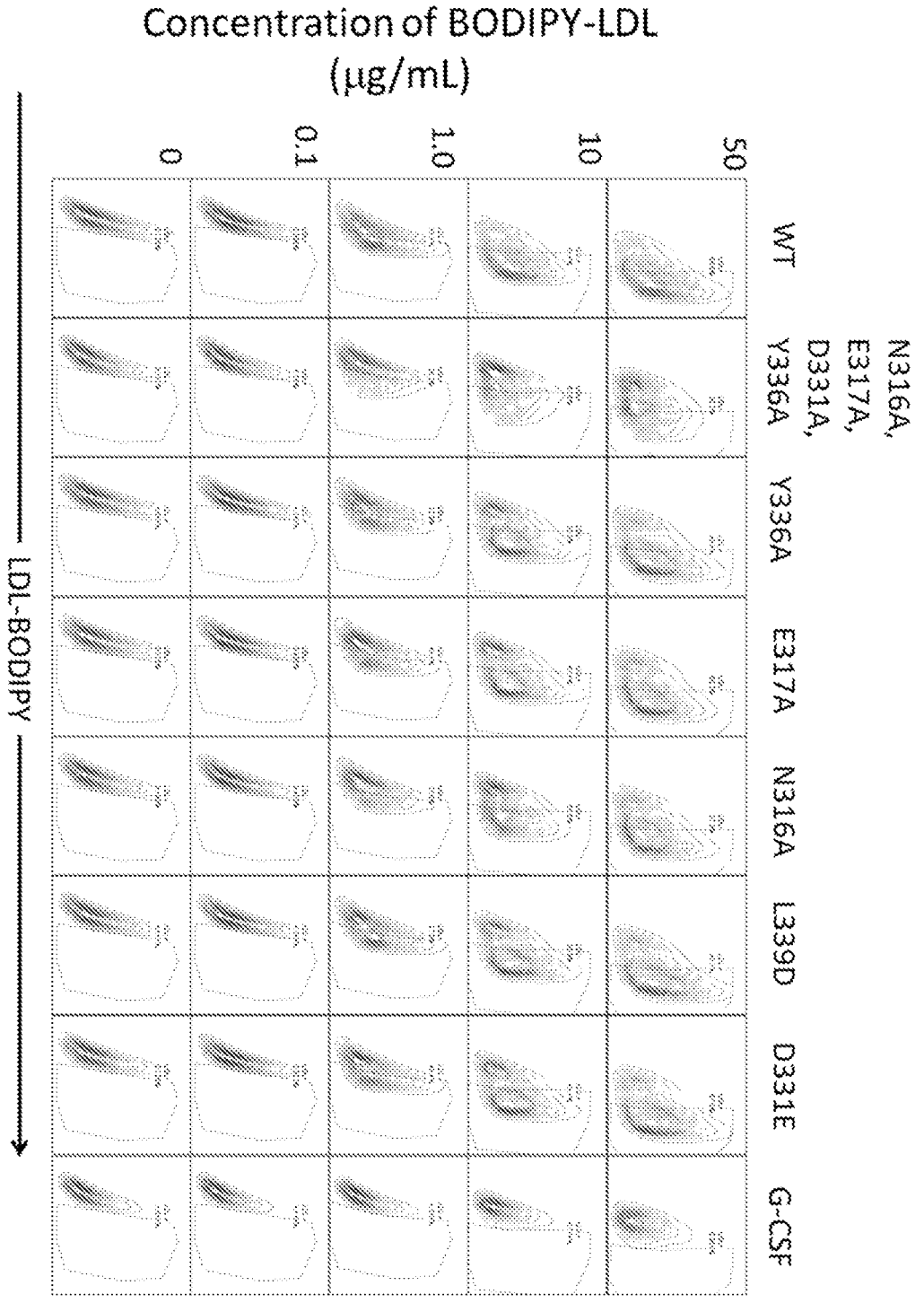

Concentration of BODIPY-LDL
(µg/mL)
0
0.1
1.0
10
50
LDL-BODIPY
WT
N316A, E317A, D331A, Y336A
Y336A
E317A
N316A
L339D
D331E
G-CSF

FIGURE 13 CONT.

B.

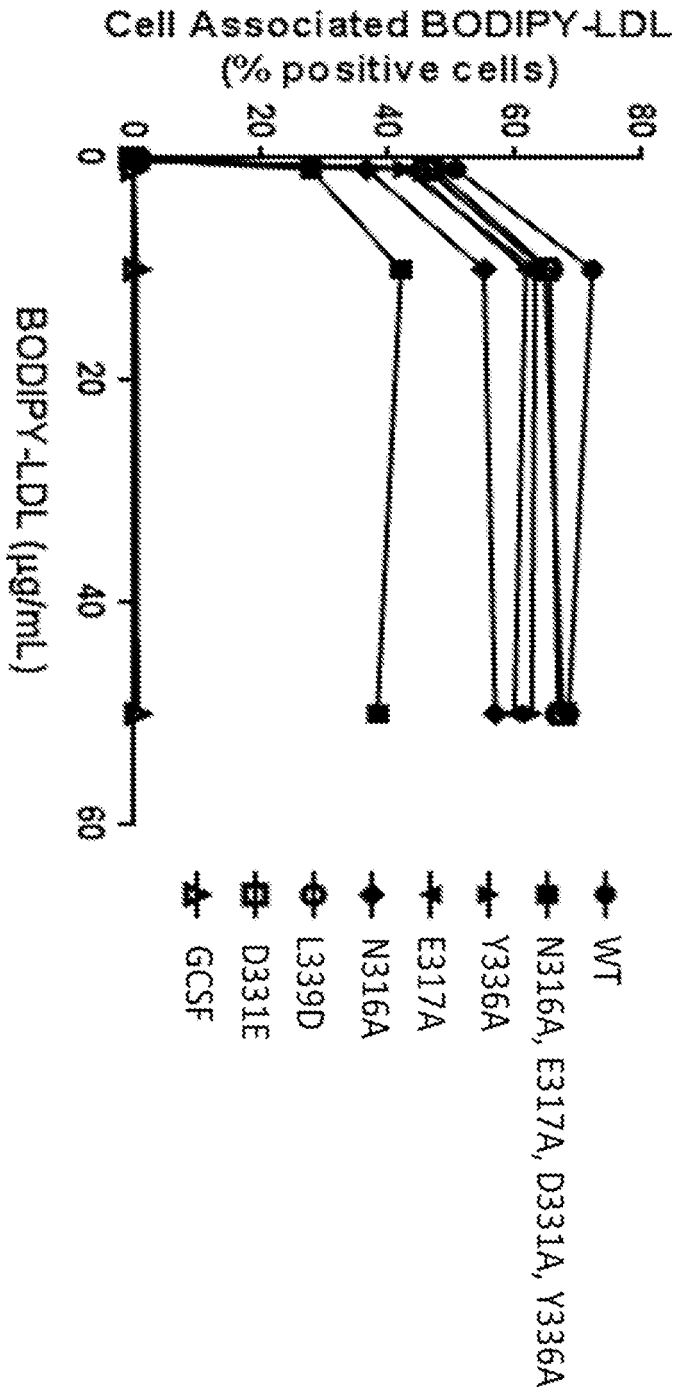
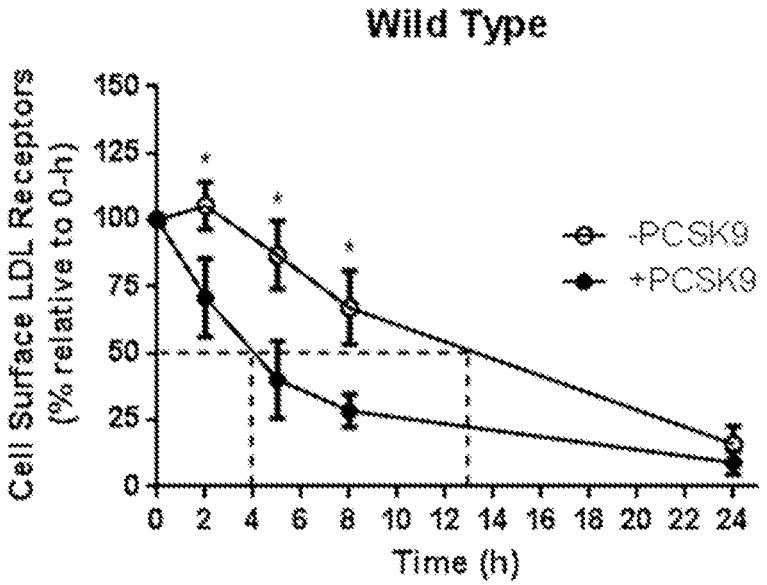


FIGURE 14

A.


Wild Type
Cell Surface LDL Receptors (% relative to 0-h)
150
125
100
75
50
25
0
0 2 4 6 8 10 12 14 16 18 20 22 24
Time (h)
-PCSK9
+PCSK9
*
*
*

B.

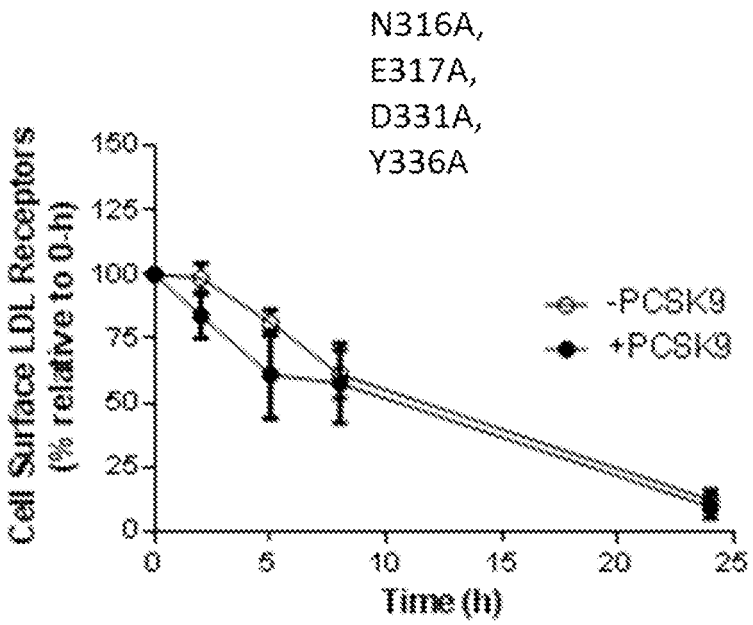
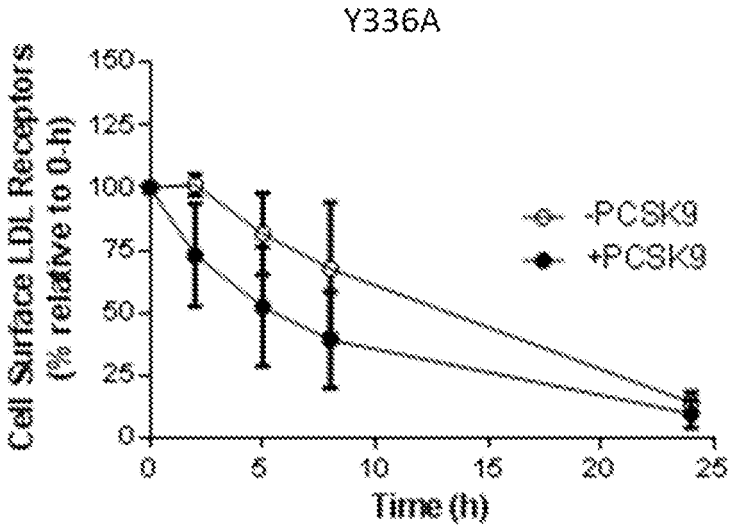

N316A,
E317A,
D331A,
Y336A
Cell Surface LDL Receptors (% relative to 0-h)
150
125
100
75
50
25
0
0 5 10 15 20 25
Time (h)
-PCSK9
+PCSK9

FIGURE 14 CONT.

C.



D.

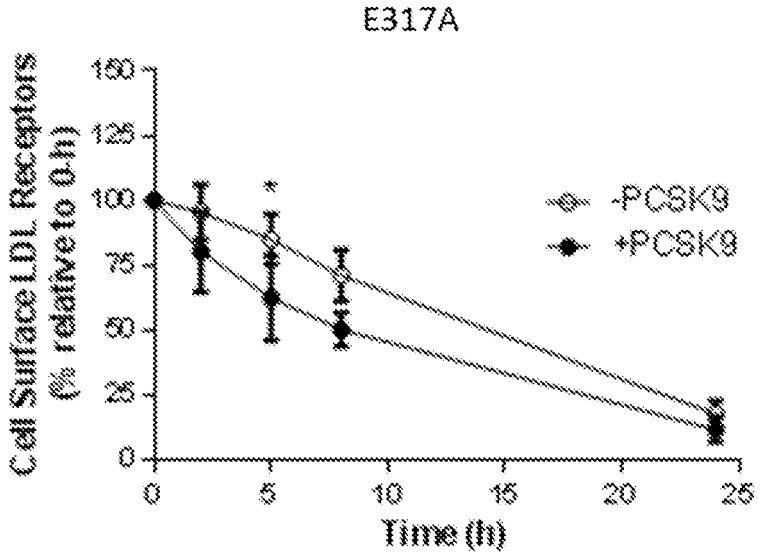
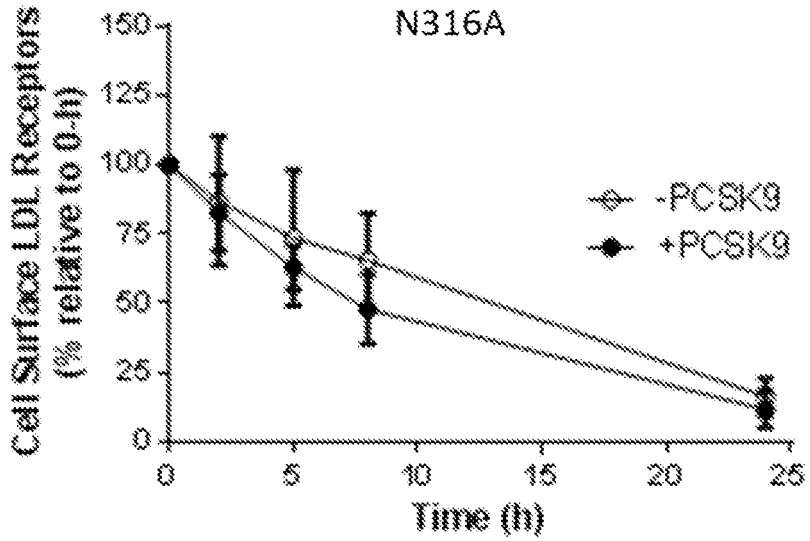


FIGURE 14 CONT.

E.



F.

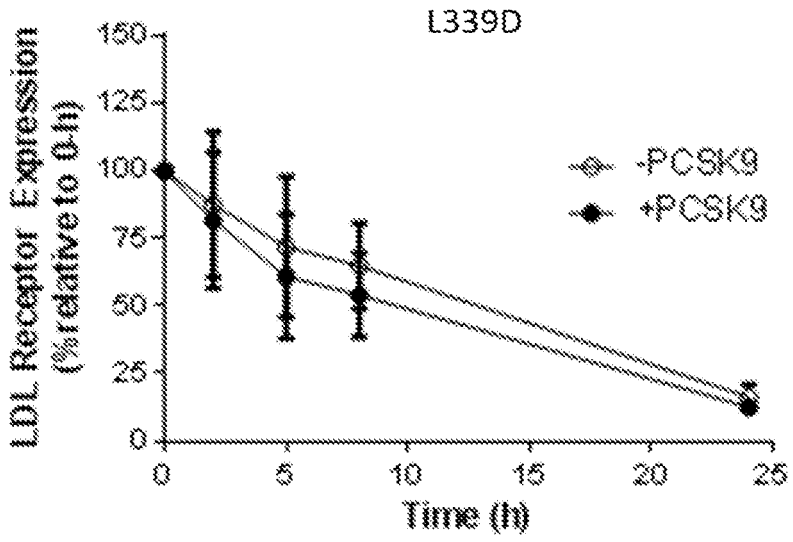


FIGURE 14 CONT.

G.

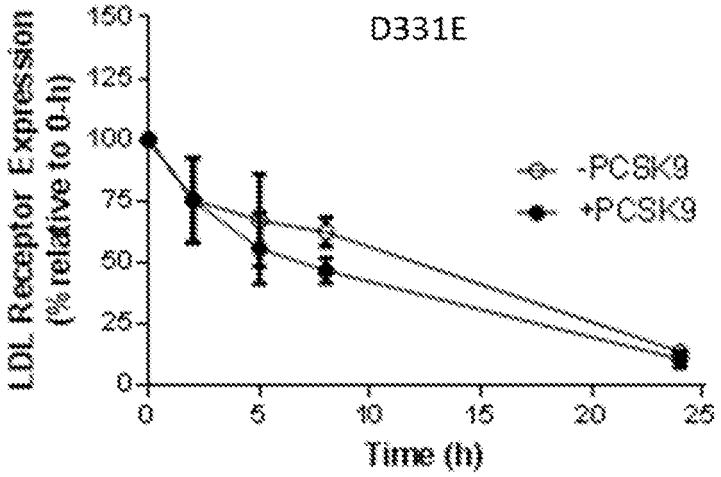
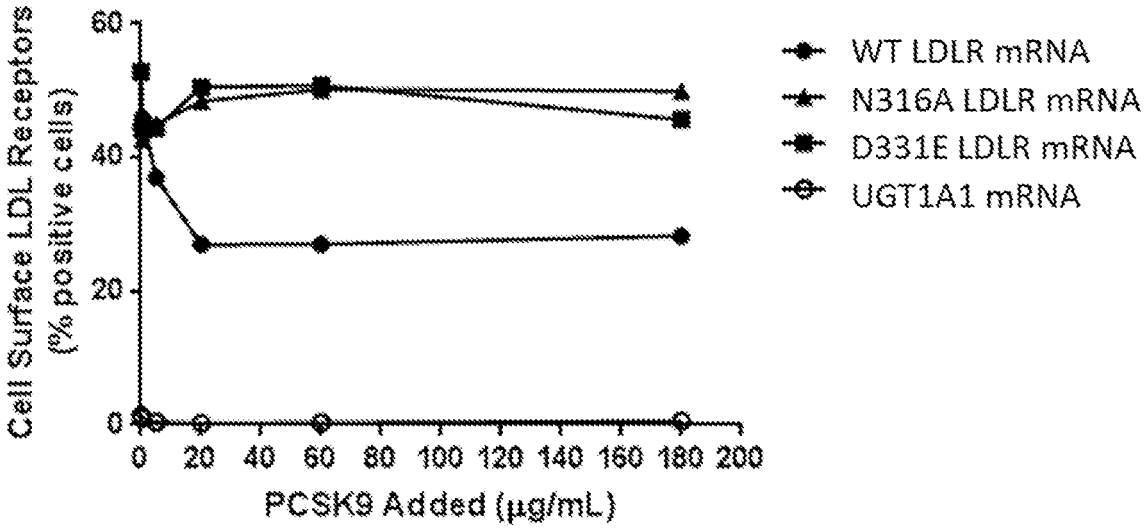


FIGURE 15


Cell Surface LDL Receptors (% positive cells)
60
40
20
0
0 20 40 60 80 100 120 140 160 180 200
PCSK9 Added (µg/mL)
WT LDLR mRNA
N316A LDLR mRNA
D331E LDLR mRNA
UGT1A1 mRNA