FIGURE 1

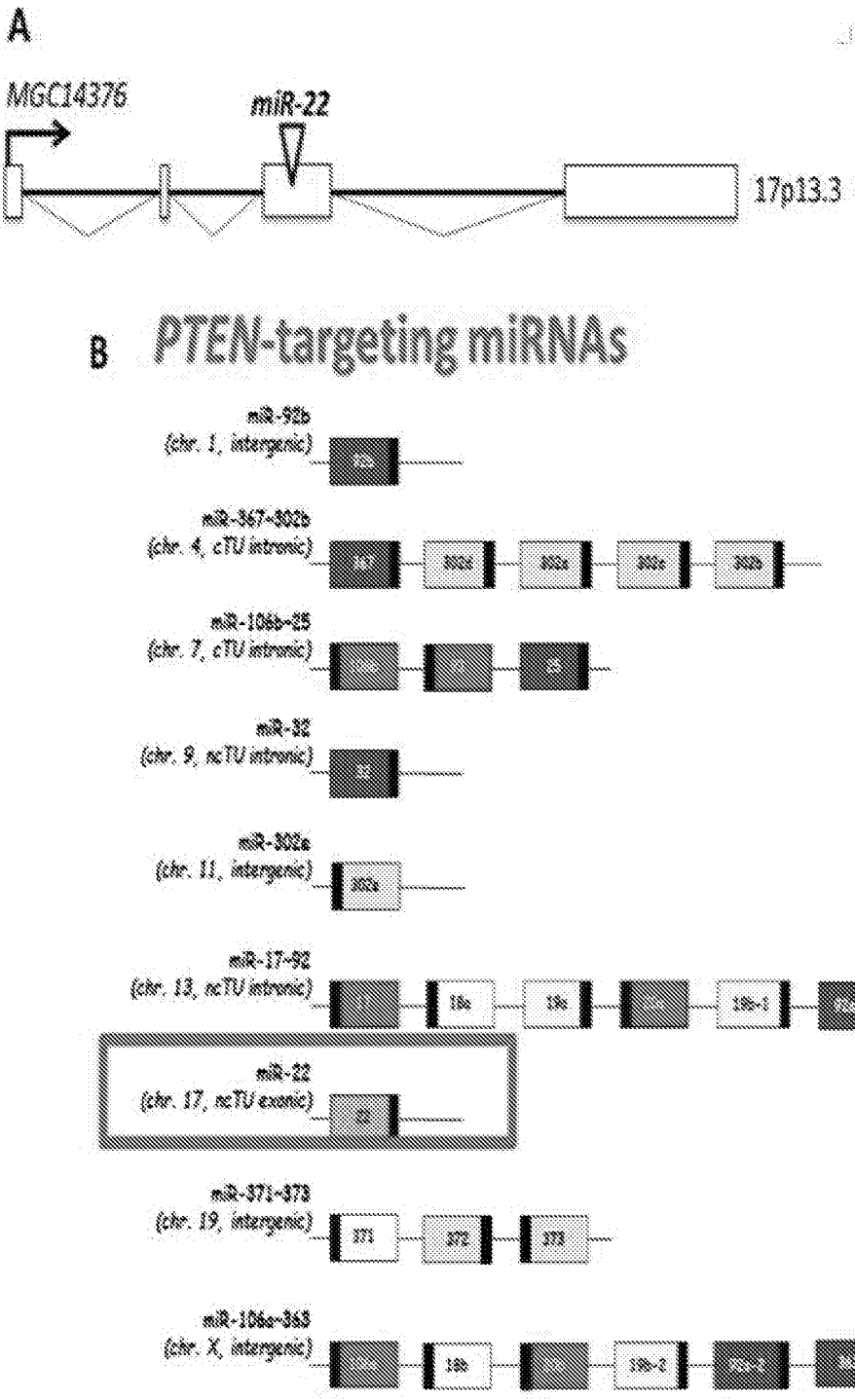

A
MGC14376
miR-22
17p13.3
B
PTEN-targeting miRNAs
miR-92b
(chr. 1, intergenic)
miR-367~302b
(chr. 4, cTU intronic)
miR-106b~25
(chr. 7, cTU intronic)
miR-32
(chr. 9, ncTU intronic)
miR-302a
(chr. 11, intergenic)
miR-17~92
(chr. 13, ncTU intronic)
miR-22
(chr. 17, ncTU exonic)
miR-371~373
(chr. 19, intergenic)
371
372
373
miR-106a~363
(chr. X, intergenic)

FIGURE 1 (Continued)

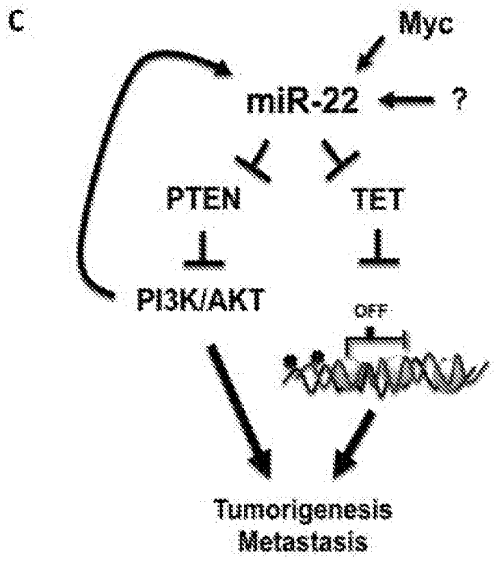


FIGURE 2

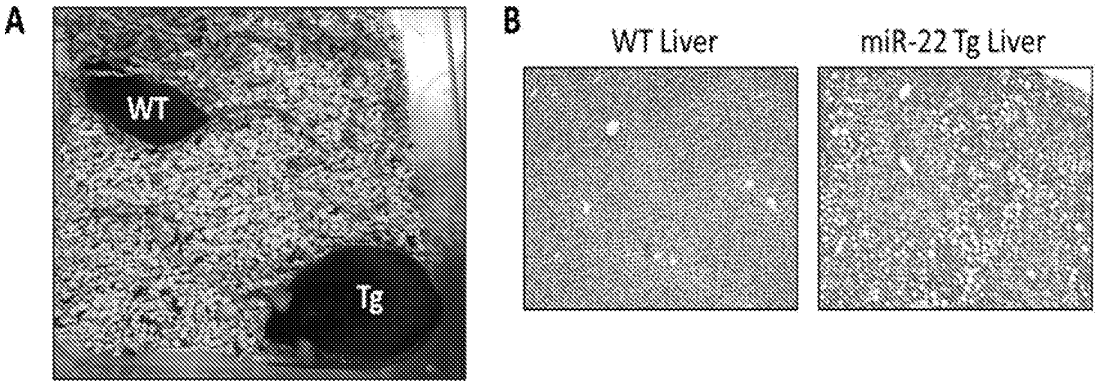
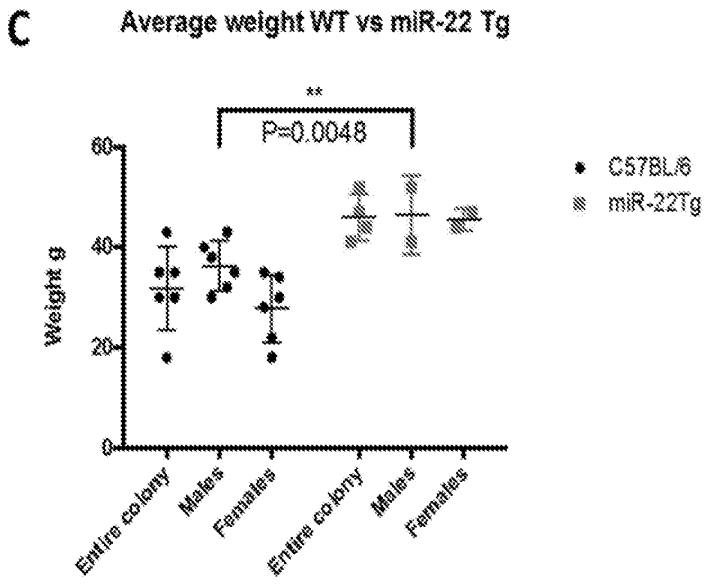


FIGURE 2 (Continued)



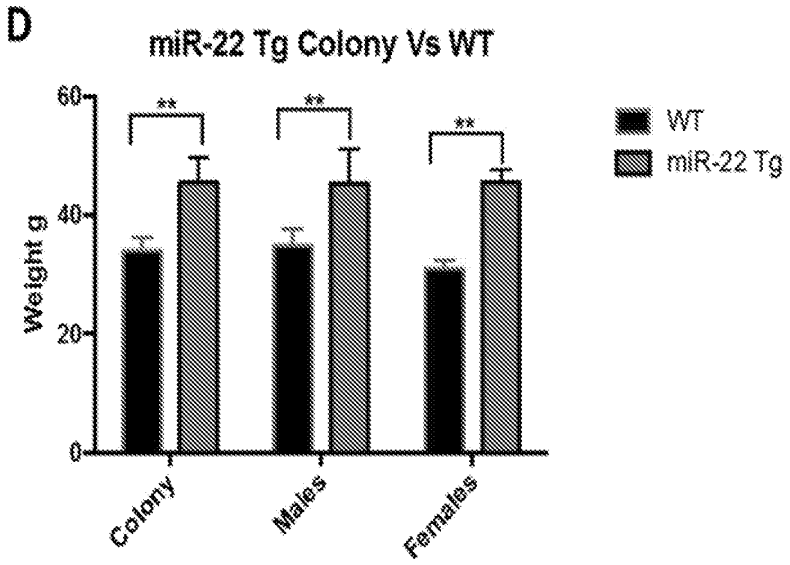


FIGURE 3

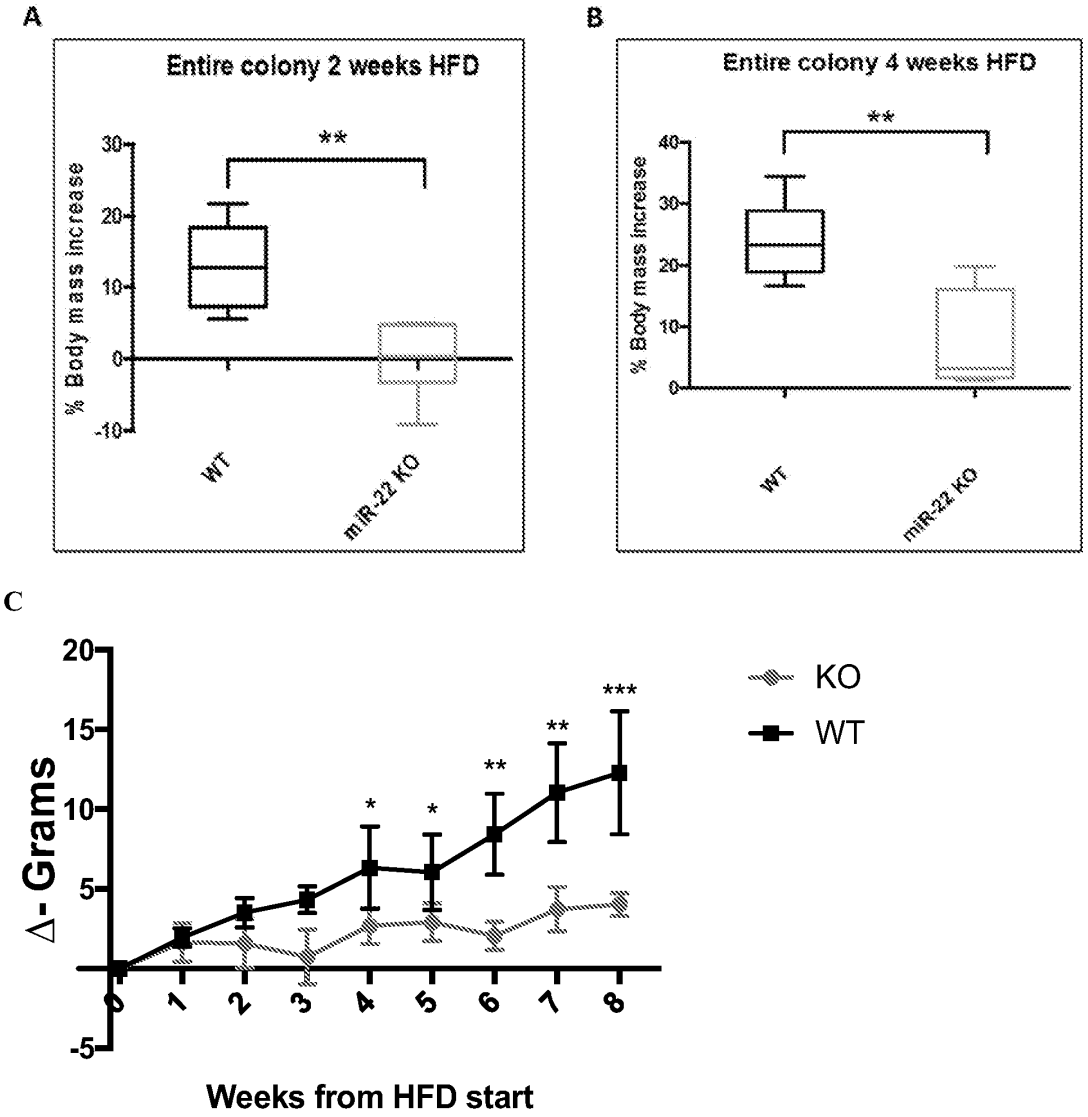
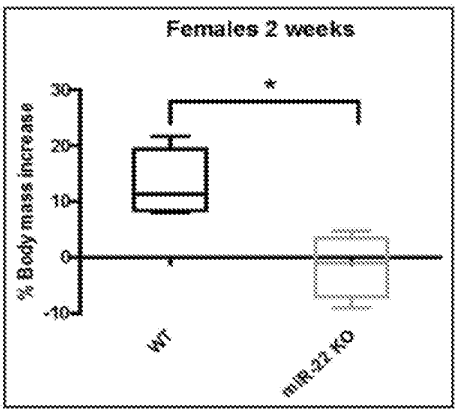
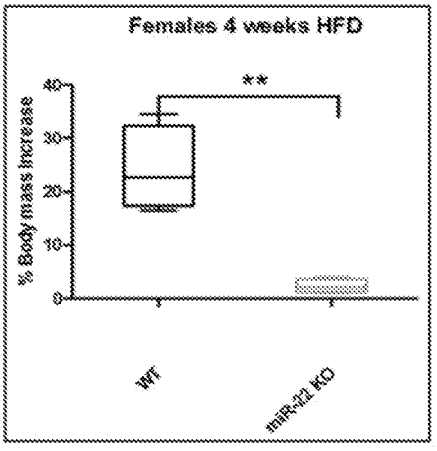

A
Entire colony 2 weeks HFD
% Body mass increase
30
20
10
0
-10
**
WT
miR-22 KO
B
Entire colony 4 weeks HFD
% Body mass increase
40
30
20
10
0
**
WT
miR-22 KO
C
Δ- Grams
20
15
10
5
-5
0
1
2
3
4
5
6
7
8
*
*
**
**
***
KO
WT
Weeks from HFD start

FIGURE 4

A


Females 2 weeks
*
% Body mass increase
30
20
10
0
-10
WT
miR-22 KO

B


Females 4 weeks HFD
**
% Body mass increase
40
30
20
10
0
WT
miR-22 KO

C

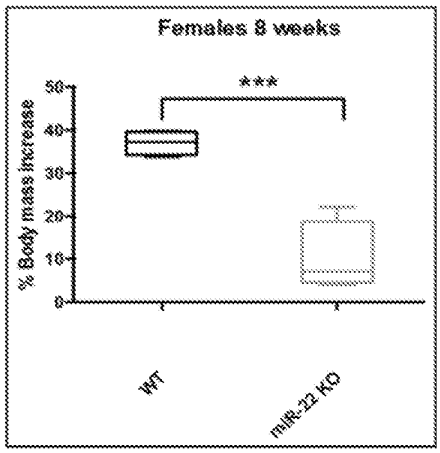

Females 8 weeks
***
% Body mass increase
50
40
30
20
10
0
WT
miR-22 KO

FIGURE 4 (Continued)

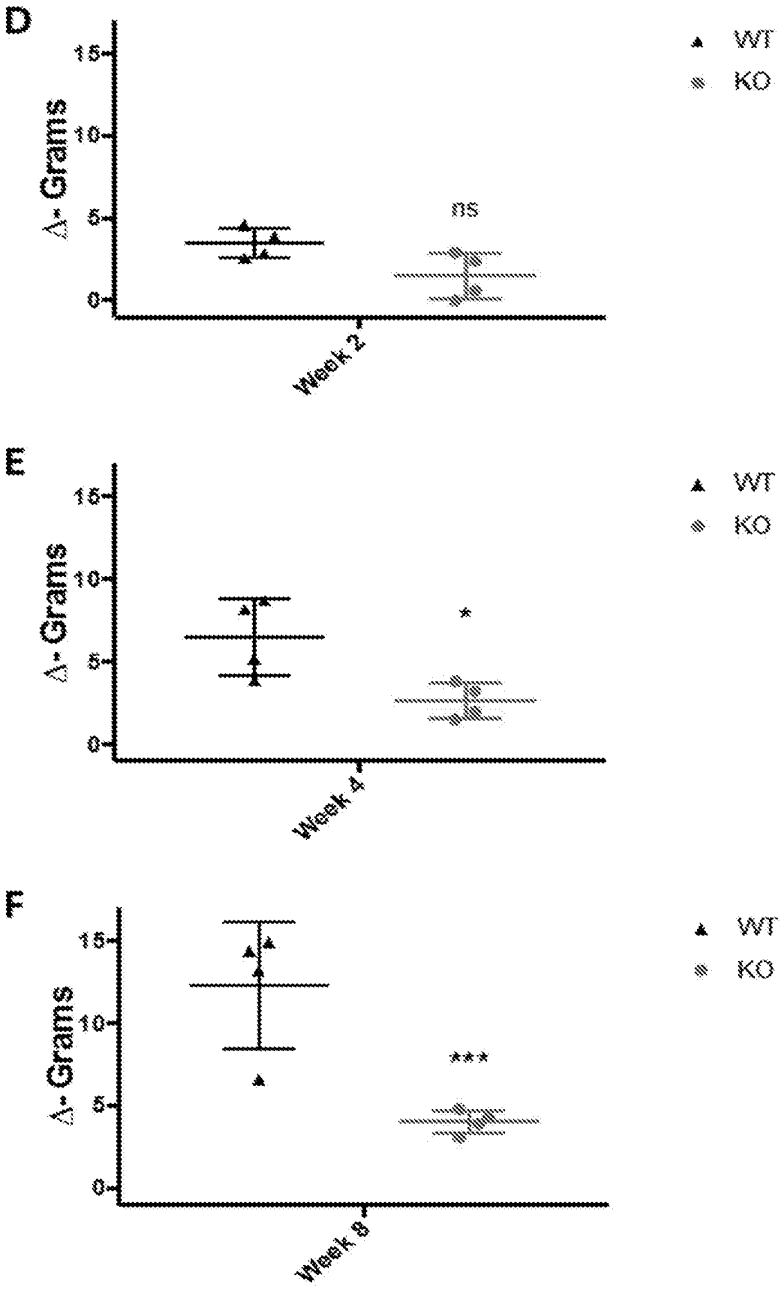


FIGURE 5

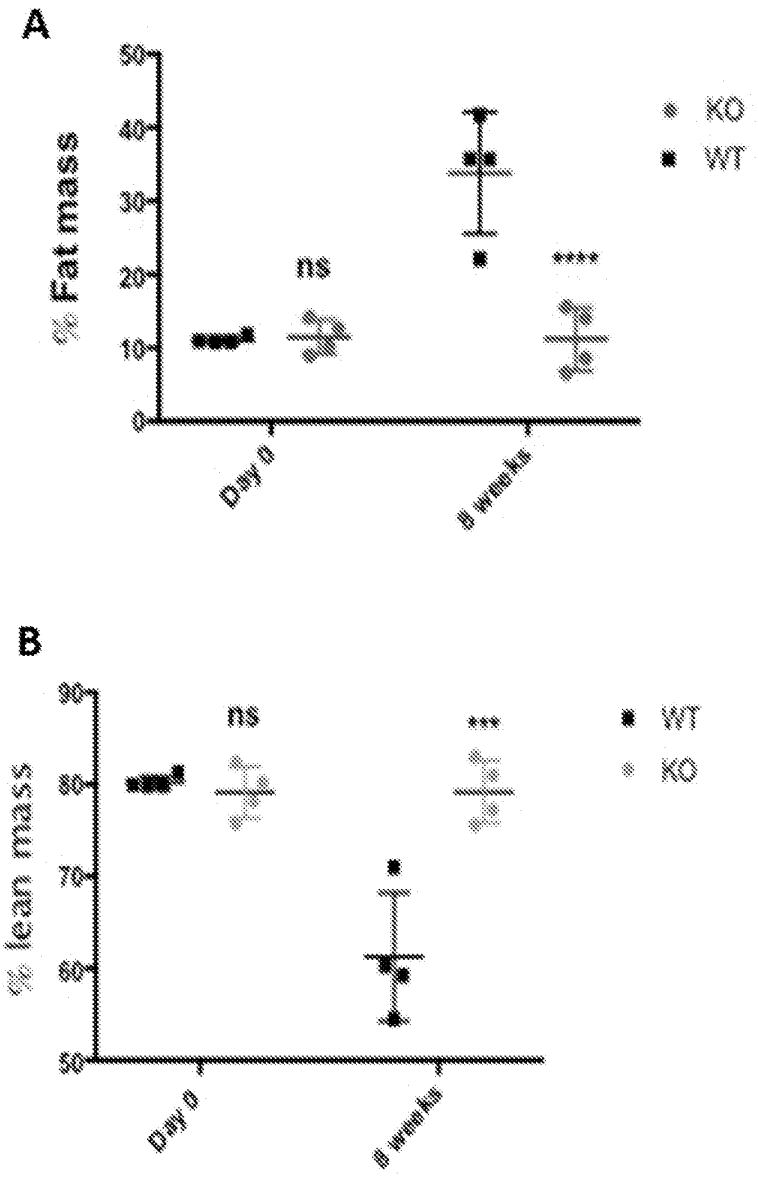

A
% Fat mass
50
40
30
20
10
0
ns
****
KO
WT
Day 0
8 weeks
B
% lean mass
90
80
70
60
50
ns
***
WT
KO
Day 0
8 weeks

FIGURE 5 (Continued)

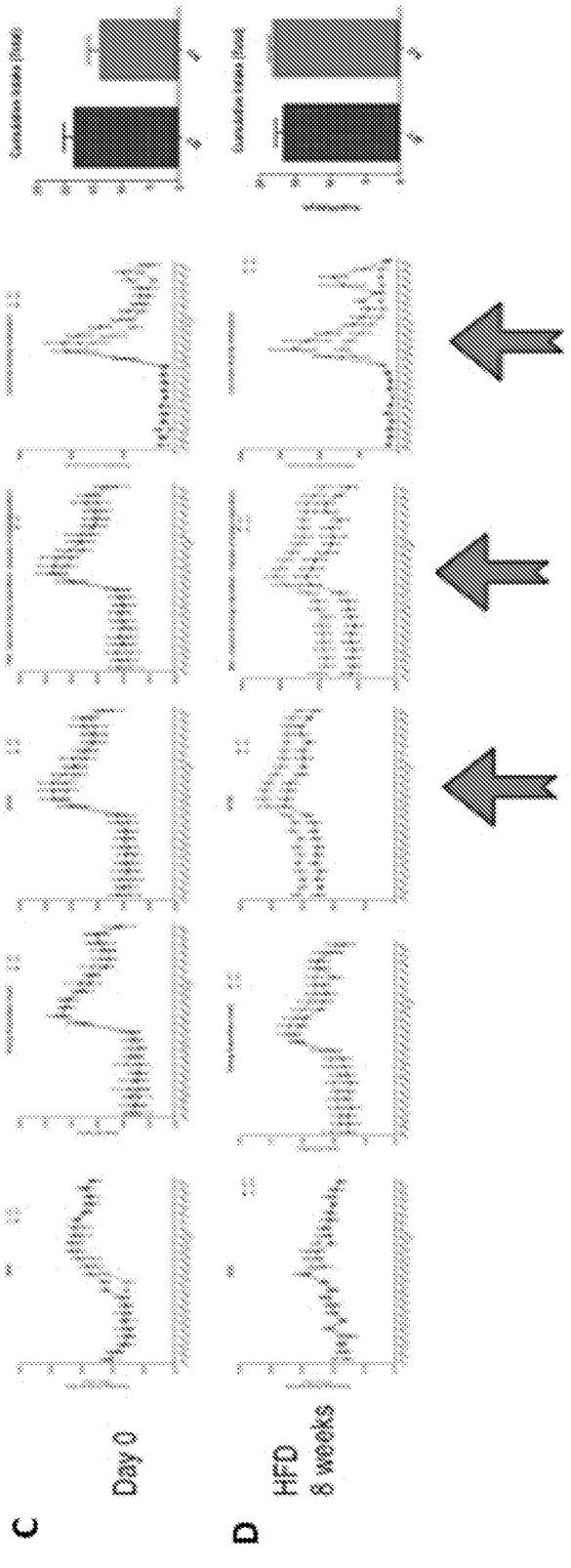


FIGURE 6

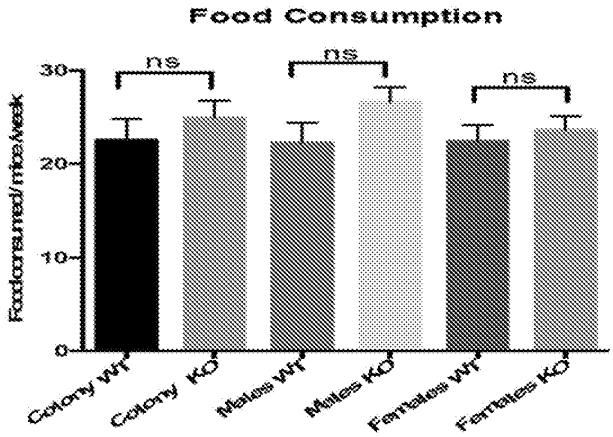


FIGURE 7

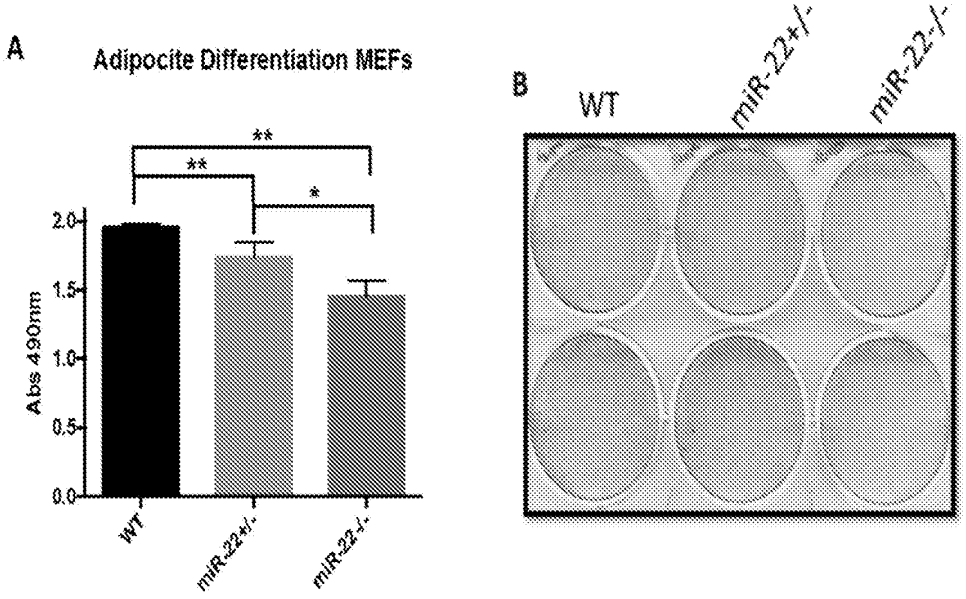


FIGURE 8

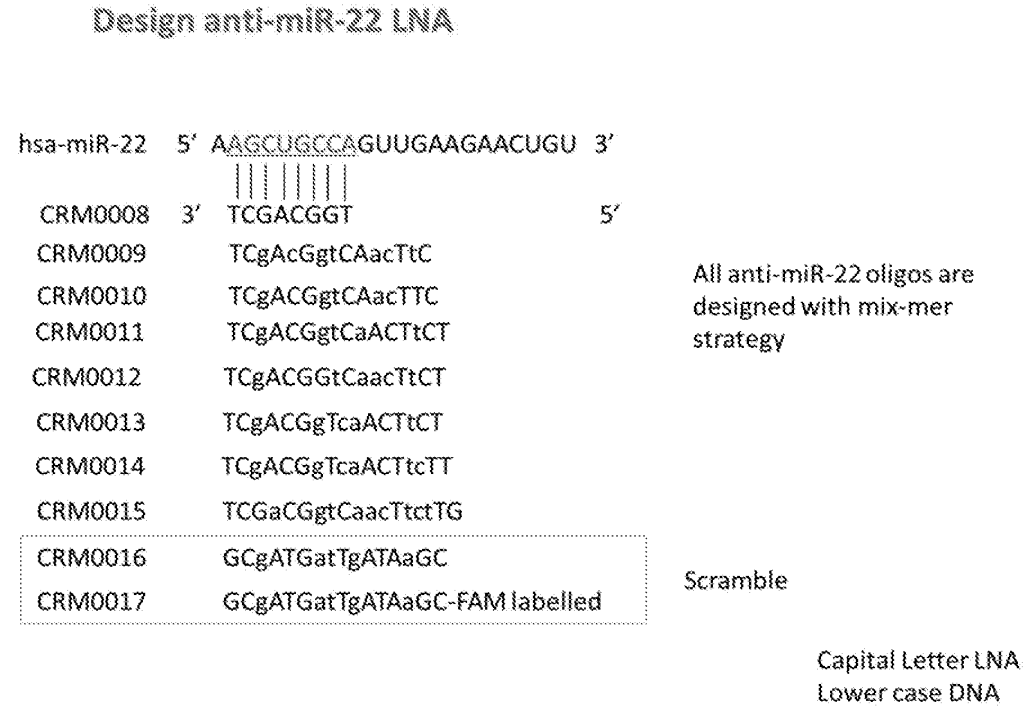
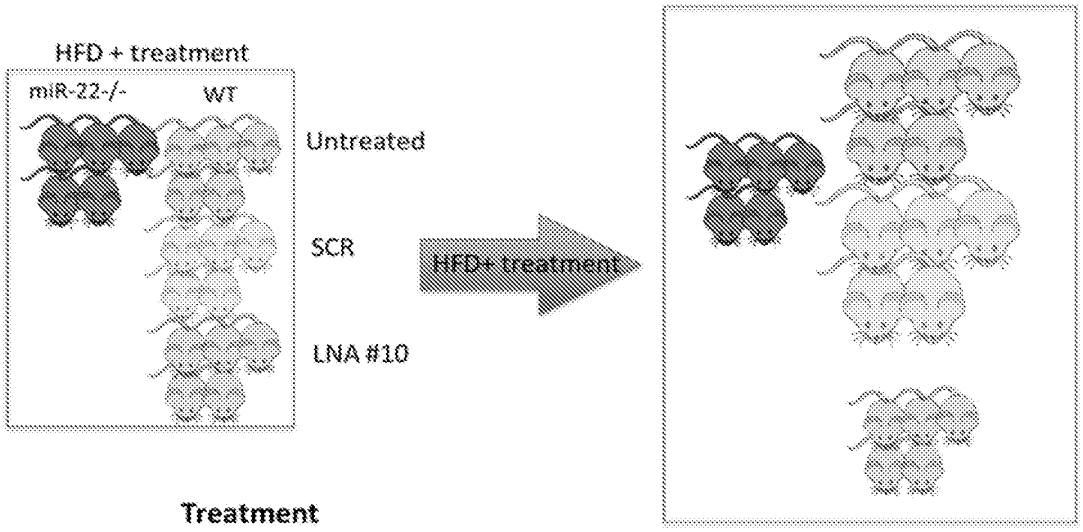

Design anti-miR-22 LNA
hsa-miR-22 5' AAGCUGCCAGUUGAAGAACUGU 3'
CRM0008 3' TCGACGGT 5'
CRM0009 TCgAcGgtCAacTtC
CRM0010 TCgACGgtCAacTTC
CRM0011 TCgACGgtCaACTtCT
CRM0012 TCgACGGtCaacTtCT
CRM0013 TCgACGgTcaACTtCT
CRM0014 TCgACGgTcaACTtcTT
CRM0015 TCGaCGgtCaacTtctTG
CRM0016 GCgATGatTgATAaGC
CRM0017 GCgATGatTgATAaGC-FAM labelled
All anti-miR-22 oligos are designed with mix-mer strategy
Scramble
Capital Letter LNA
Lower case DNA

FIGURE 9



Treatment

Loading dose 20mg/kg (first time)
Maintenance dose 10mg/kg weekly
IP injection un-assisted uptake

All mice were 2 months old at the beginning of the experiment

FIGURE 10

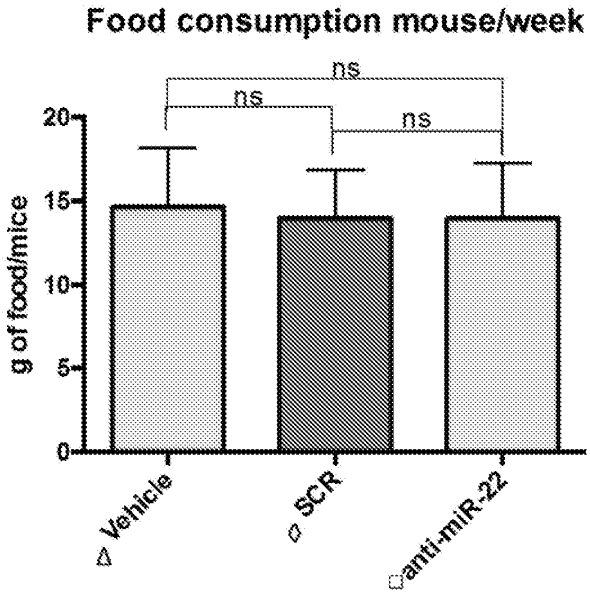
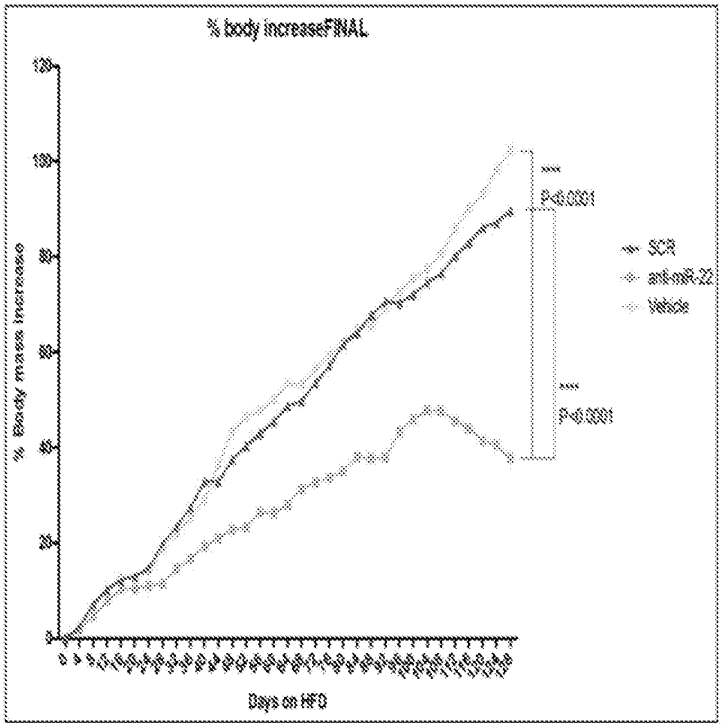


FIGURE 11

A


% body increaseFINAL
% Body mass increase
Days on HFD
SCR
anti-miR-22
Vehicle
****
P<0.0001
****
P<0.0001

B

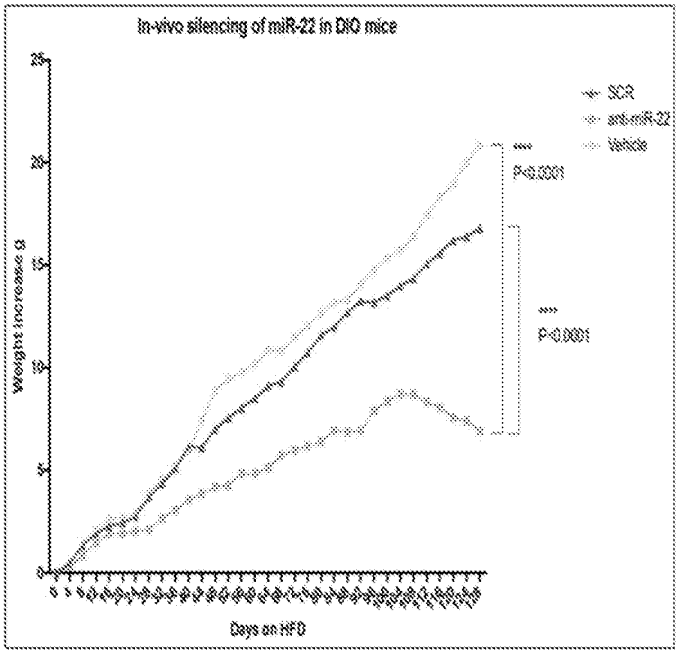
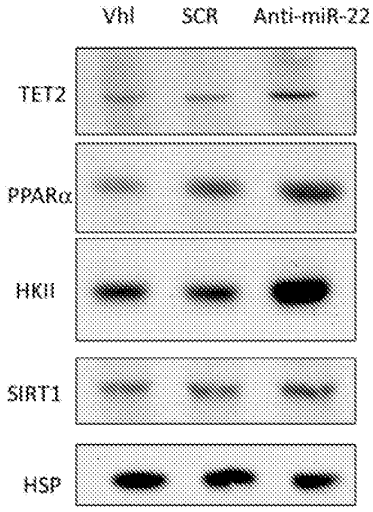

In-vivo silencing of miR-22 in DIO mice
Weight increase g
Days on HFD
SCR
anti-miR-22
Vehicle
****
P<0.0001
****
P<0.0001

FIGURE 12



Liver sample from treated and un-treated mice

FIGURE 13

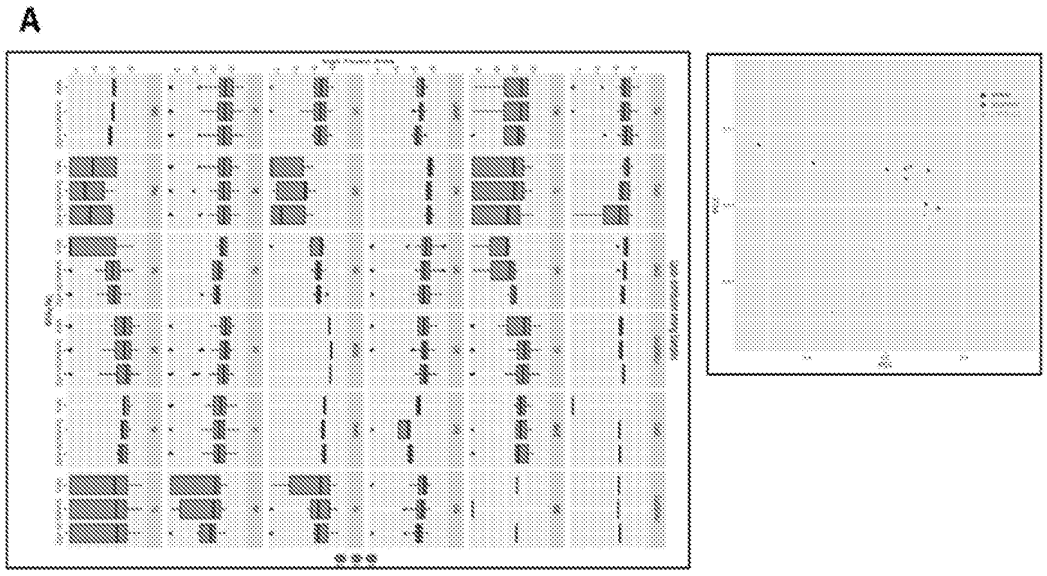


FIGURE 13 (Continued)

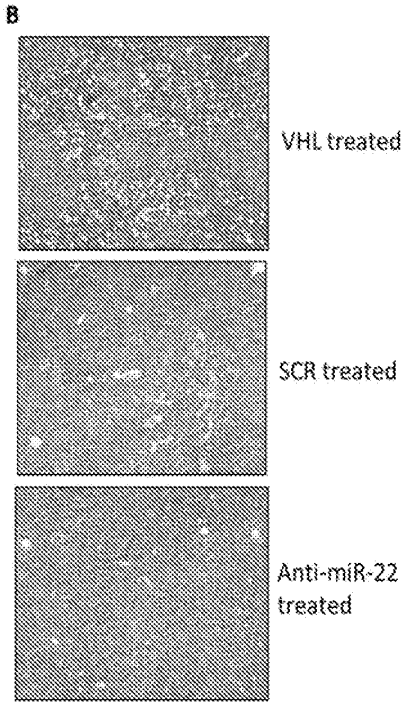


FIGURE 14

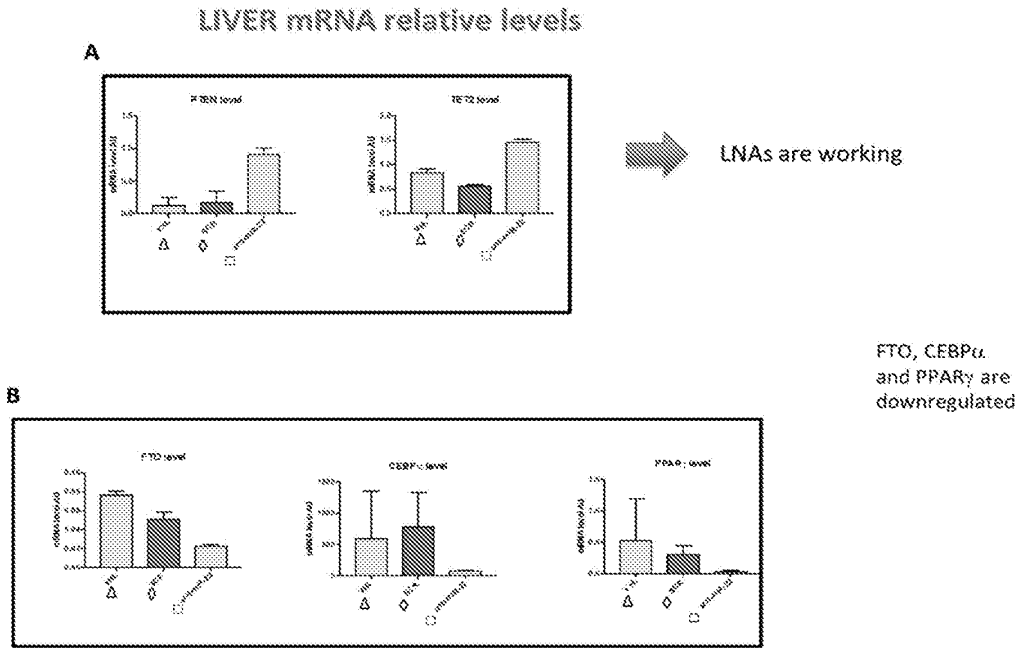


FIGURE 15

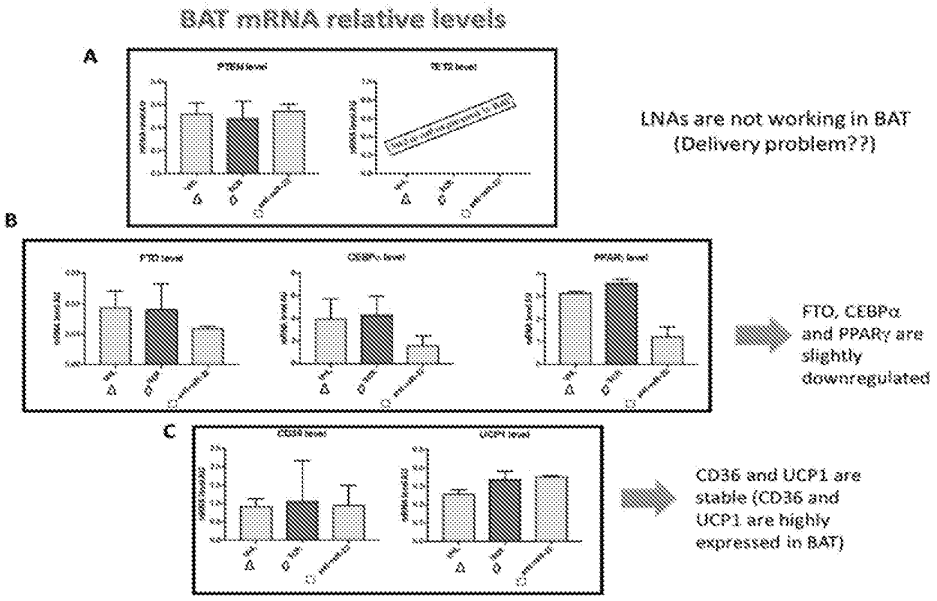


FIGURE 16

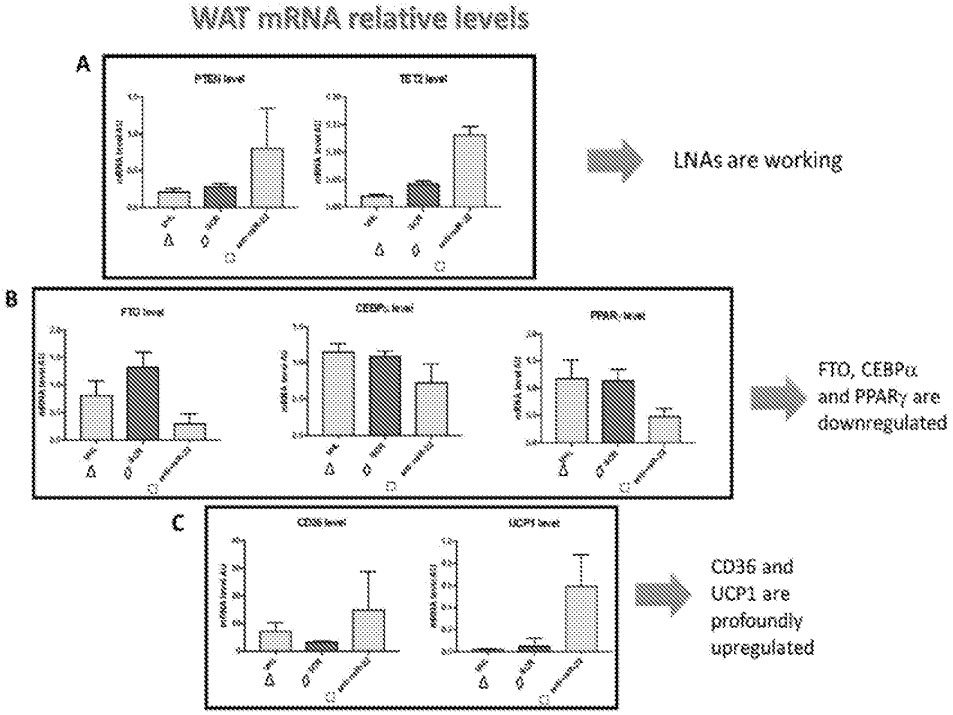


FIGURE 17

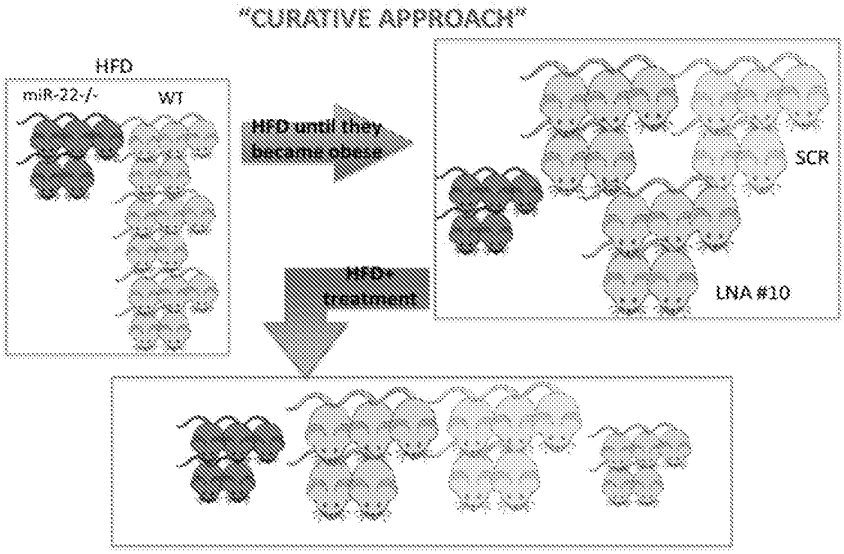


FIGURE 18

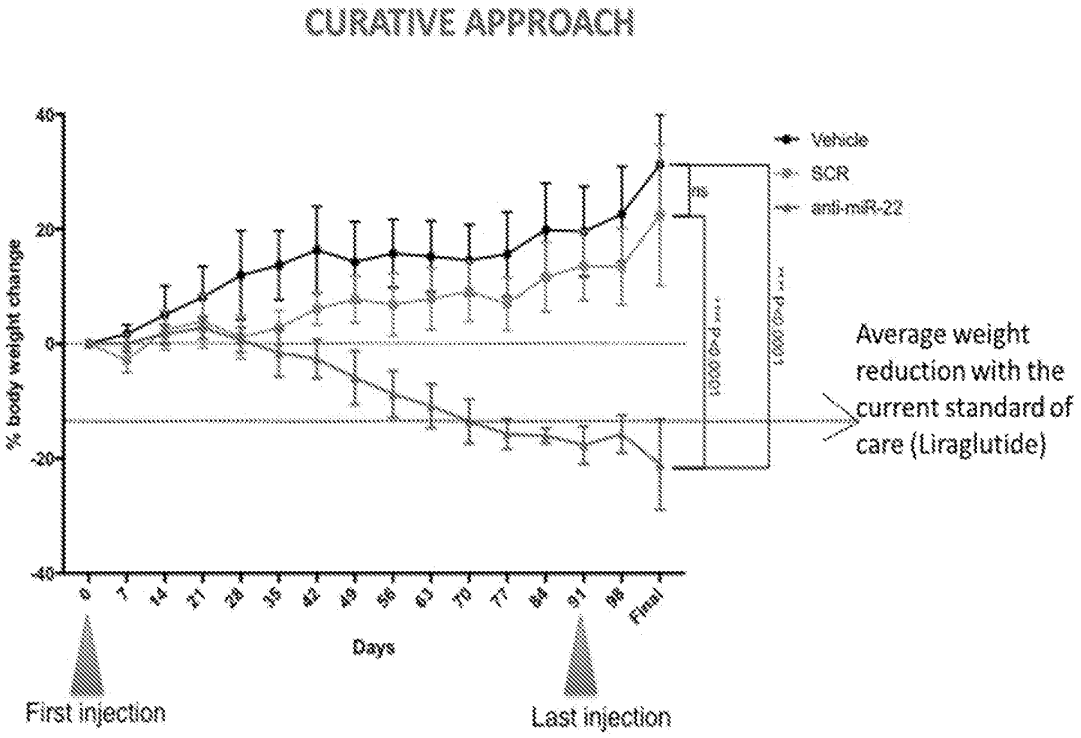


FIGURE 19

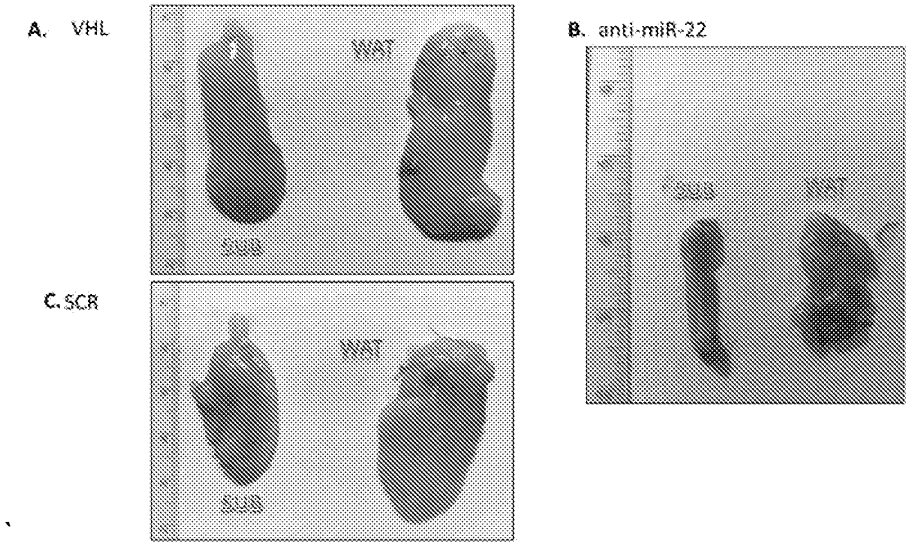


FIGURE 20

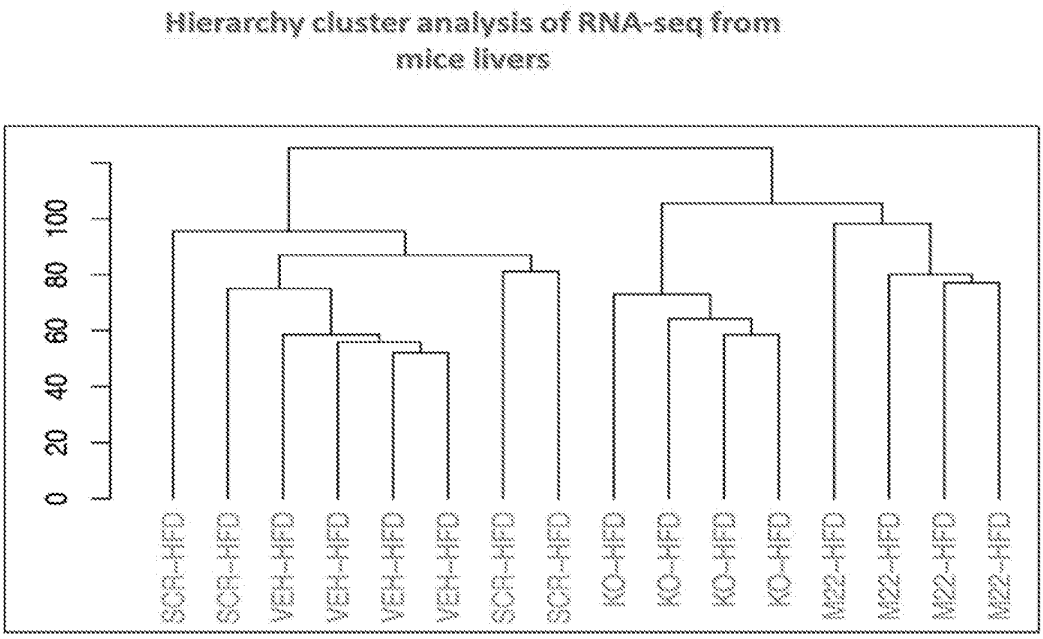


FIGURE 21

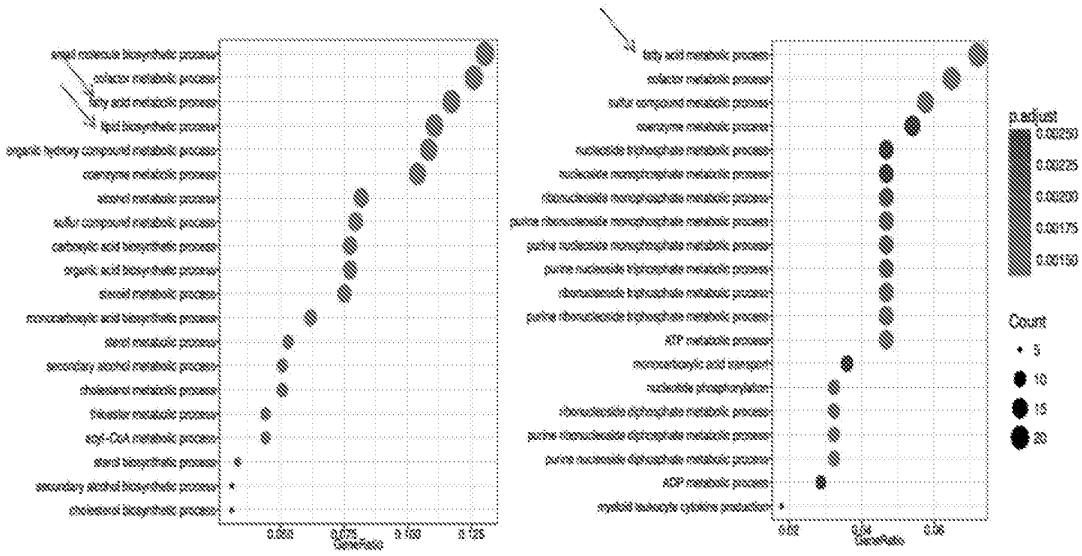


FIGURE 22

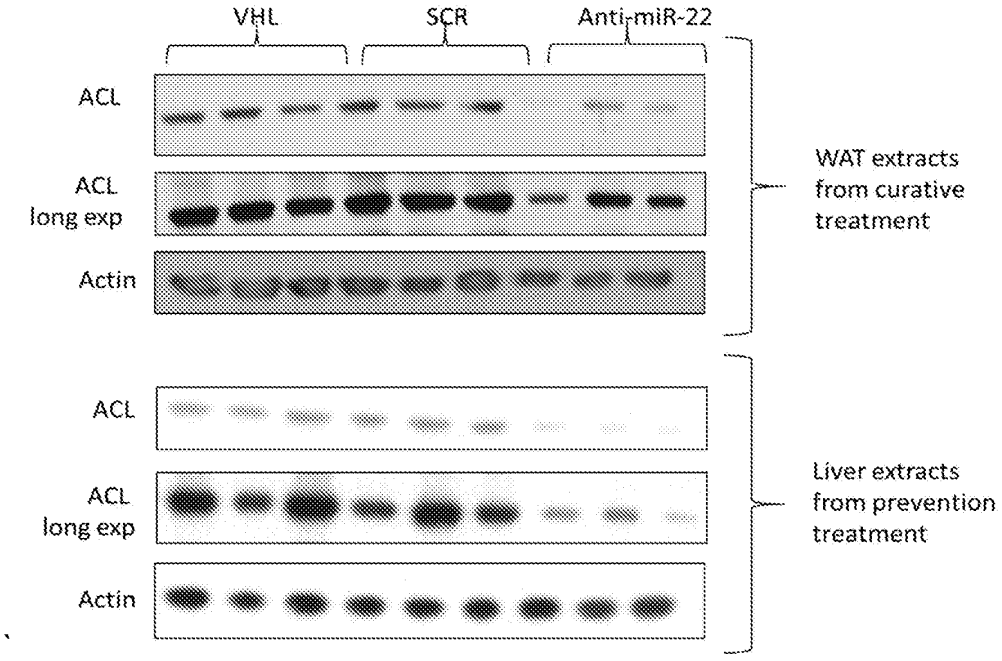


FIGURE 23

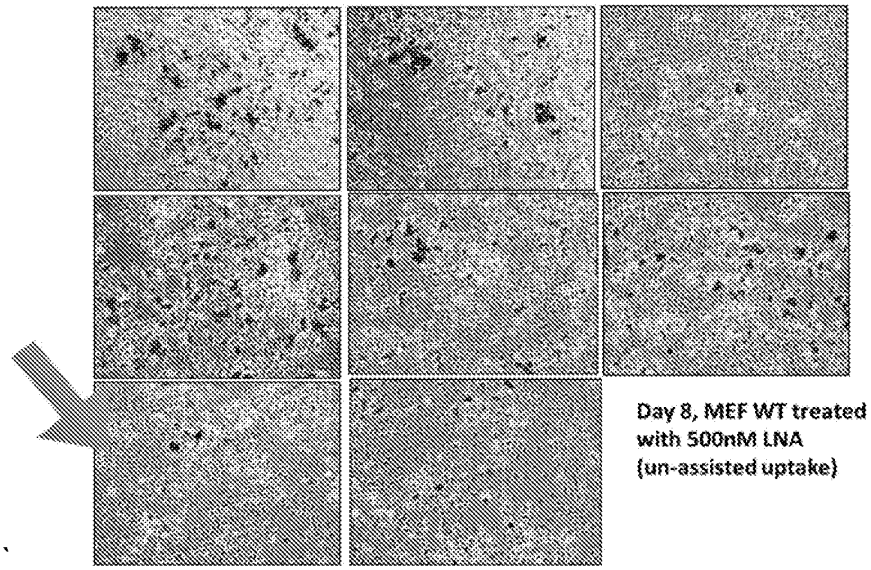


FIGURE 24

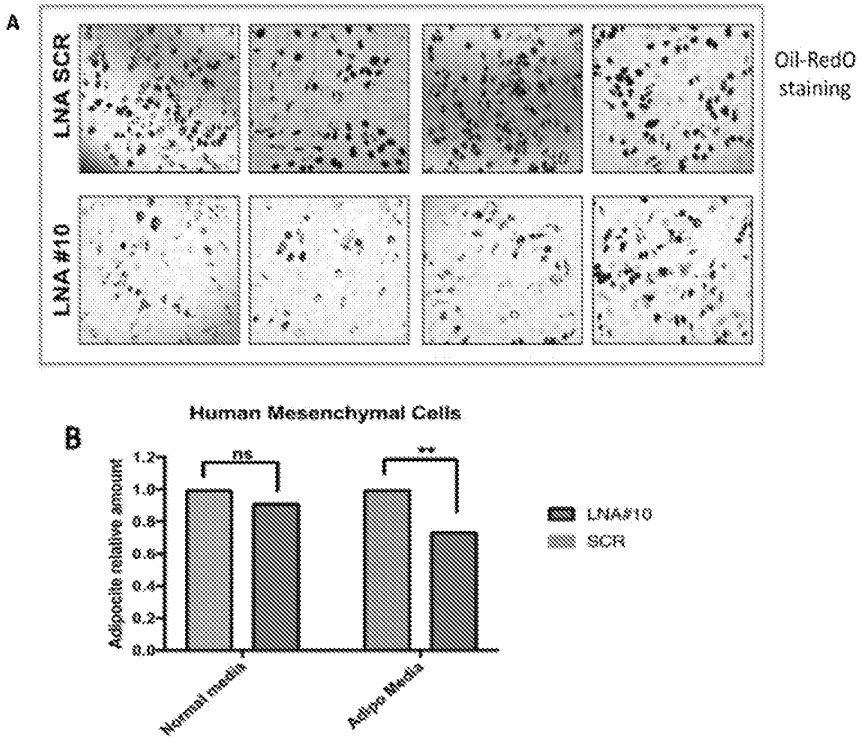


FIGURE 25

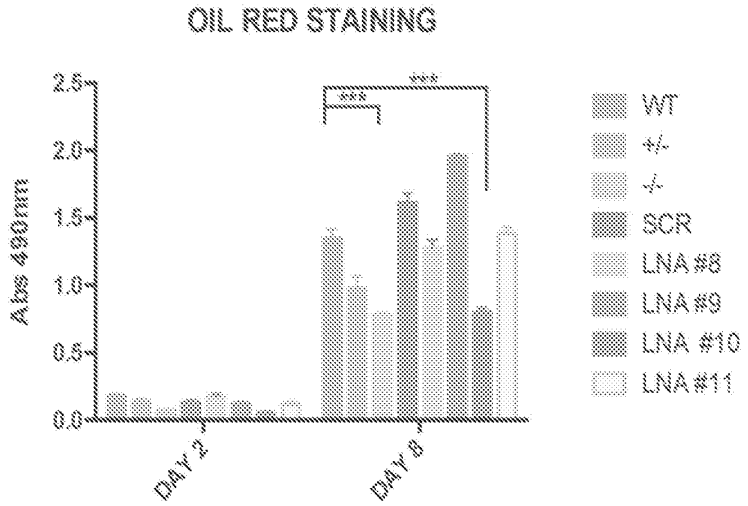


FIGURE 26

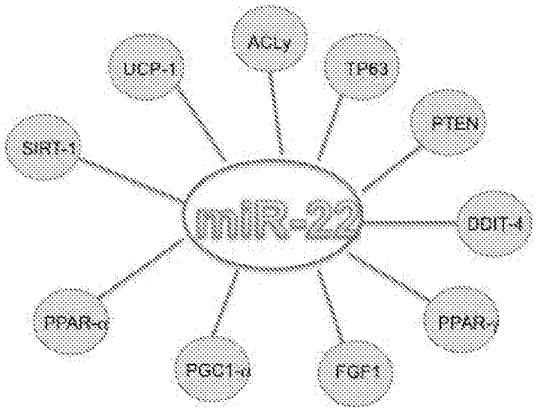


FIGURE 27

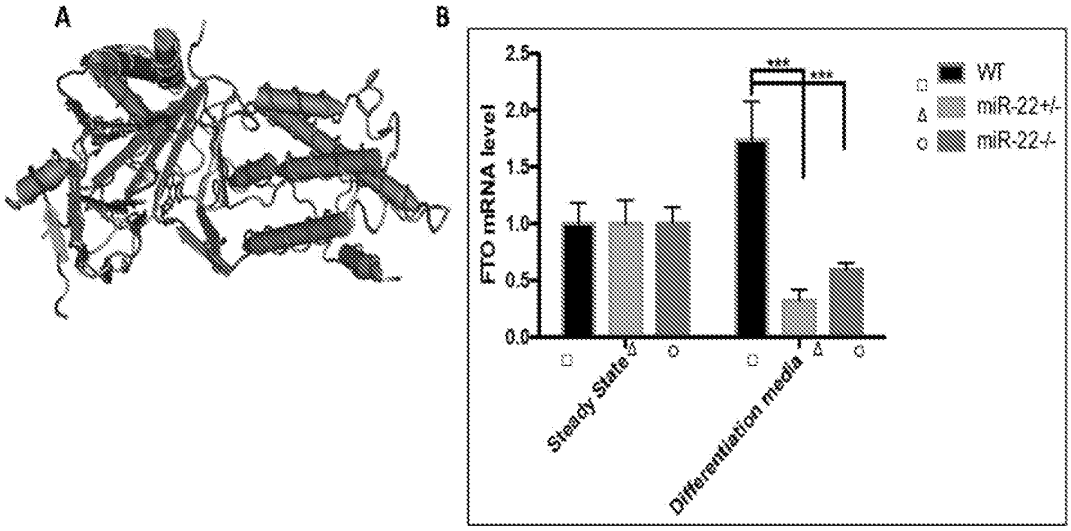
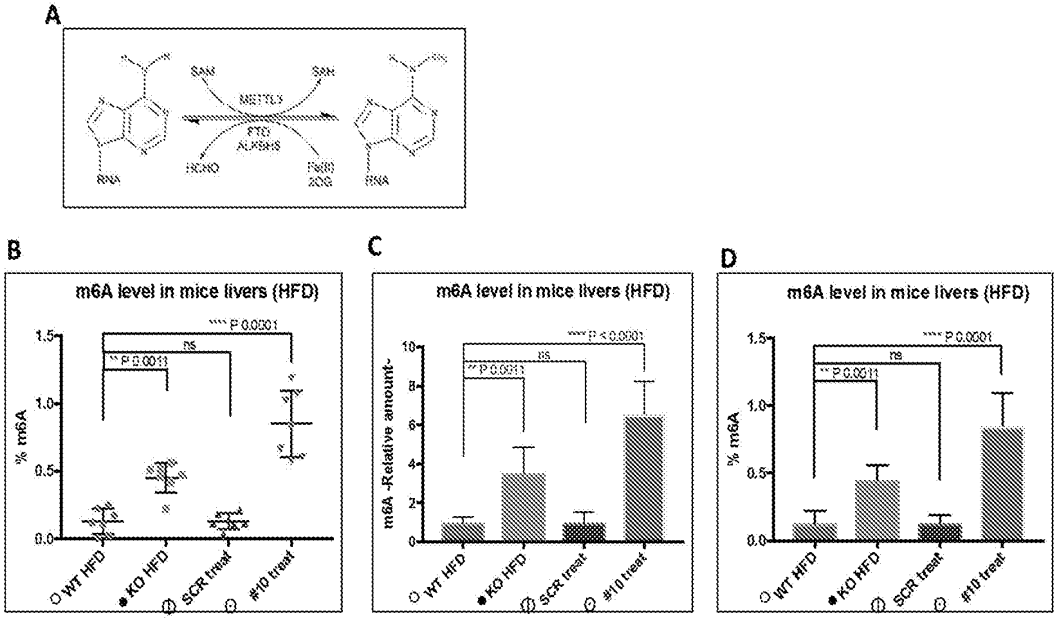


FIGURE 28



RNA from Liver (n=7)
Colorimetric assay

FIGURE 29

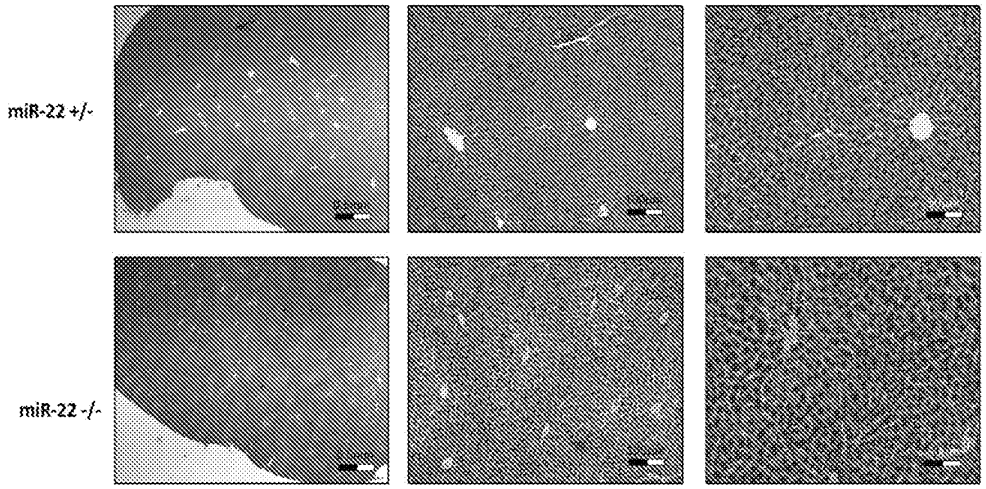


FIGURE 30

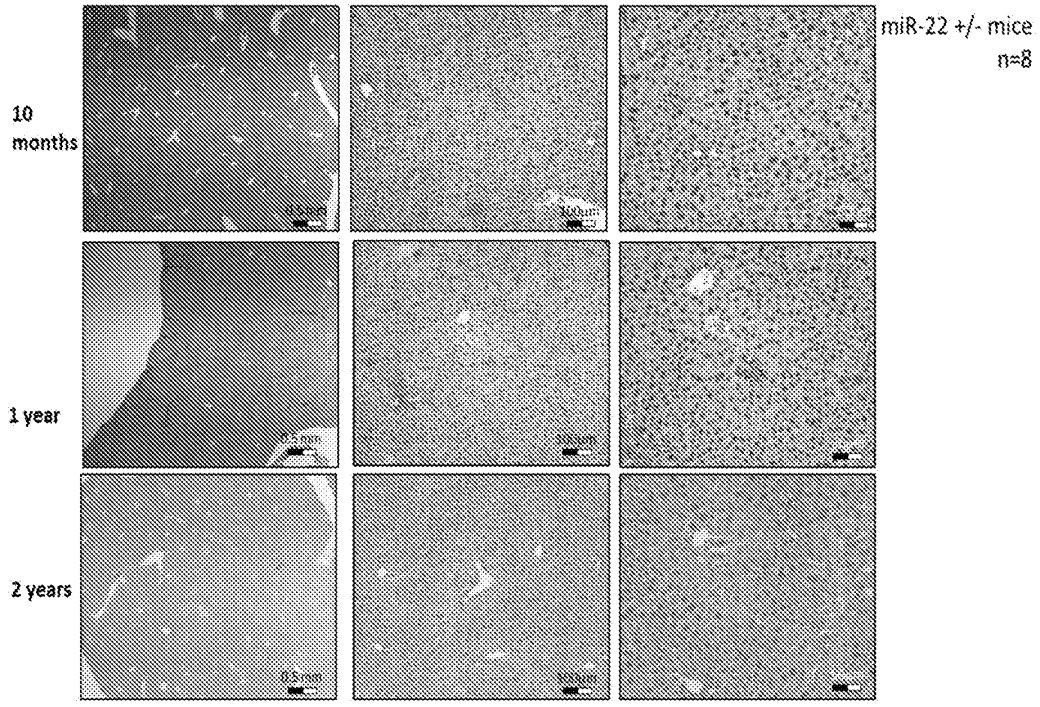


FIGURE 31

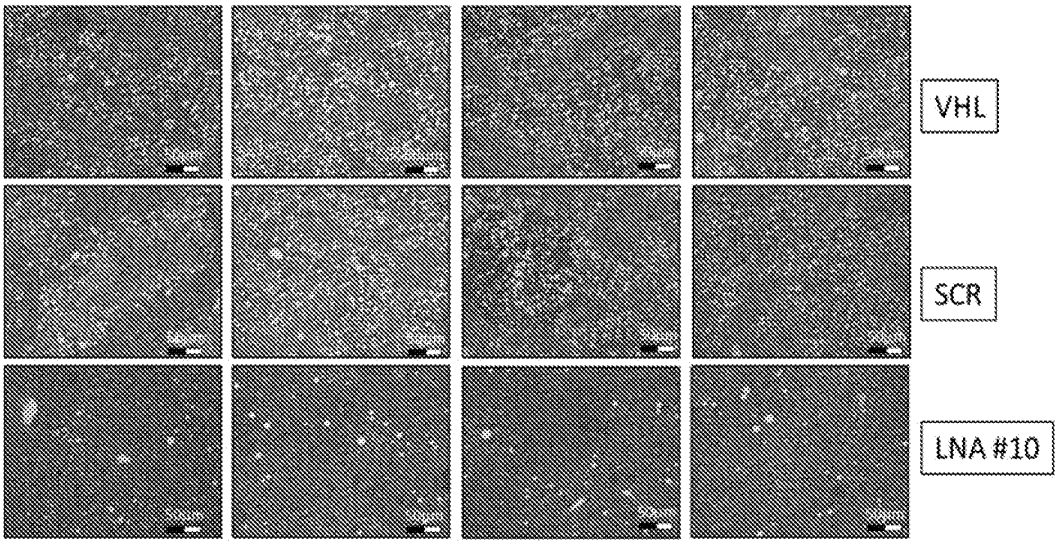


FIGURE 32

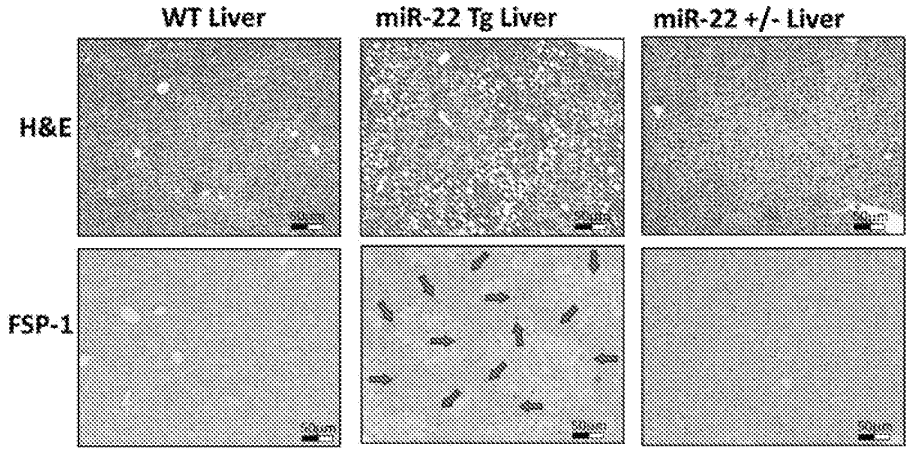


FIGURE 33

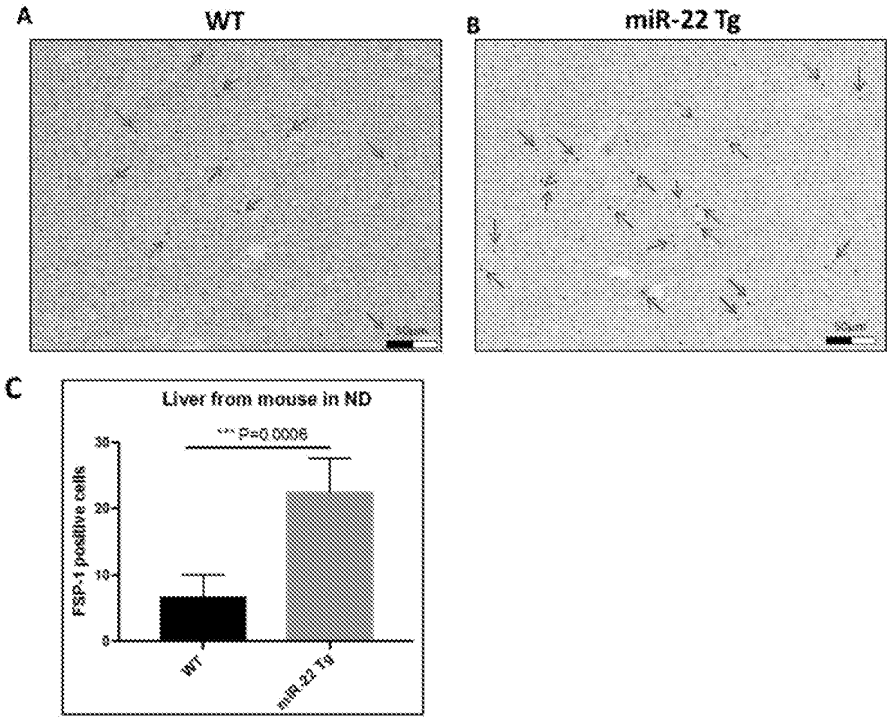


FIGURE 34

