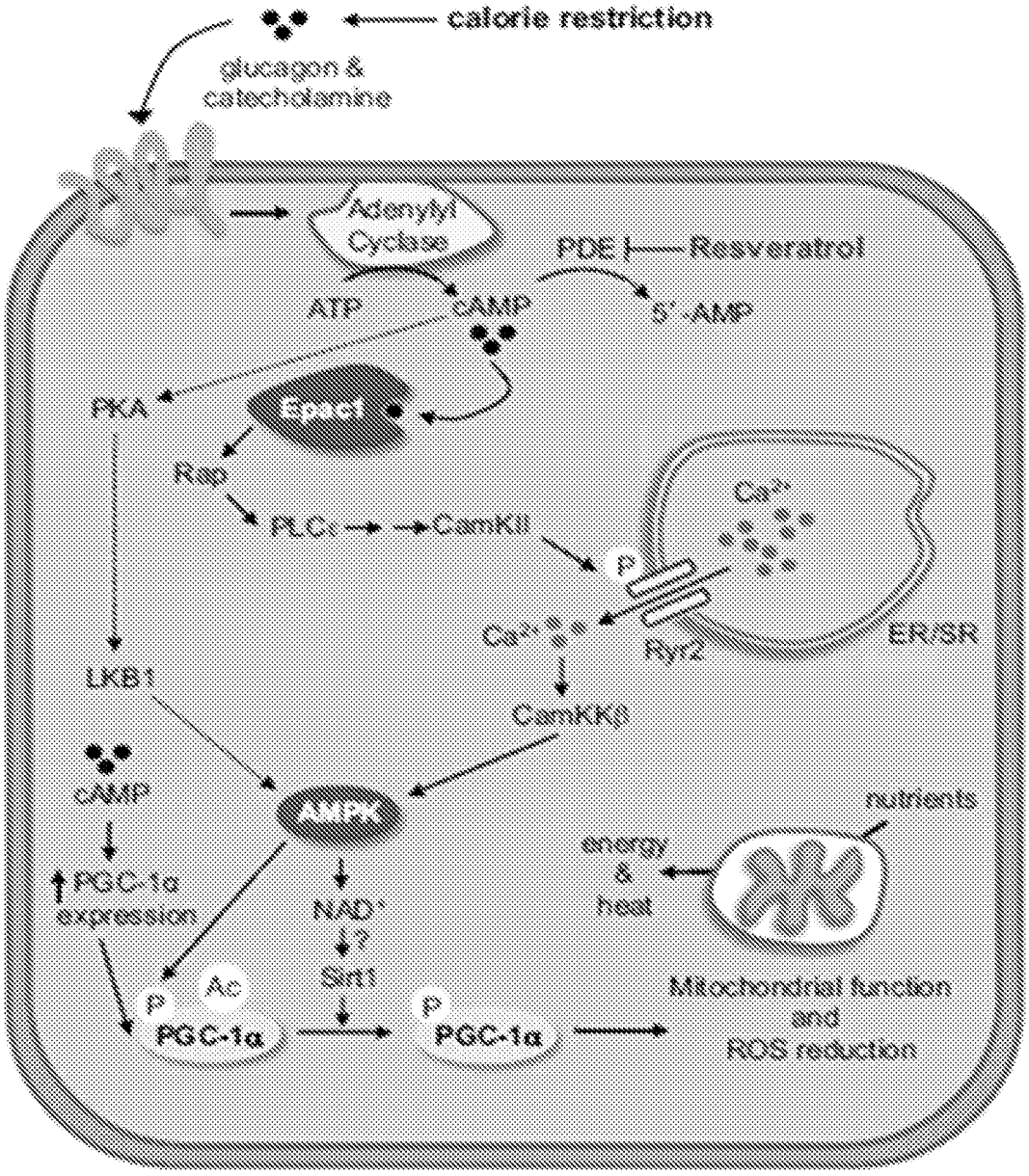

calorie restriction
glucagon &
catecholamine
Adenylyl
Cyclase
PDE
Resveratrol
ATP
cAMP
5'-AMP
PKA
Epac1
Rap
PLCε
CamKII
P
Ca2+
Ca2+
Ryr2
ER/SR
LKB1
CamKKβ
cAMP
AMPK
nutrients
energy
&
heat
PGC-1α
expression
NAD+
Sirt1
P
Ac
PGC-1α
P
PGC-1α
Mitochondrial function
and
ROS reduction

FIG. 1

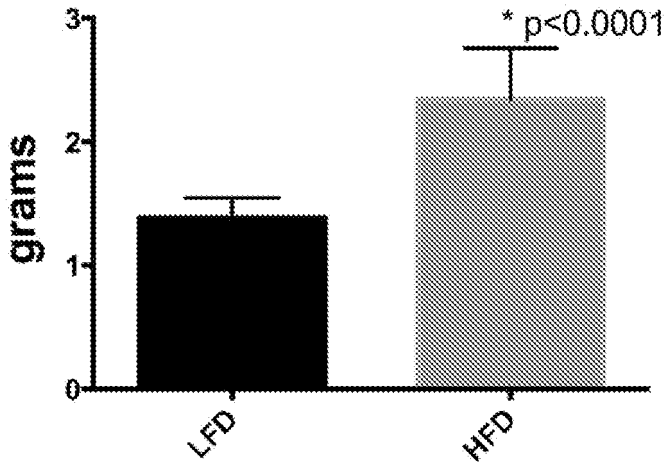

* p<0.0001
grams
3
2
1
0
LFD
HFD

FIG. 2

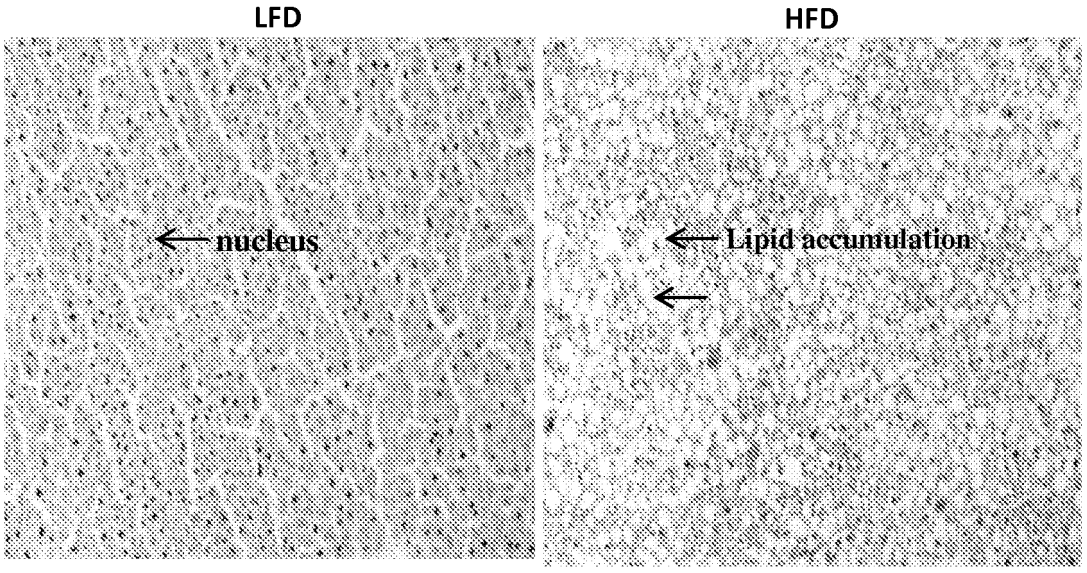

LFD
HFD
nucleus
Lipid accumulation

FIG. 3

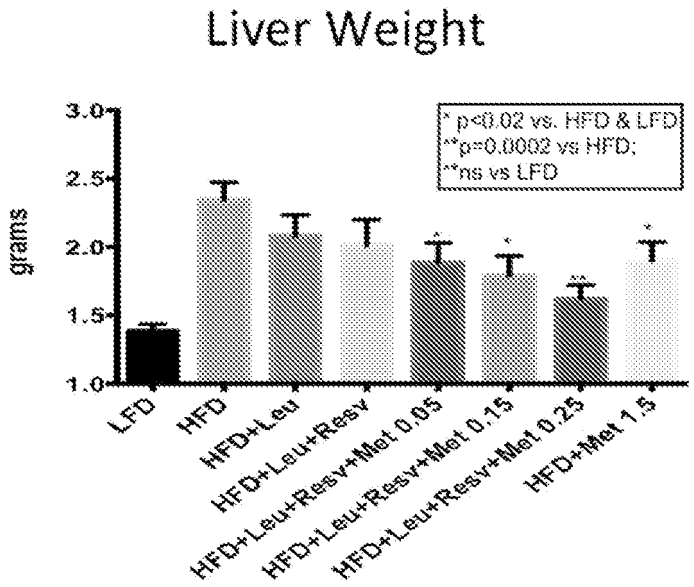

Liver Weight
* p<0.02 vs. HFD & LFD
**p=0.0002 vs HFD;
***ns vs LFD
grams
3.0
2.5
2.0
1.5
1.0
LFD
HFD
HFD+Leu
HFD+Leu+Resv
HFD+Leu+Resv+Met 0.05
HFD+Leu+Resv+Met 0.15
HFD+Leu+Resv+Met 0.25
HFD+Met 1.5

FIG. 4

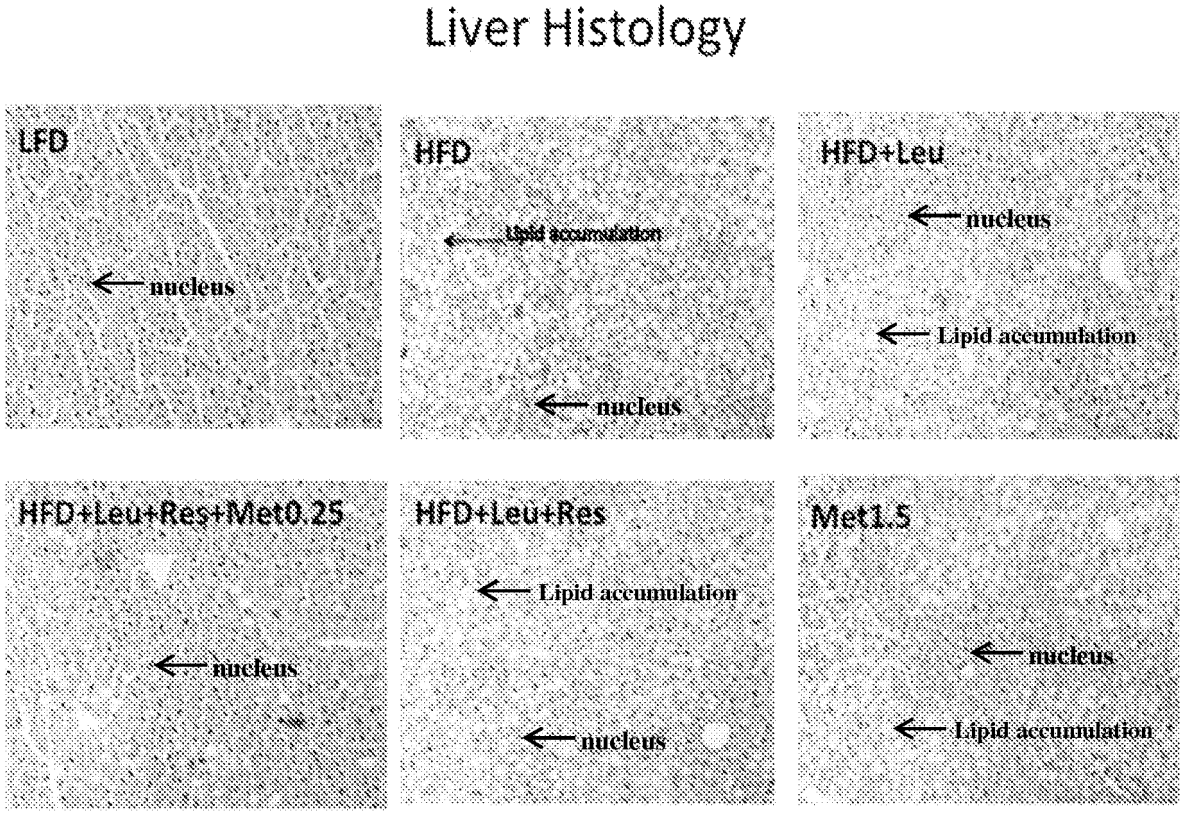

Liver Histology
LFD
nucleus
HFD
Lipid accumulation
nucleus
HFD+Leu
nucleus
Lipid accumulation
HFD+Leu+Res+Met0.25
nucleus
HFD+Leu+Res
Lipid accumulation
nucleus
Met1.5
nucleus
Lipid accumulation

FIG. 5

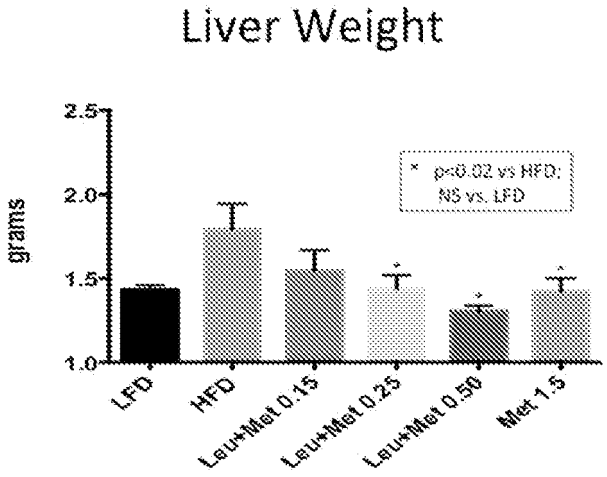

Liver Weight
grams
2.5
2.0
1.5
1.0
* p<0.02 vs HFD;
NS vs. LFD
LFD
HFD
Leu+Met 0.15
Leu+Met 0.25
Leu+Met 0.50
Met 1.5

FIG. 6

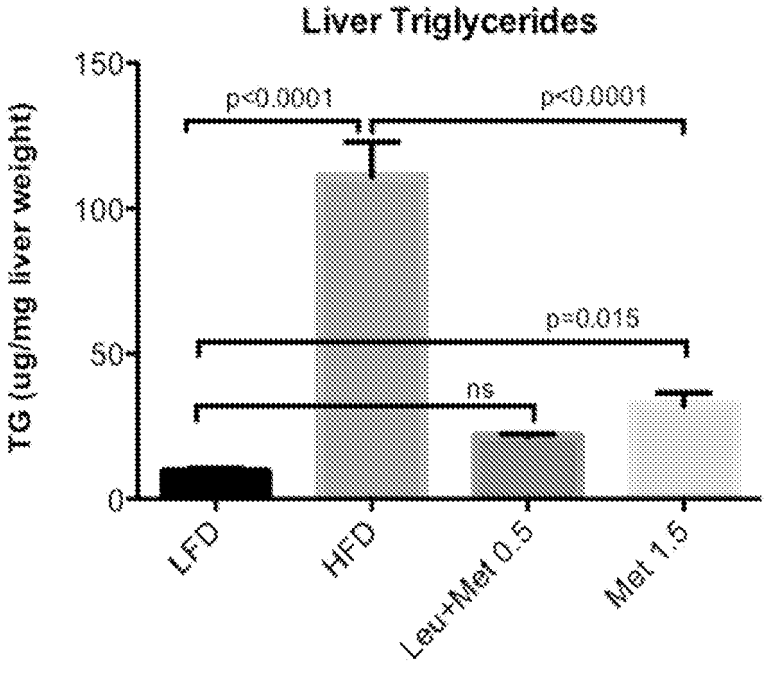

Liver Triglycerides
TG (ug/mg liver weight)
150
100
50
0
p<0.0001
p<0.0001
p=0.015
ns
LFD
HFD
Leu+Met 0.5
Met 1.5

FIG. 7

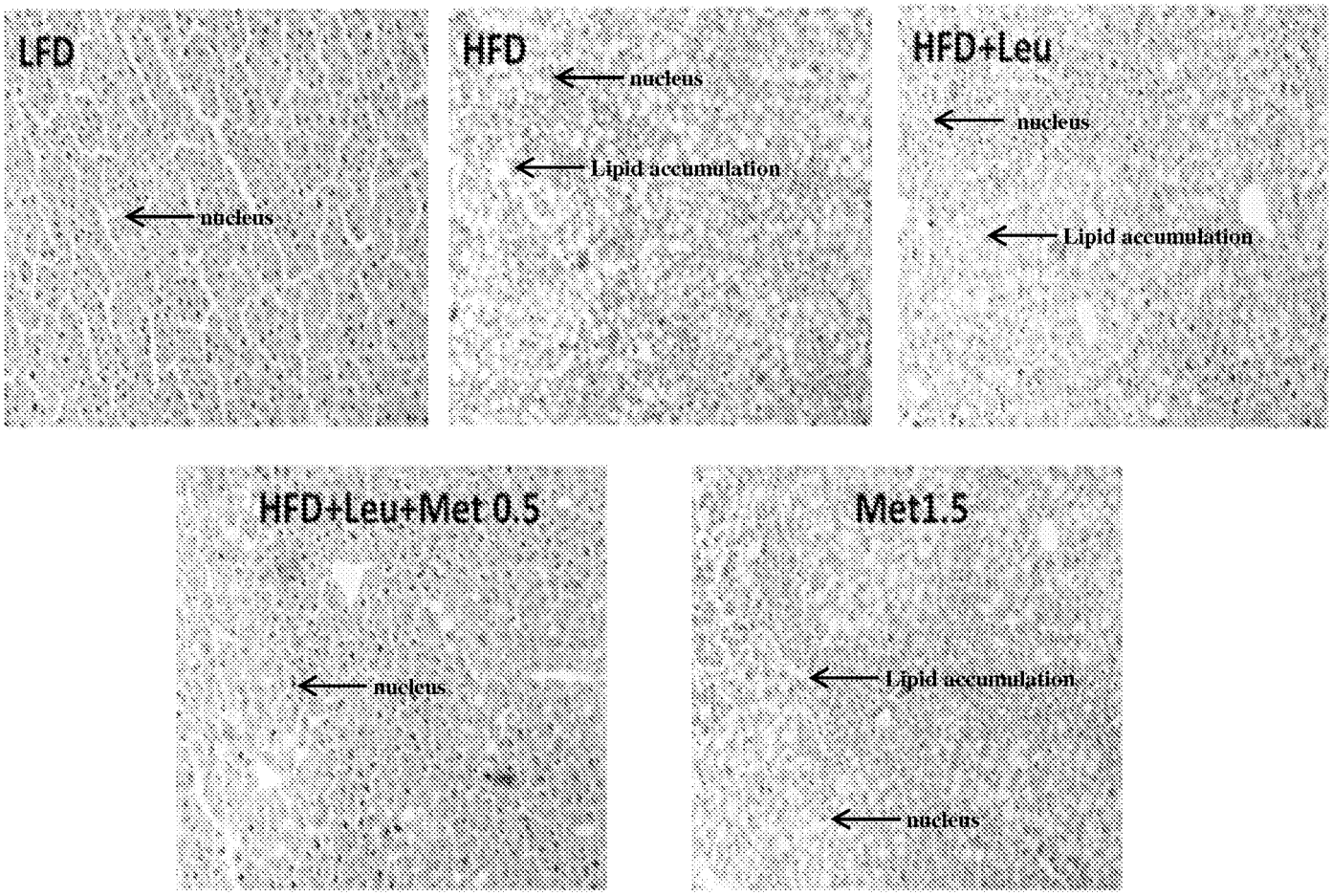

LFD
nucleus
HFD
nucleus
Lipid accumulation
HFD+Leu
nucleus
Lipid accumulation
HFD+Leu+Met 0.5
nucleus
Met1.5
Lipid accumulation
nucleus

FIG. 8

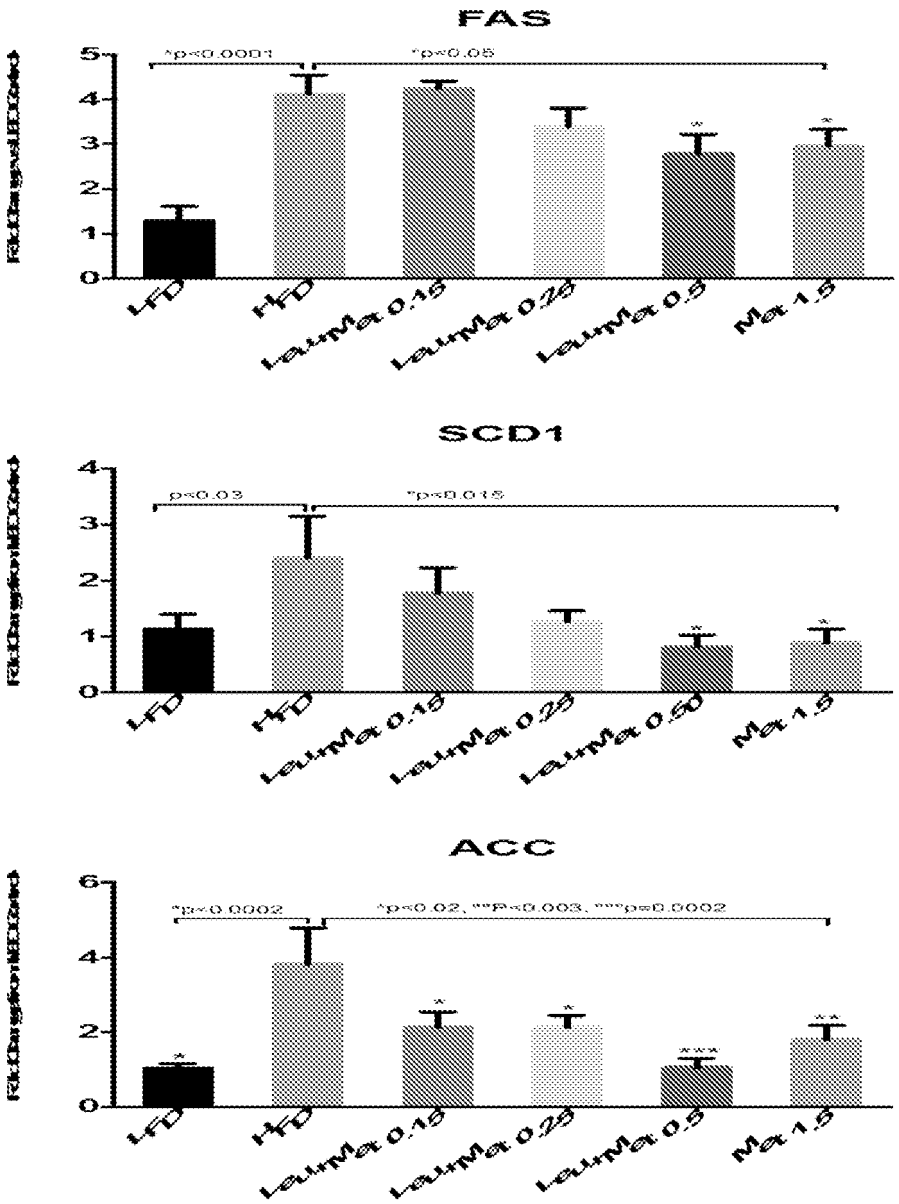


FIG. 9

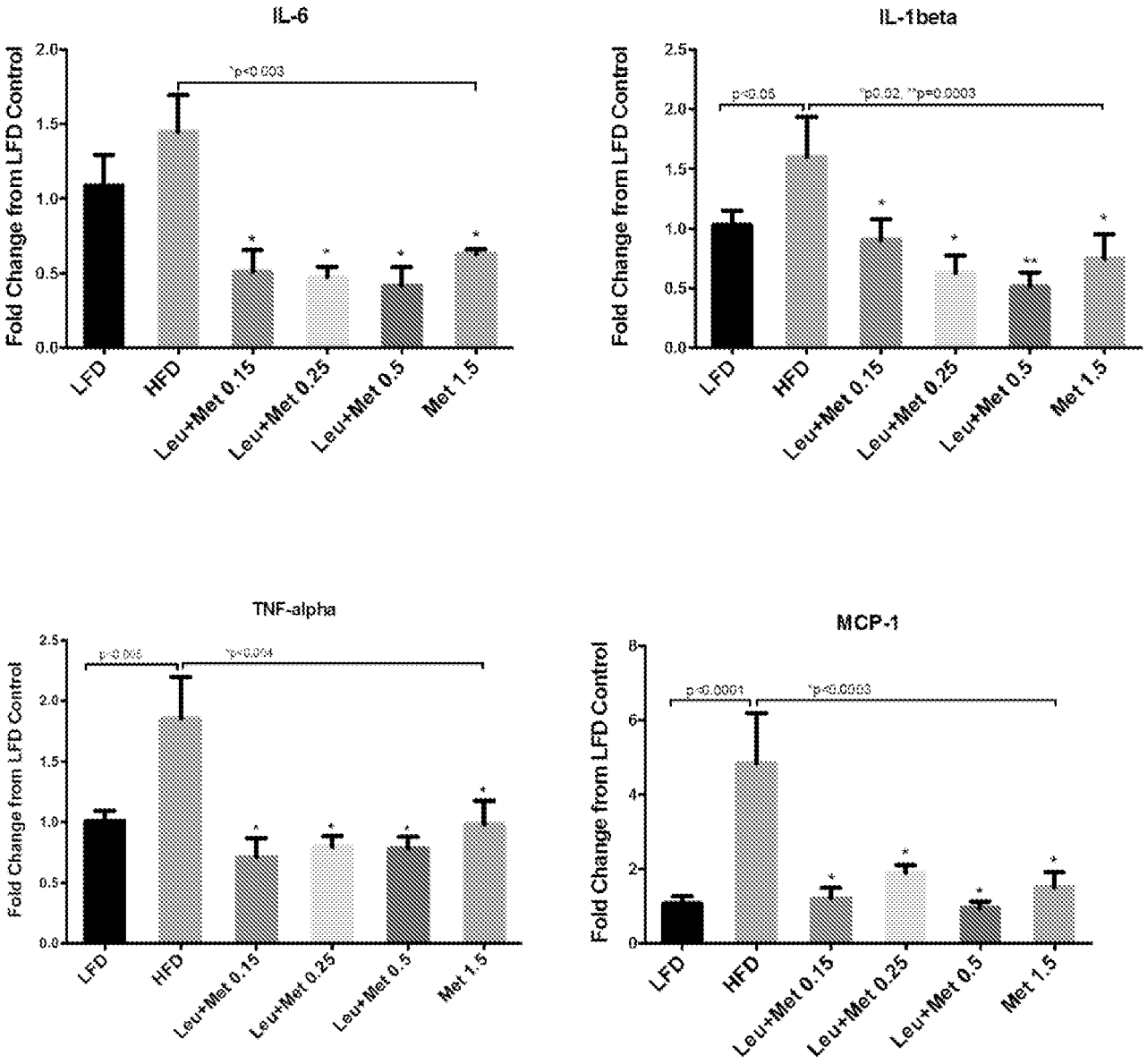

IL-6
Fold Change from LFD Control
*p<0.003
LFD
HFD
Leu+Met 0.15
Leu+Met 0.25
Leu+Met 0.5
Met 1.5
IL-1beta
Fold Change from LFD Control
p<0.05
*p0.02, **p=0.0003
LFD
HFD
Leu+Met 0.15
Leu+Met 0.25
Leu+Met 0.5
Met 1.5
TNF-alpha
Fold Change from LFD Control
p<0.005
*p<0.004
LFD
HFD
Leu+Met 0.15
Leu+Met 0.25
Leu+Met 0.5
Met 1.5
MCP-1
Fold Change from LFD Control
p<0.0001
*p<0.0003
LFD
HFD
Leu+Met 0.15
Leu+Met 0.25
Leu+Met 0.5
Met 1.5

FIG. 10

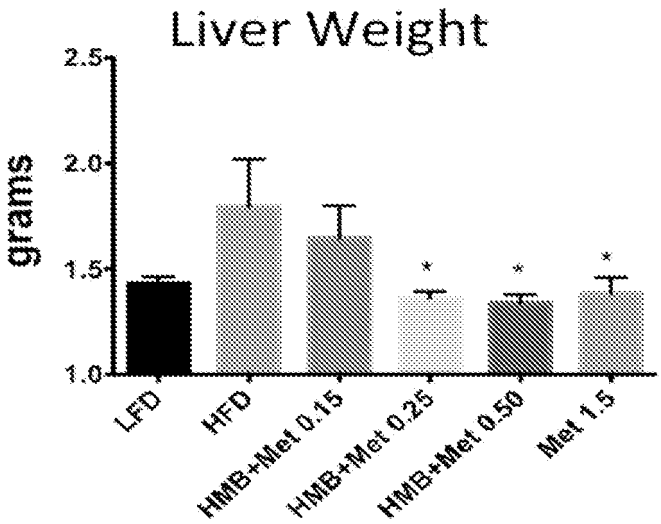

Liver Weight
grams
2.5
2.0
1.5
1.0
LFD
HFD
HMB+Met 0.15
HMB+Met 0.25
HMB+Met 0.50
Met 1.5

FIG. 11

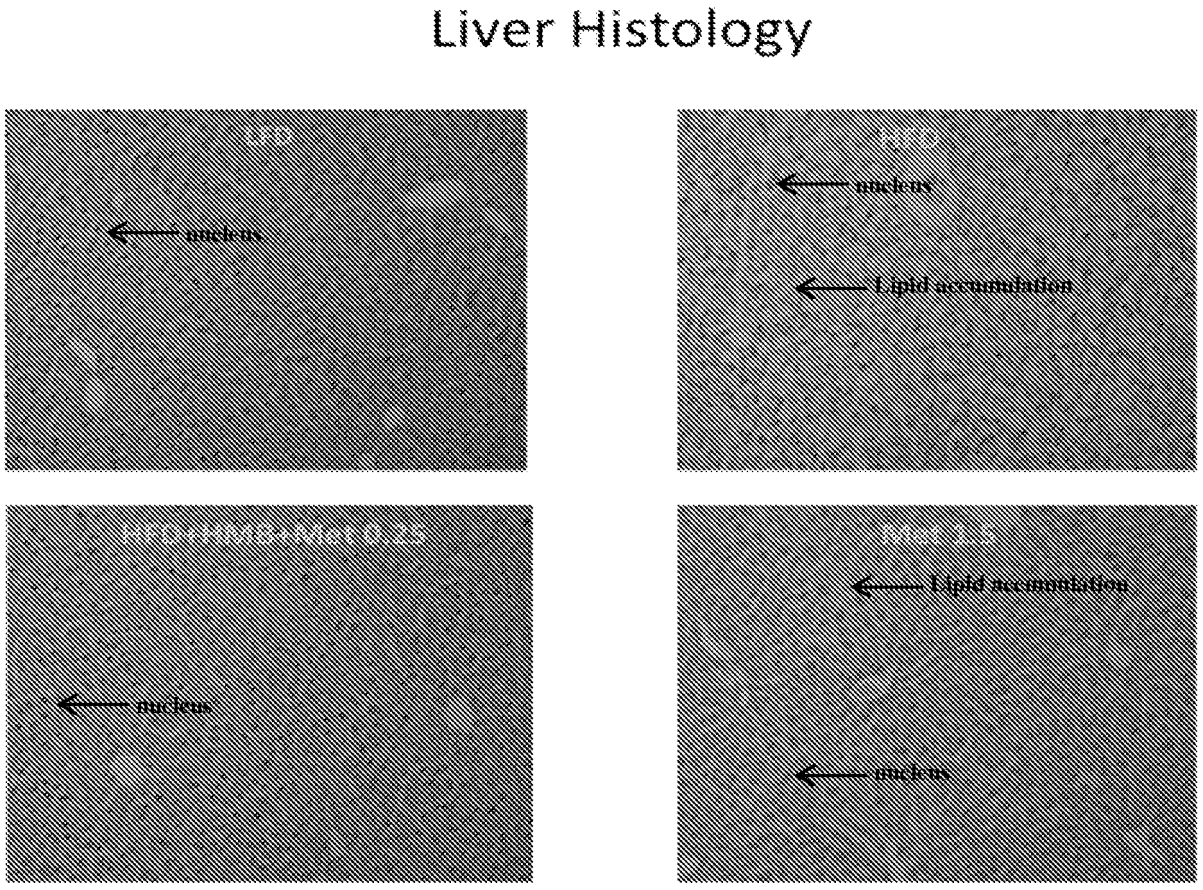

Liver Histology
nucleus
nucleus
Lipid accumulation
nucleus
Lipid accumulation
nucleus

FIG. 12

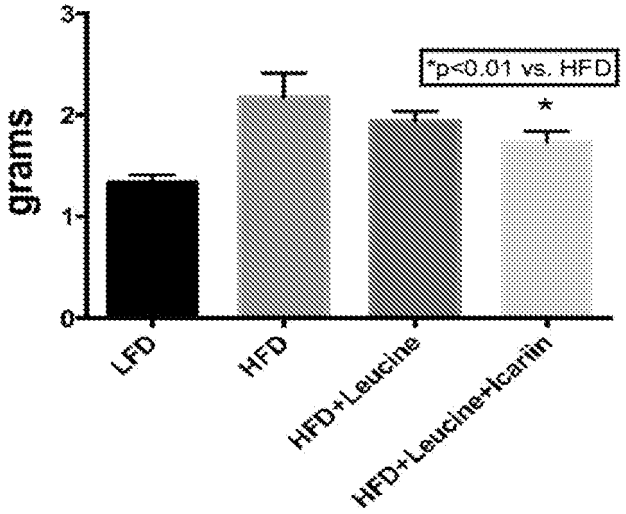

grams
3
2
1
0
*p<0.01 vs. HFD
*
LFD
HFD
HFD+Leucine
HFD+Leucine+Icariin

FIG. 13

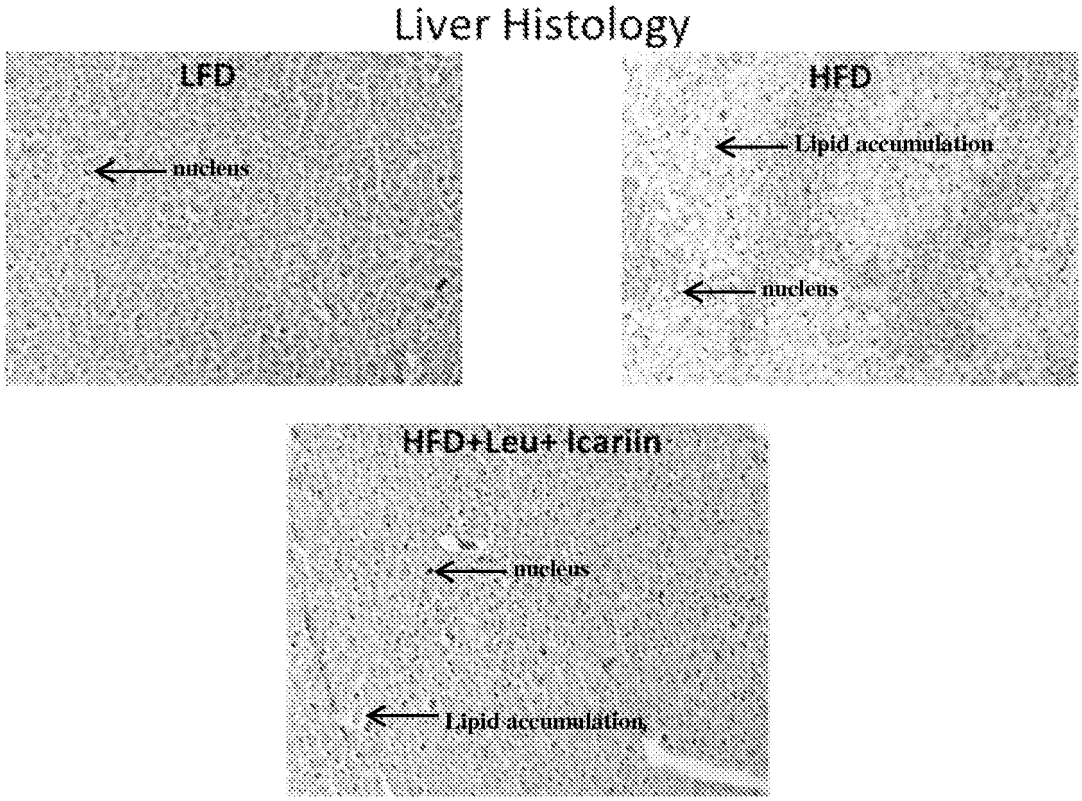

Liver Histology
LFD
nucleus
HFD
Lipid accumulation
nucleus
HFD+Leu+ Icariin
nucleus
Lipid accumulation

FIG. 14

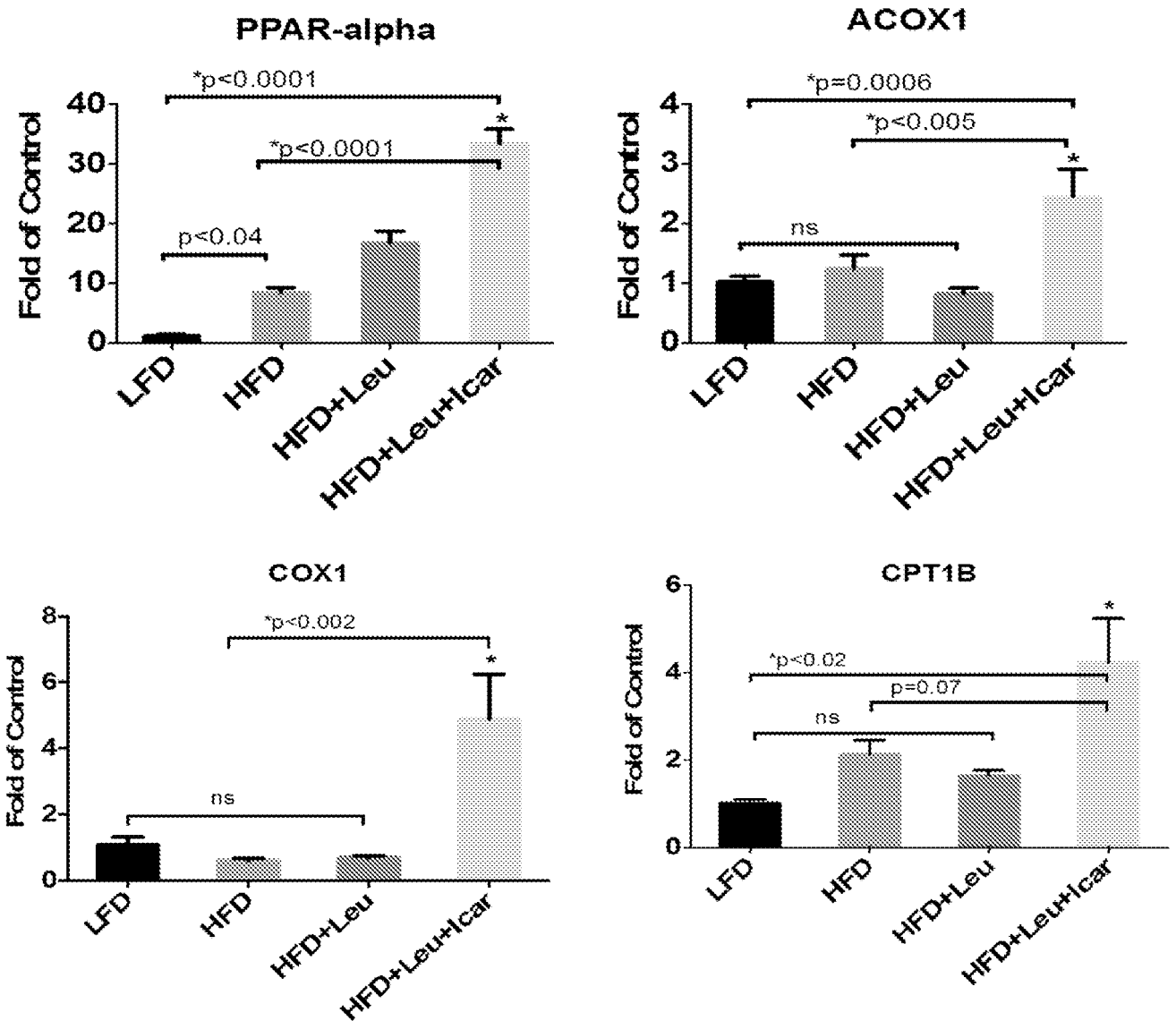

PPAR-alpha
*p<0.0001
*p<0.0001
p<0.04
Fold of Control
40
30
20
10
0
LFD
HFD
HFD+Leu
HFD+Leu+Icar
ACOX1
*p=0.0006
*p<0.005
ns
Fold of Control
4
3
2
1
0
LFD
HFD
HFD+Leu
HFD+Leu+Icar
COX1
*p<0.002
ns
Fold of Control
8
6
4
2
0
LFD
HFD
HFD+Leu
HFD+Leu+Icar
CPT1B
*p<0.02
p=0.07
ns
Fold of Control
6
4
2
0
LFD
HFD
HFD+Leu
HFD+Leu+Icar

FIG. 15

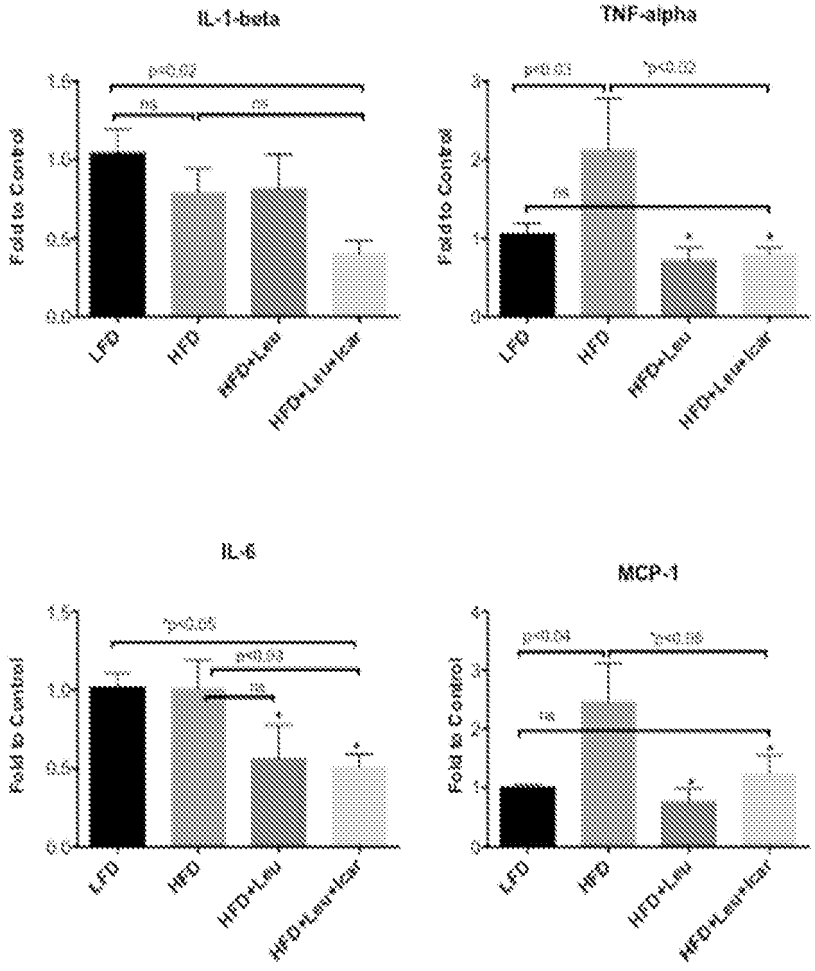

IL-1-beta
TNF-alpha
IL-6
MCP-1
Fold to Control
LFD
HFD
HFD+Leu
HFD+Leu+Icar

FIG. 16

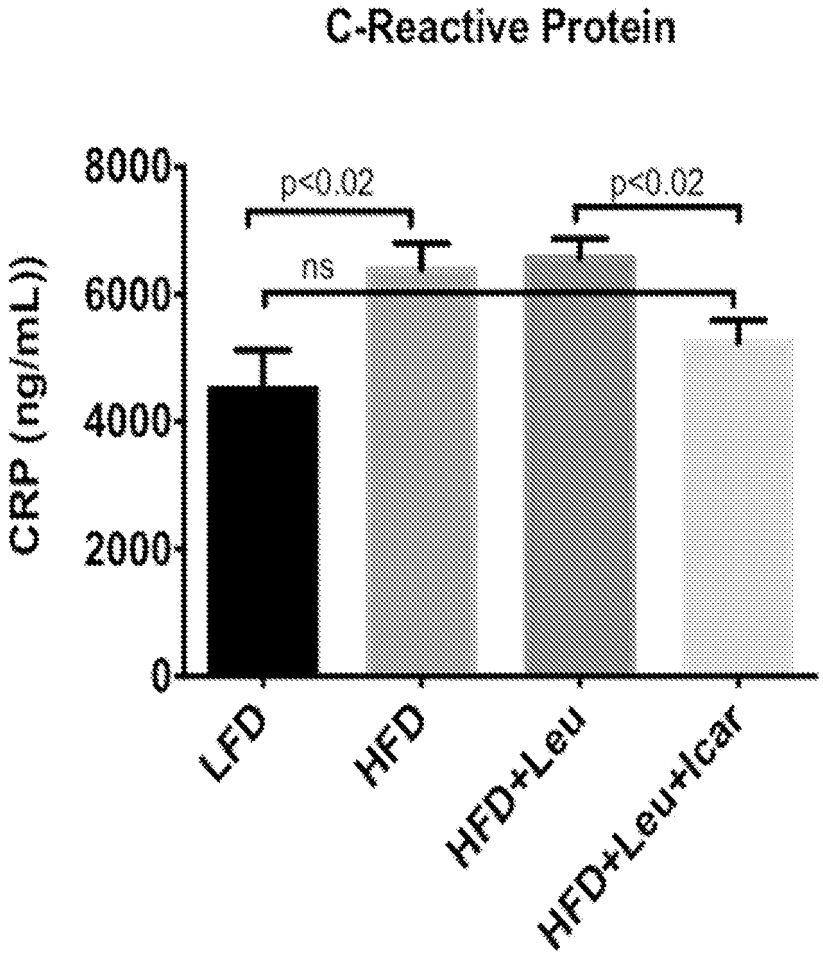

C-Reactive Protein
CRP (ng/mL))
8000
6000
4000
2000
0
p<0.02
p<0.02
ns
LFD
HFD
HFD+Leu
HFD+Leu+Icar

FIG. 17

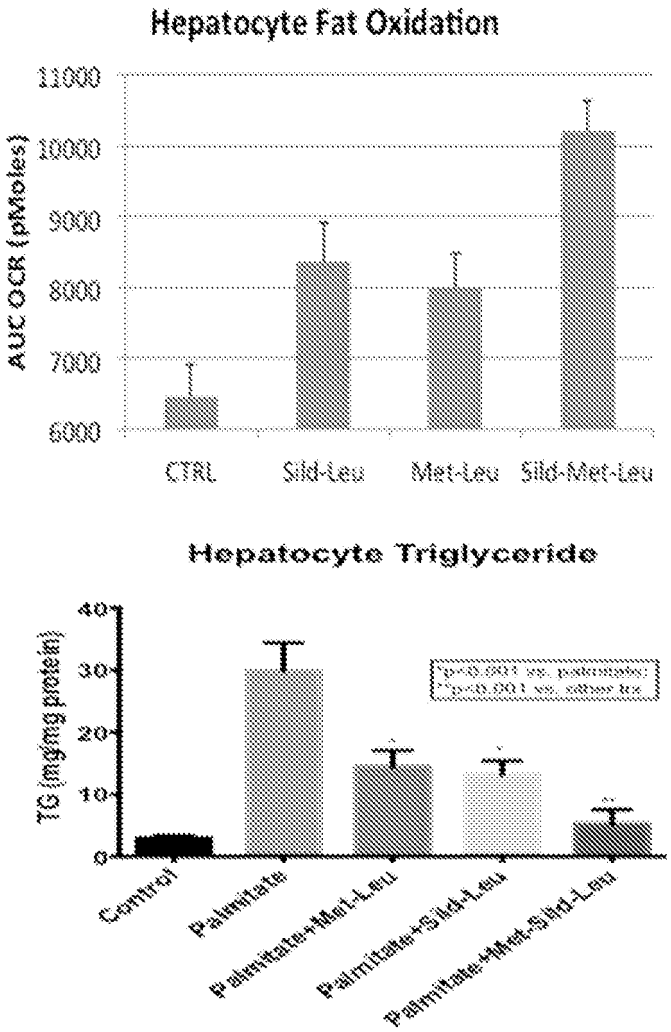

Hepatocyte Fat Oxidation
AUC OCR (pMoles)
11000
10000
9000
8000
7000
6000
CTRL
Sild-Leu
Met-Leu
Sild-Met-Leu
Hepatocyte Triglyceride
TG (mg/mg protein)
40
30
20
10
0
Control
Palmitate
Palmitate+Met-Leu
Palmitate+Sild-Leu
Palmitate+Met-Sild-Leu

FIG. 18

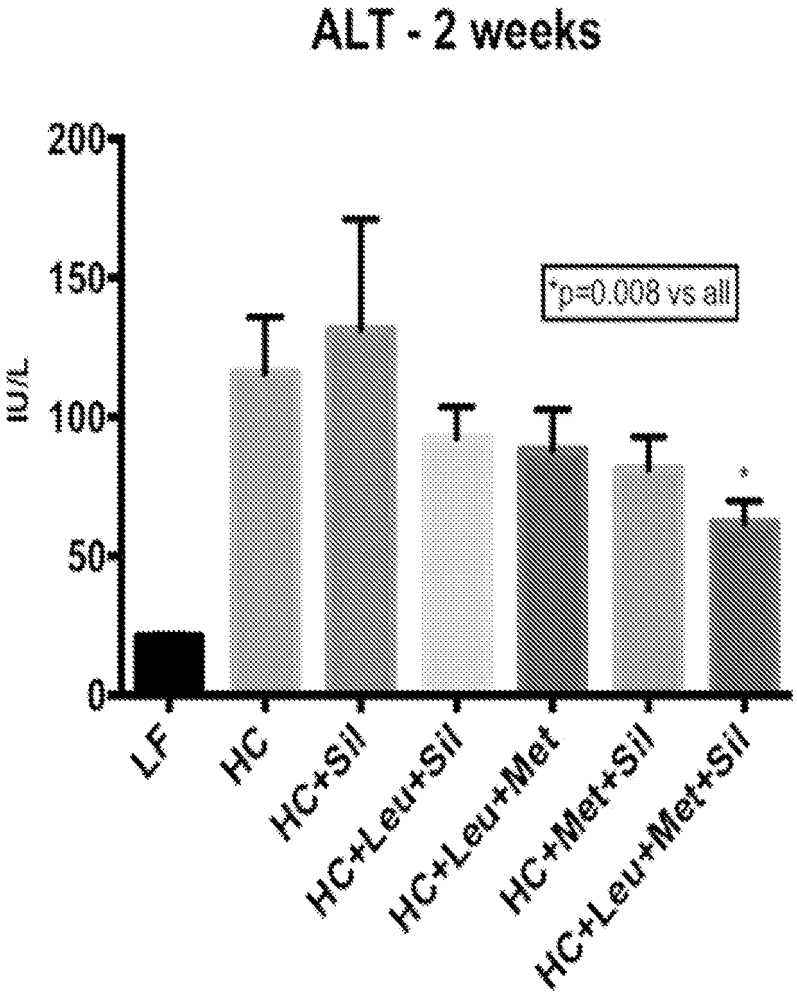

ALT - 2 weeks
IU/L
200
150
100
50
0
*p=0.008 vs all
*
LF
HC
HC+Sil
HC+Leu+Sil
HC+Leu+Met
HC+Met+Sil
HC+Leu+Met+Sil

FIG. 19

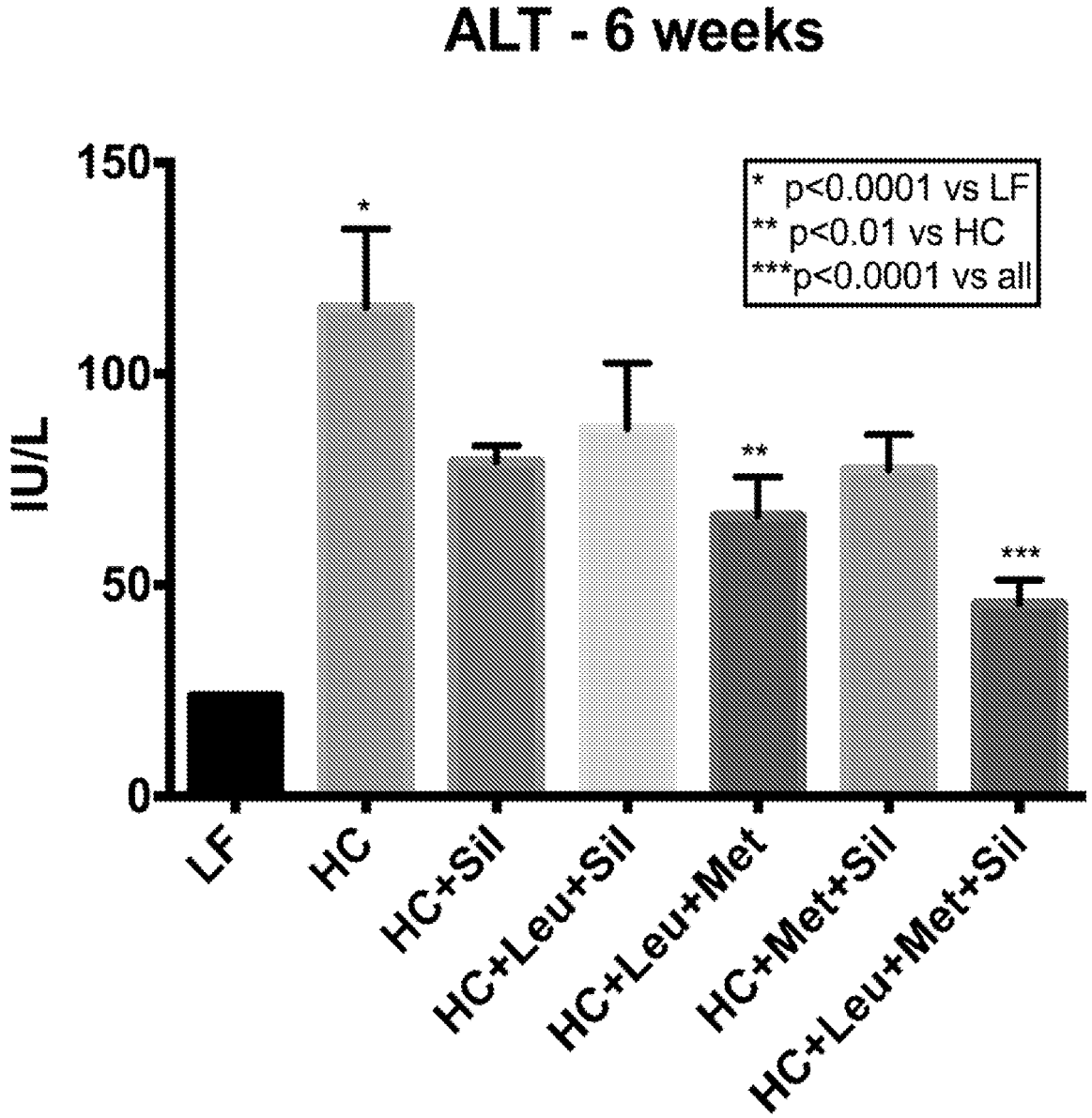

ALT - 6 weeks
IU/L
150
100
50
0
* p<0.0001 vs LF
** p<0.01 vs HC
***p<0.0001 vs all
*
**
***
LF
HC
HC+Sil
HC+Leu+Sil
HC+Leu+Met
HC+Met+Sil
HC+Leu+Met+Sil

FIG. 20

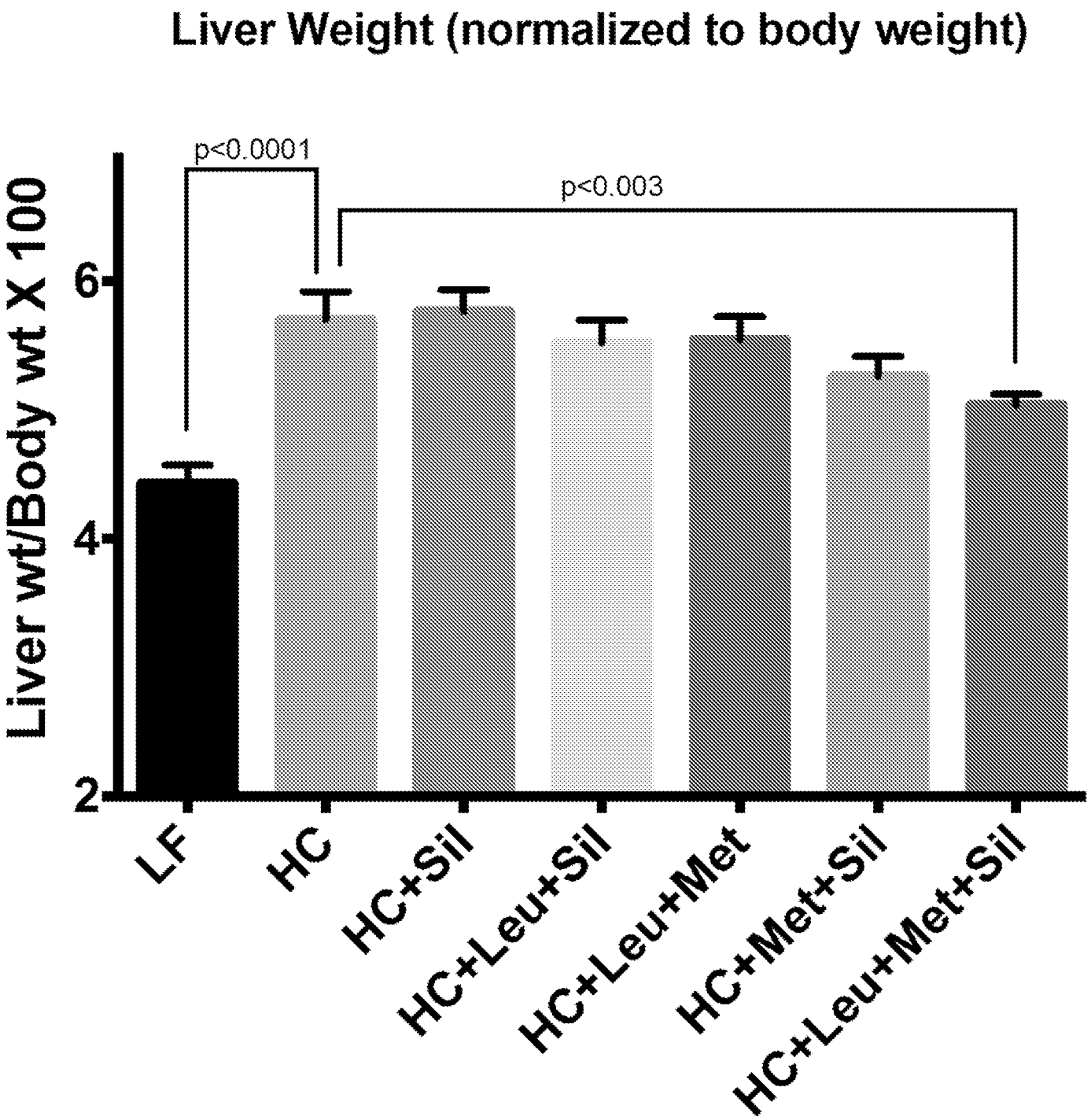

Liver Weight (normalized to body weight)
Liver wt/Body wt X 100
2
4
6
p<0.0001
p<0.003
LF
HC
HC+Sil
HC+Leu+Sil
HC+Leu+Met
HC+Met+Sil
HC+Leu+Met+Sil

FIG. 21