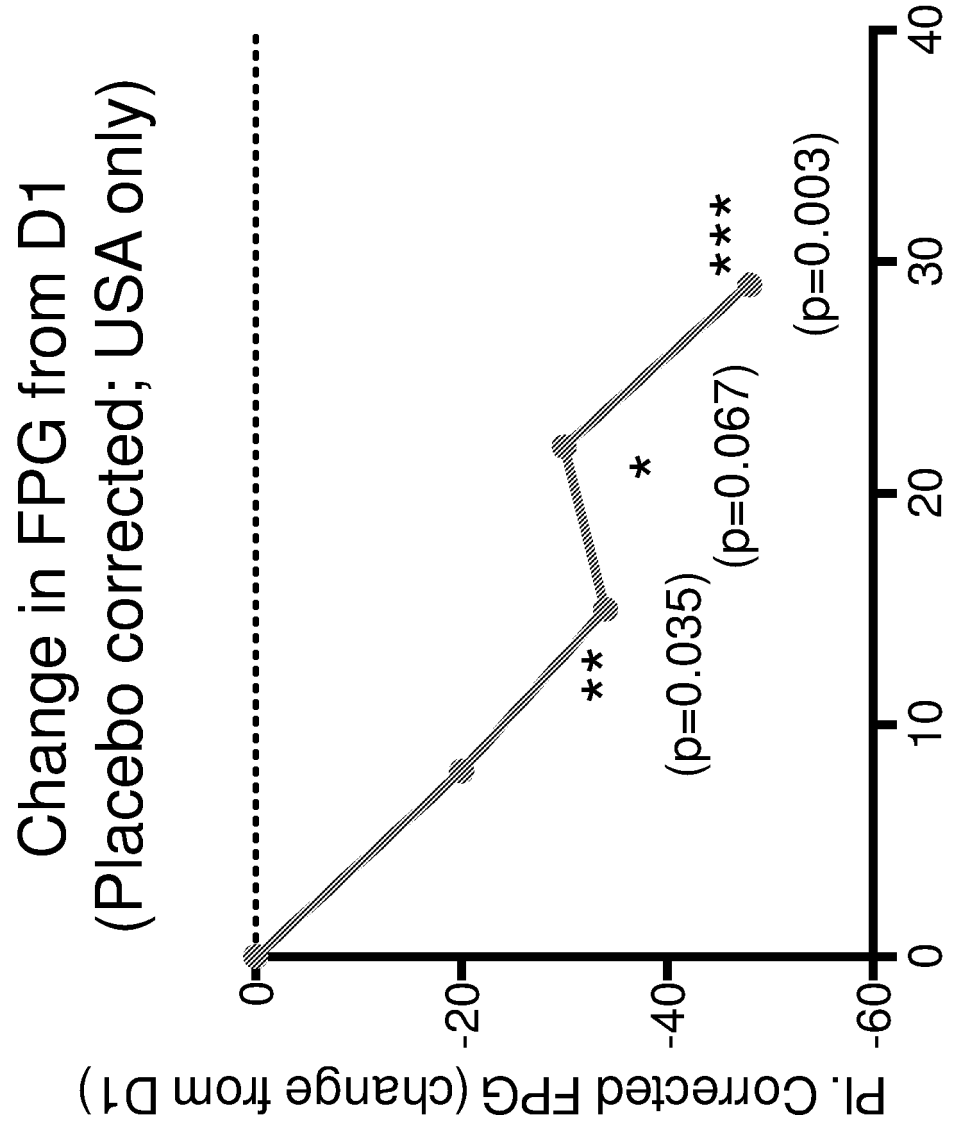

Change in FPG from D1
(Placebo corrected; USA only)
Pl. Corrected FPG (change from D1)
0
-20
-40
-60
0
10
20
30
40
Days on Treatment
**
*
***
(p=0.035)
(p=0.067)
(p=0.003)

Figure 1

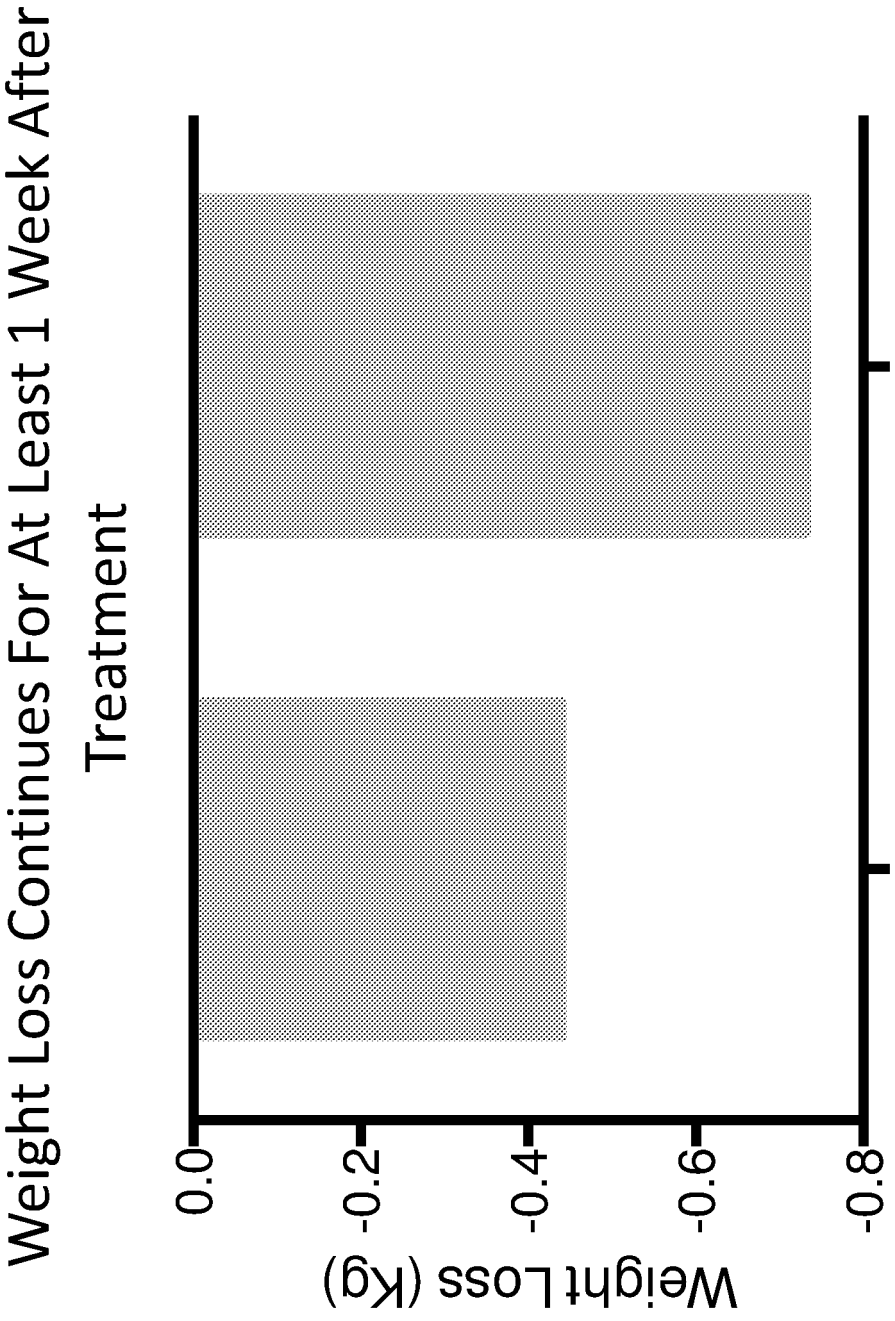

Weight Loss Continues For At Least 1 Week After Treatment
0.0
-0.2
-0.4
-0.6
-0.8
Weight Loss (Kg)
Day 29
Day 36
Days after Start of MLR-1023

Figure 2

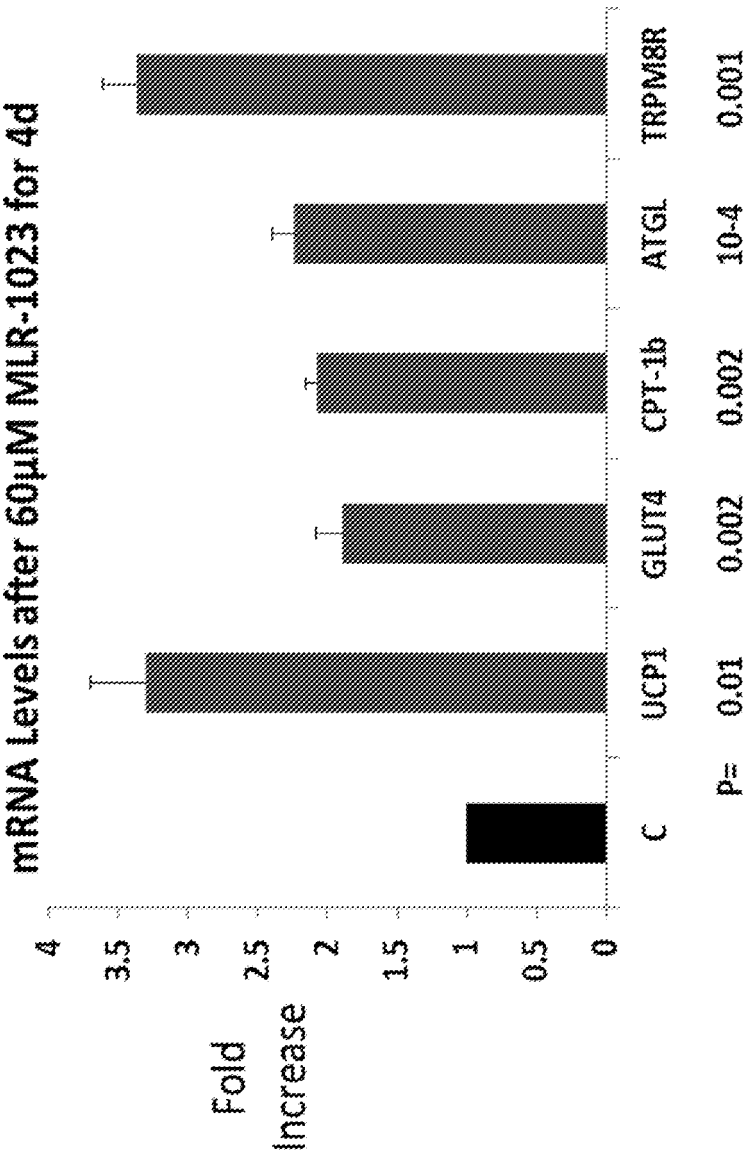

mRNA Levels after 60μM MLR-1023 for 4d
Fold Increase
4
3.5
3
2.5
2
1.5
1
0.5
0
C
UCP1
GLUT4
CPT-1b
ATGL
TRPM8R
P= 0.01 0.002 0.002 10-4 0.001

Figure 3

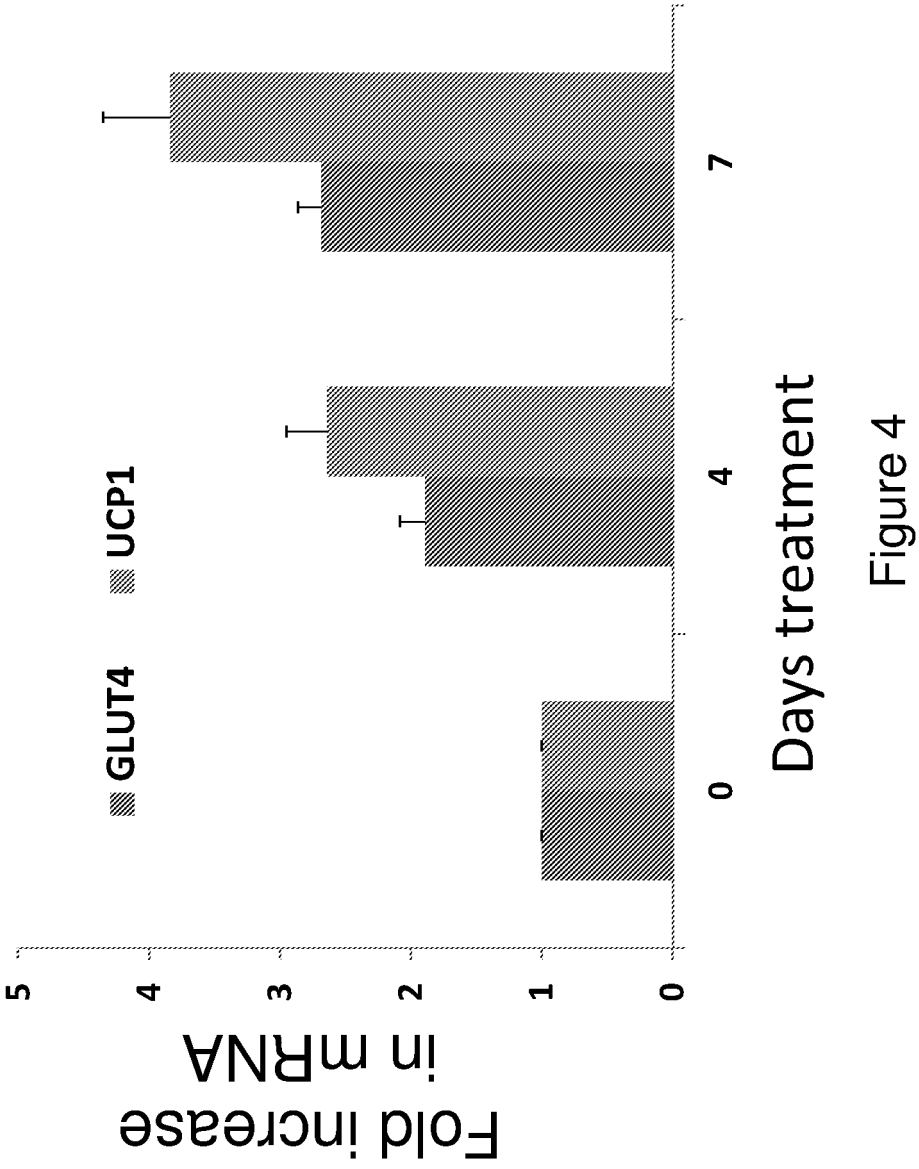


Figure 4

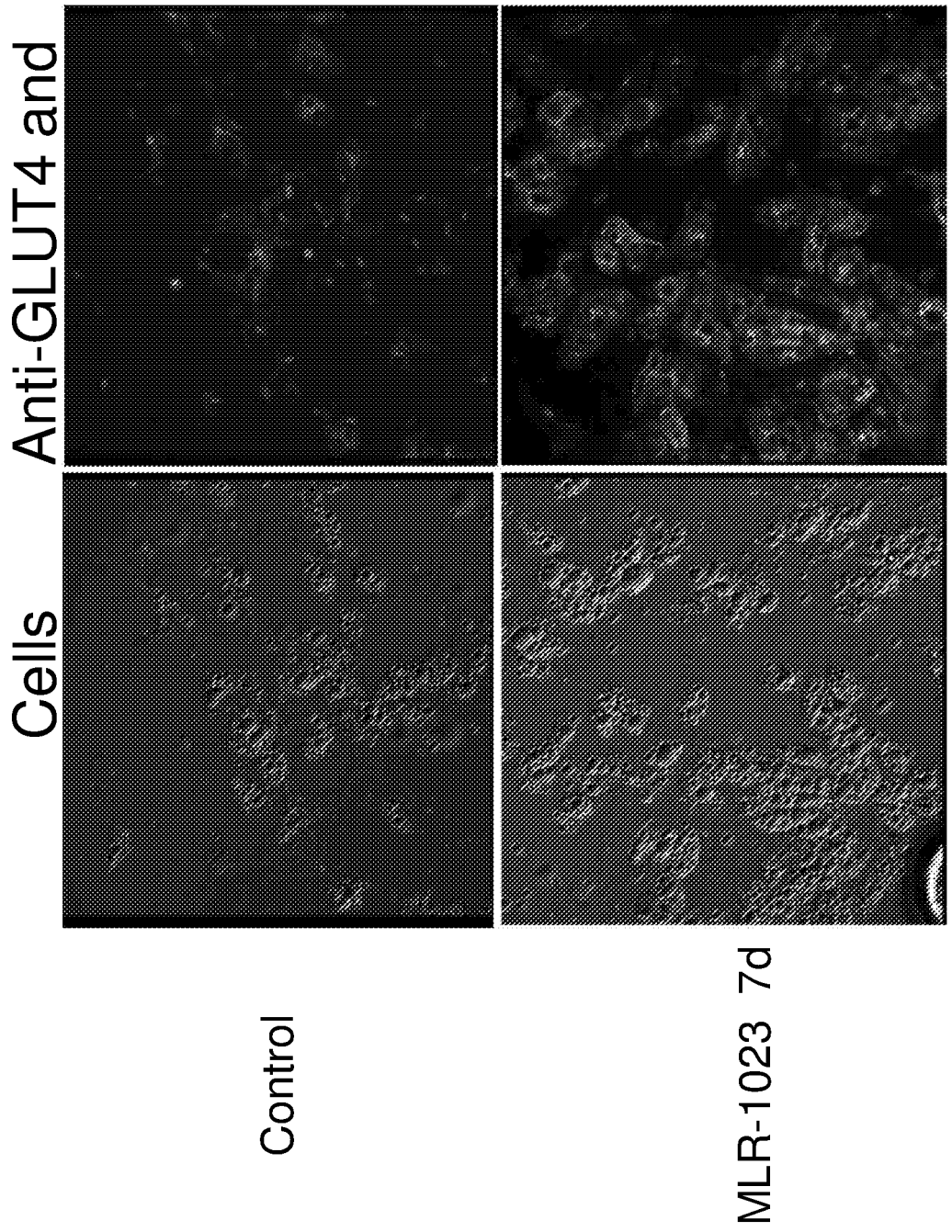


Figure 5

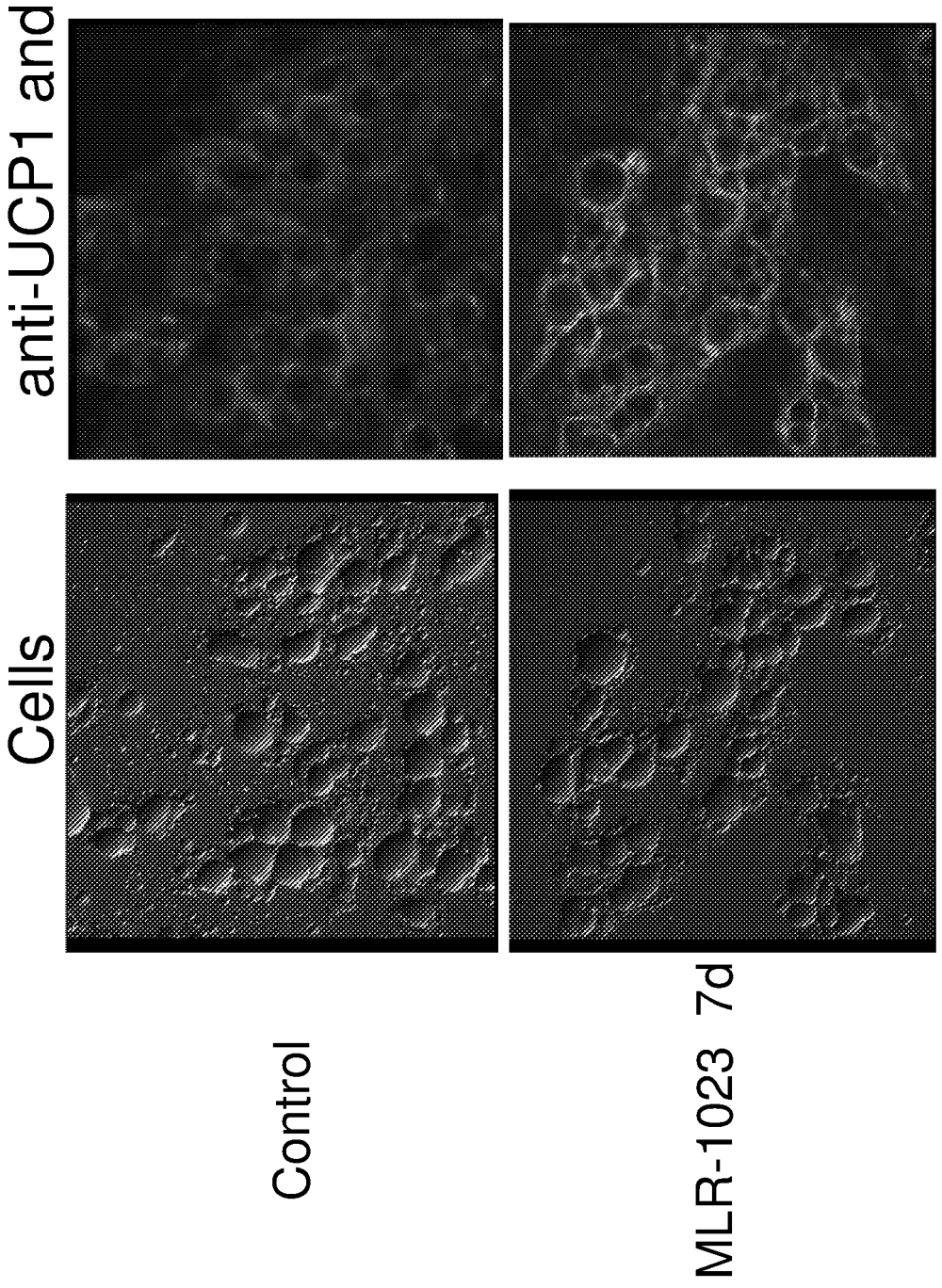


Figure 6

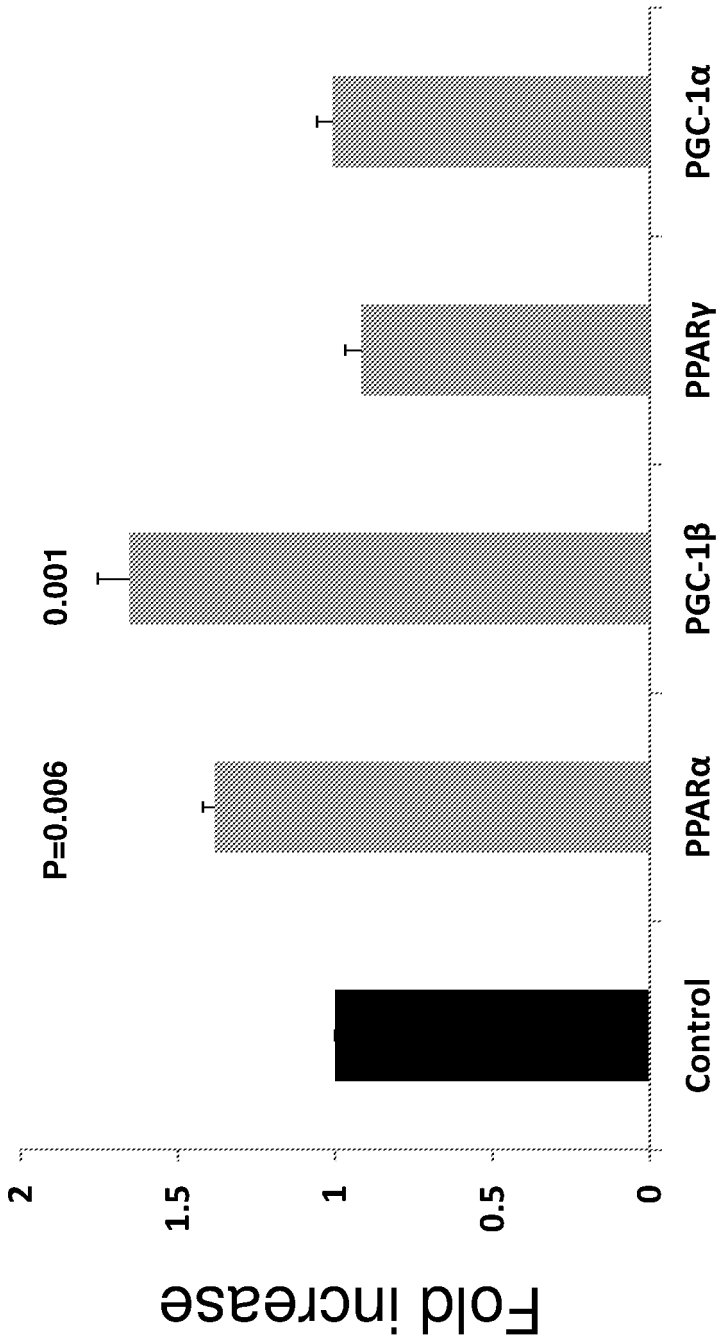

Fold increase
2
1.5
1
0.5
0
Control
PPARα
PGC-1β
PPARγ
PGC-1α
P=0.006
0.001
4 Day Treatment

Figure 7

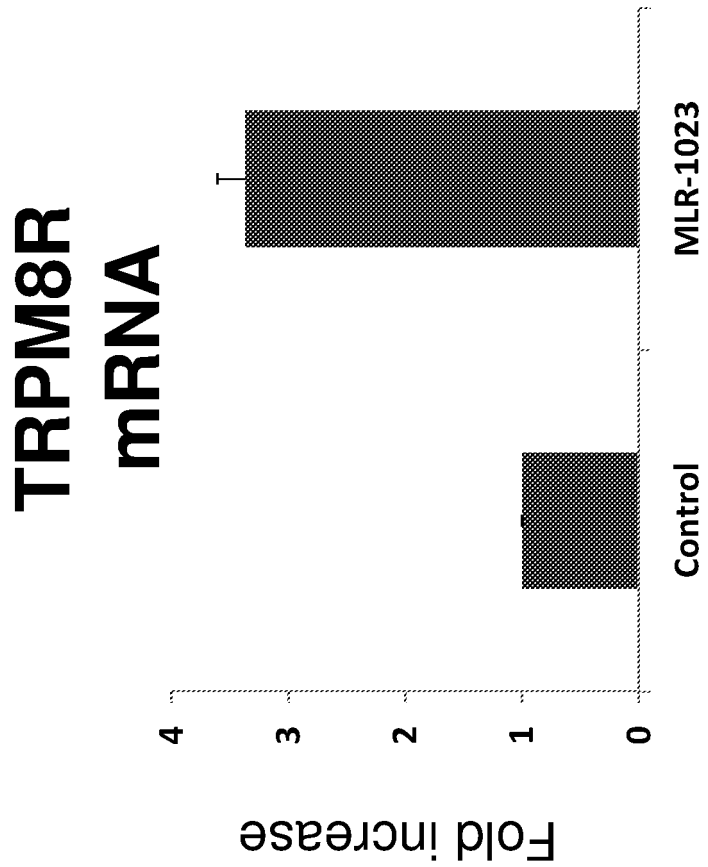

TRPM8R mRNA
Fold increase
4
3
2
1
0
Control
MLR-1023
4 day Treatment

Figure 8

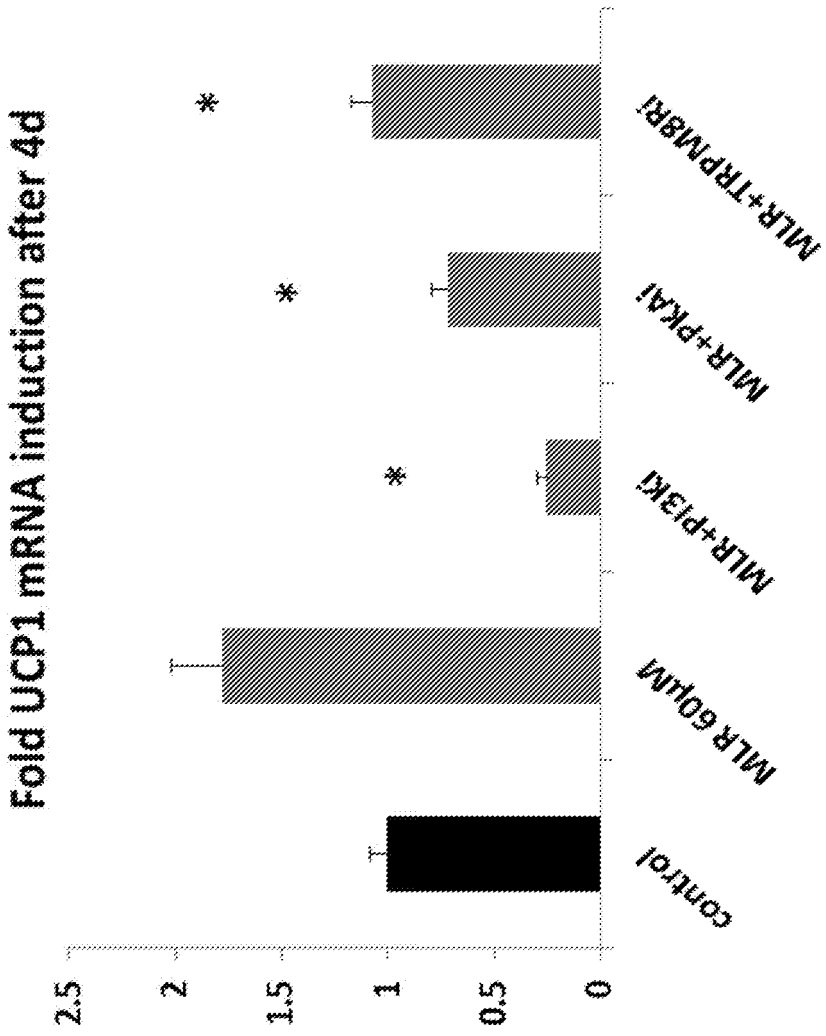

Fold UCP1 mRNA induction after 4d
2.5
2
1.5
1
0.5
0
control
MLR 6OLIM
MLR+PI3KI
MLR+PKAI
MLR+TRPVM8RI
*
*
*

Figure 9

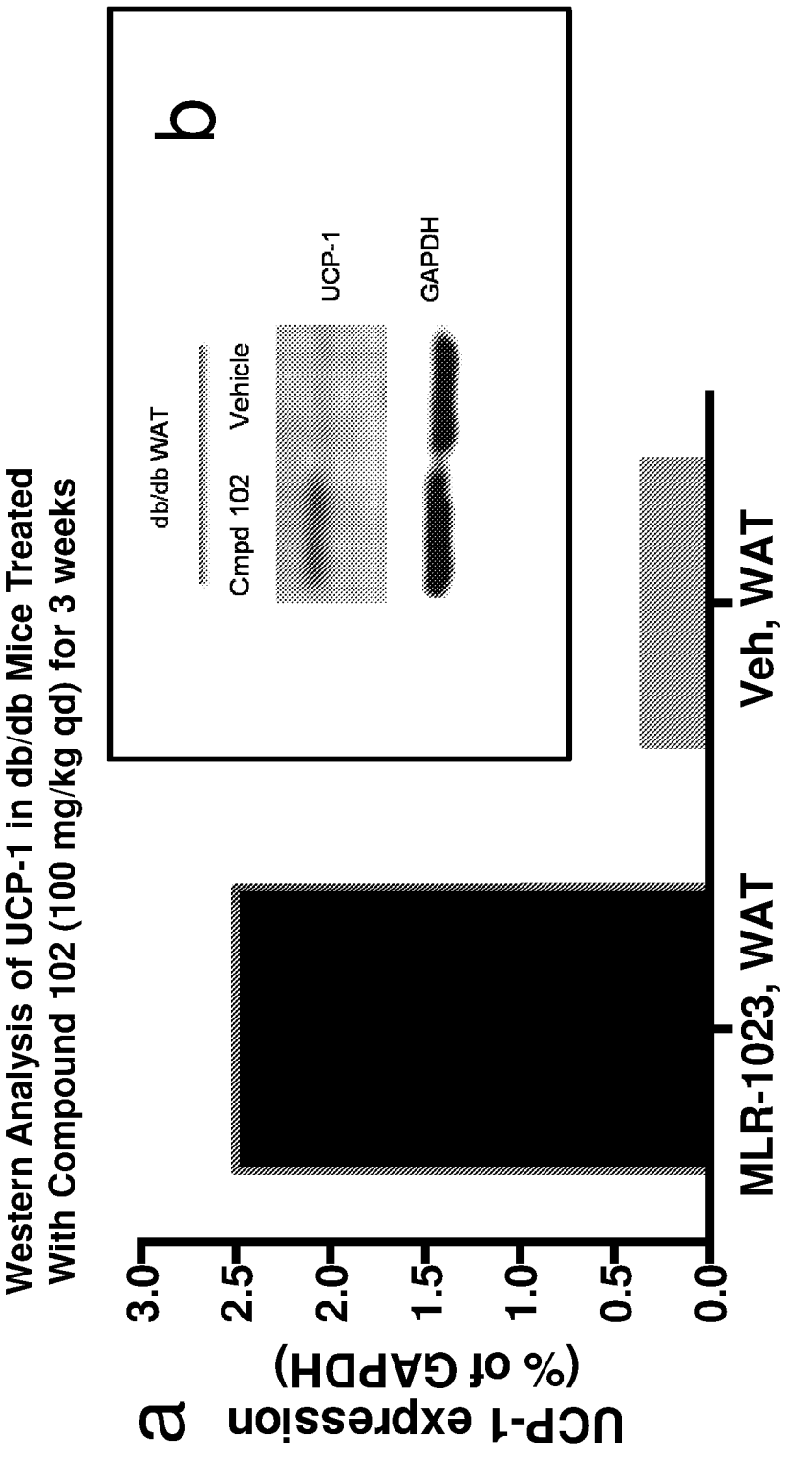

Western Analysis of UCP-1 in db/db Mice Treated
With Compound 102 (100 mg/kg qd) for 3 weeks
a
UCP-1 expression
(% of GAPDH)
3.0
2.5
2.0
1.5
1.0
0.5
0.0
MLR-1023, WAT
Veh, WAT
N=4/ group
b
db/db WAT
Cmpd 102
Vehicle
UCP-1
GAPDH

Figure 10

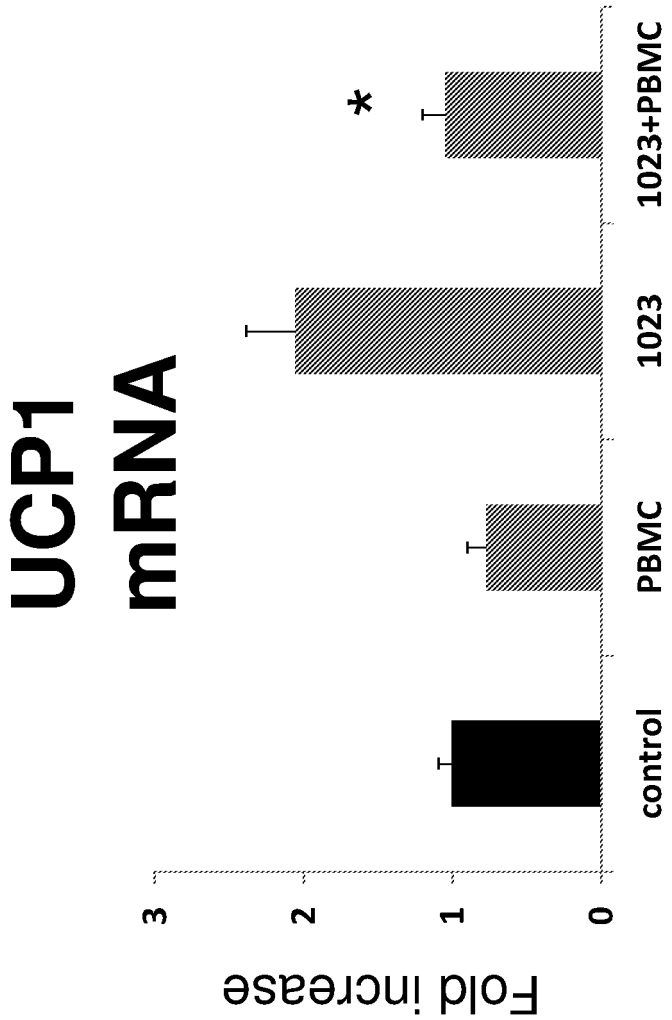

UCP1
mRNA
Fold increase
3
2
1
0
control
PBMC
1023
1023+PBMC
*
4 Day Treatment

Figure 11

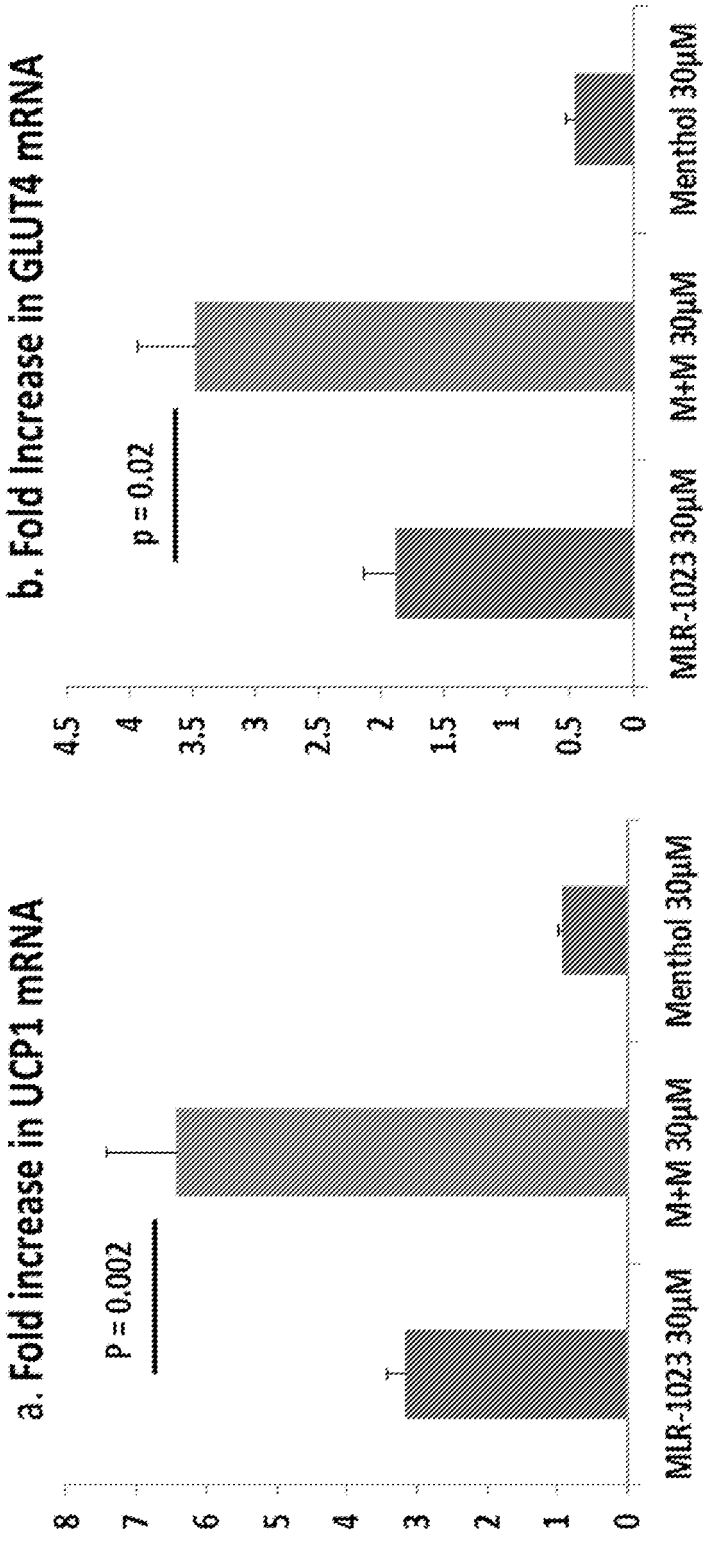
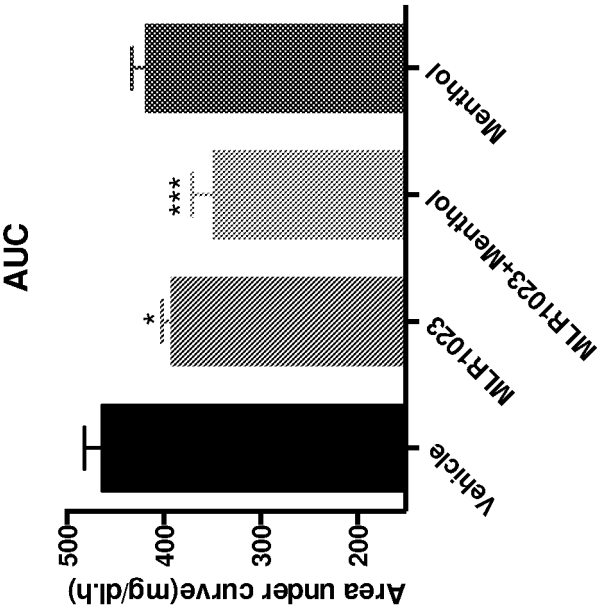

a. Fold increase in UCP1 mRNA
P = 0.002
8
7
6
5
4
3
2
1
0
MLR-1023 30µM
M+M 30µM
Menthol 30µM
b. Fold Increase in GLUT4 mRNA
p = 0.02
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
MLR-1023 30µM
M+M 30µM
Menthol 30µM

Figure 12


AUC
Area under curve(mg/dl.h)
500
400
300
200
Vehicle
MLR1023
MLR1023+Menthol
Menthol
*
***

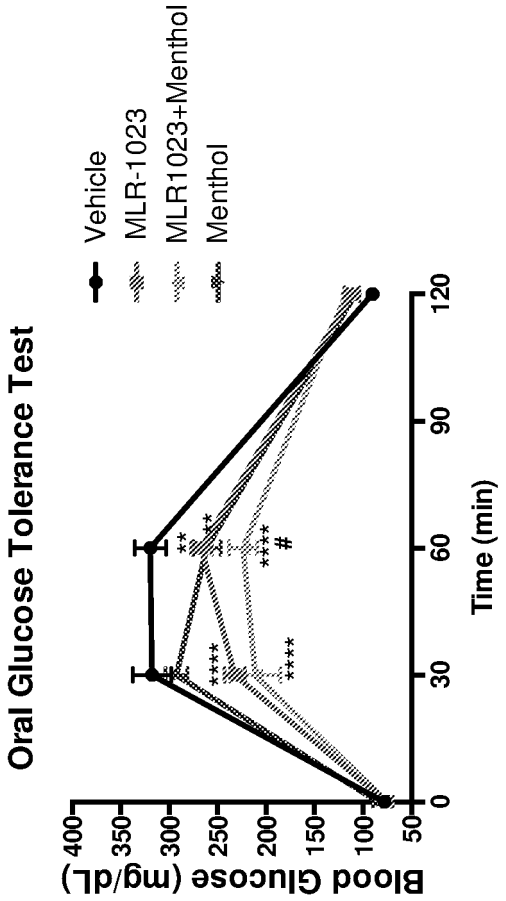

Oral Glucose Tolerance Test
Blood Glucose (mg/dL)
Time (min)
Vehicle
MLR-1023
MLR1023+Menthol
Menthol
400
350
300
250
200
150
100
50
0
30
60
90
120
**
****
#

Figure 13