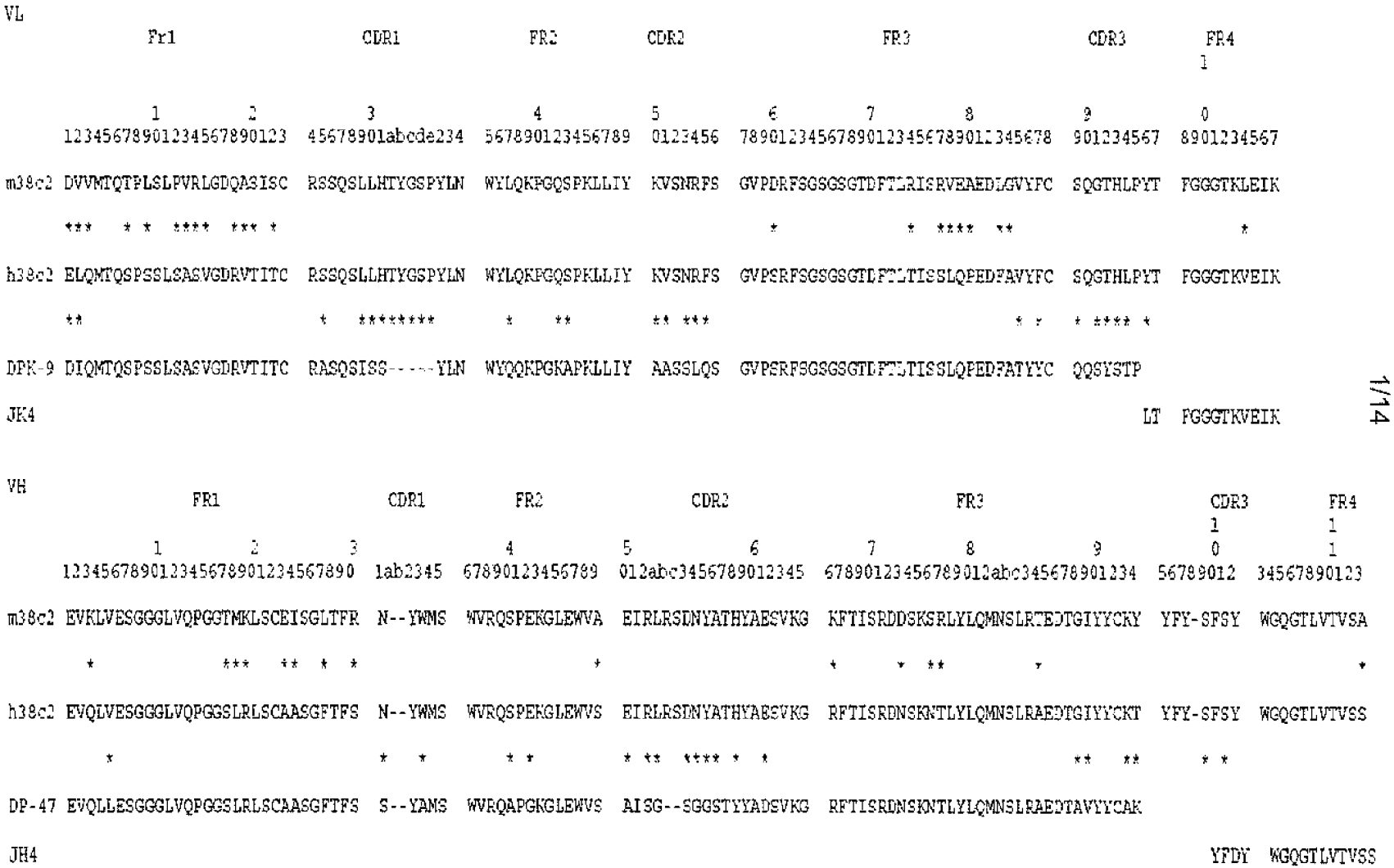
FIG. 1


VL
Fr1
CDR1
FR2
CDR2
FR3
CDR3
FR4
m38c2 DVVMTQTPLSLPVRLGDQASISC RSSQSLLHTYGSPYLN WYLQKPGQSPKLLIY KVSNRFS GVPDRFSGSGSGTDFTLRISRVEAEDLGVYFC SQGTHLPYT FGGGTKLEIK
h38c2 ELQMTQSPSSLSASVGDRVTITC RSSQSLLHTYGSPYLN WYLQKPGQSPKLLIY KVSNRFS GVPSRFSGSGSGTDFTLTISSLQPEDFAVYFC SQGTHLPYT FGGGTKVEIK
DPK-9 DIQMTQSPSSLSASVGDRVTITC RASQSISS-----YLN WYQQKPGKAPKLLIY AASSLQS GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC QQSYSTP
JK4 LT FGGGTKVEIK
VH
FR1
CDR1
FR2
CDR2
FR3
CDR3
FR4
m38c2 EVKLVESGGGLVQPGGTMKLSCEISGLTFR N--YWMS WVRQSPEKGLEWVA EIRLRSDNYATHYAESVKG KFTISRDDSKSRLYLQMNSLRTEDTGIYYCKY YFY-SFSY WGQGTLVTVSA
h38c2 EVQLVESGGGLVQPGGSLRLSCAASGFTFS N--YWMS WVRQSPEKGLEWVS EIRLRSDNYATHYAESVKG RFTISRDNSKNTLYLQMNSLRAEDTGIYYCKT YFY-SFSY WGQGTLVTVSS
DP-47 EVQLLESGGGLVQPGGSLRLSCAASGFTFS S--YAMS WVRQAPGKGLEWVS AISG--SGGSTYYADSVKG RFTISRDNSKNTLYLQMNSLRAEDTAVYYCAK
JH4 YFDY WGQGTLVTVSS

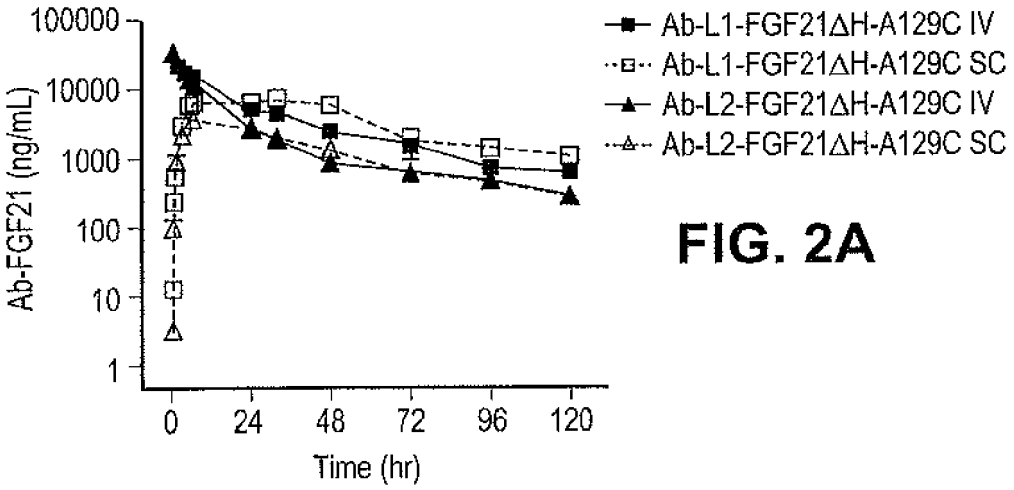


FIG. 2A

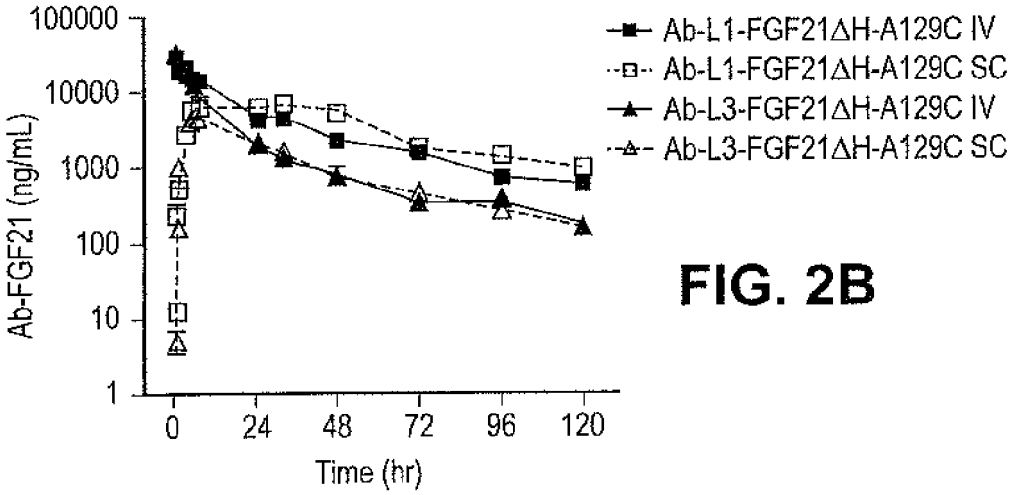


FIG. 2B

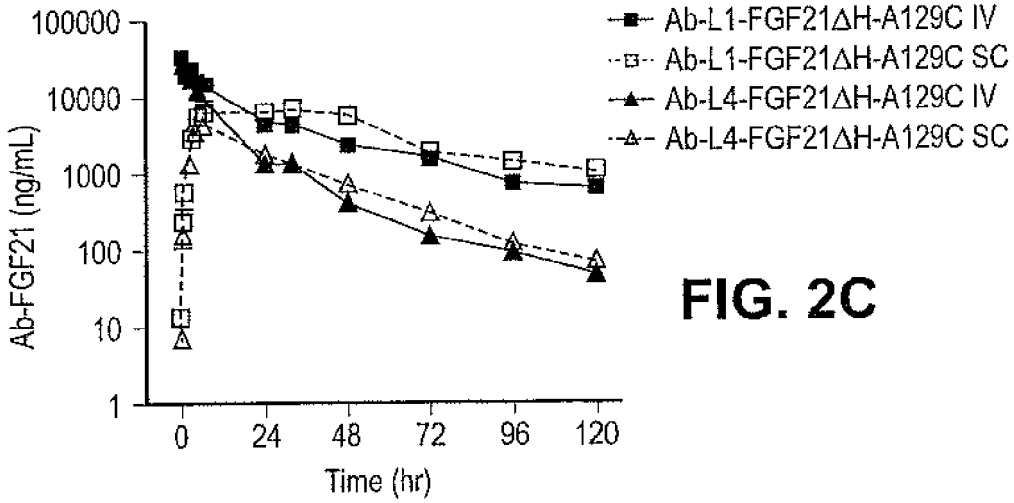


FIG. 2C

FIG. 3A

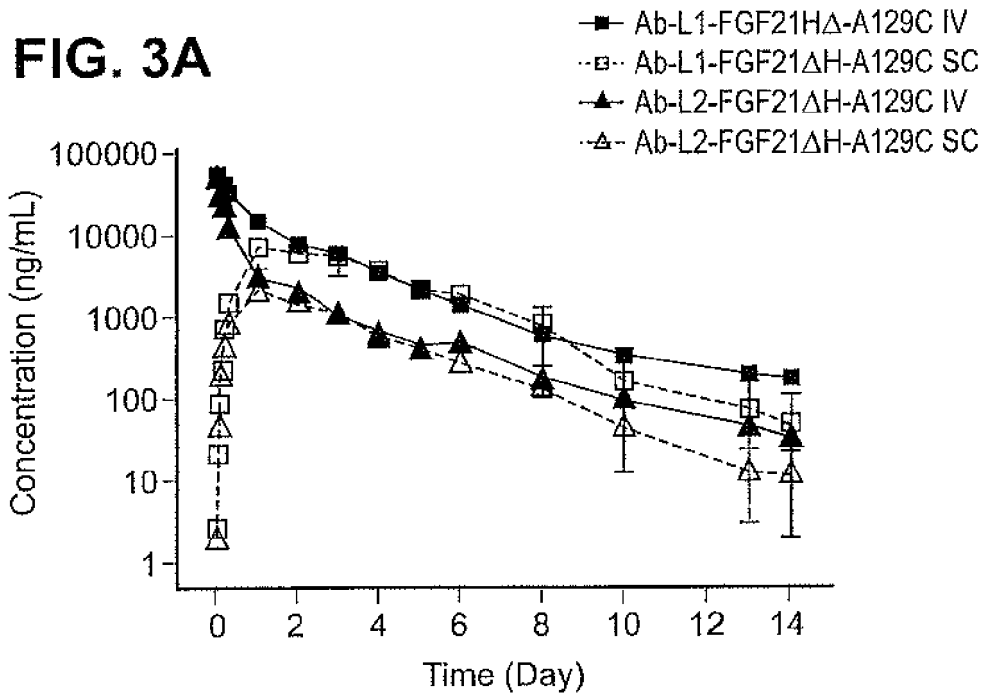

Ab-L1-FGF21HΔ-A129C IV
Ab-L1-FGF21ΔH-A129C SC
Ab-L2-FGF21ΔH-A129C IV
Ab-L2-FGF21ΔH-A129C SC
Concentration (ng/mL)
100000
10000
1000
100
10
1
0
2
4
6
8
10
12
14
Time (Day)

FIG. 3B

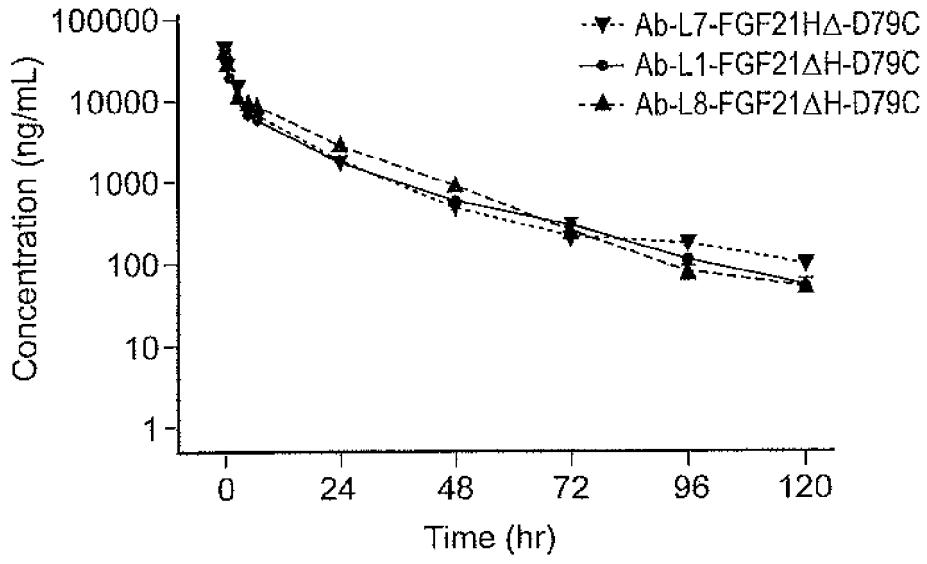

Ab-L7-FGF21HΔ-D79C
Ab-L1-FGF21ΔH-D79C
Ab-L8-FGF21ΔH-D79C
Concentration (ng/mL)
100000
10000
1000
100
10
1
0
24
48
72
96
120
Time (hr)

FIG. 4A

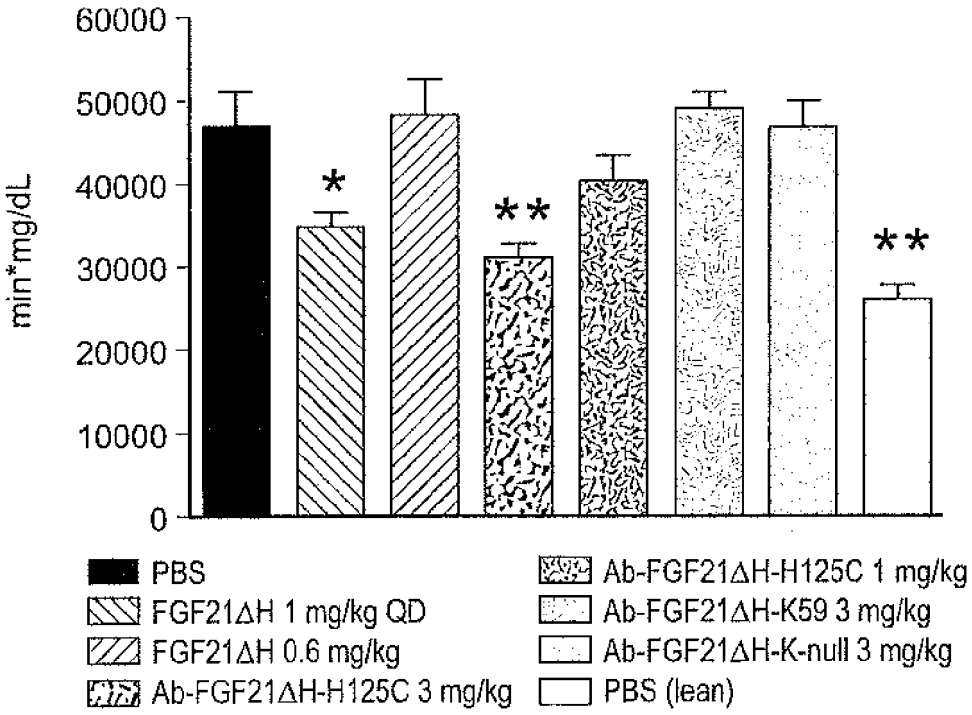

60000
50000
40000
30000
20000
10000
0
min*mg/dL
*
**
**
PBS
FGF21ΔH 1 mg/kg QD
FGF21ΔH 0.6 mg/kg
Ab-FGF21ΔH-H125C 3 mg/kg
Ab-FGF21ΔH-H125C 1 mg/kg
Ab-FGF21ΔH-K59 3 mg/kg
Ab-FGF21ΔH-K-null 3 mg/kg
PBS (lean)

FIG. 4B

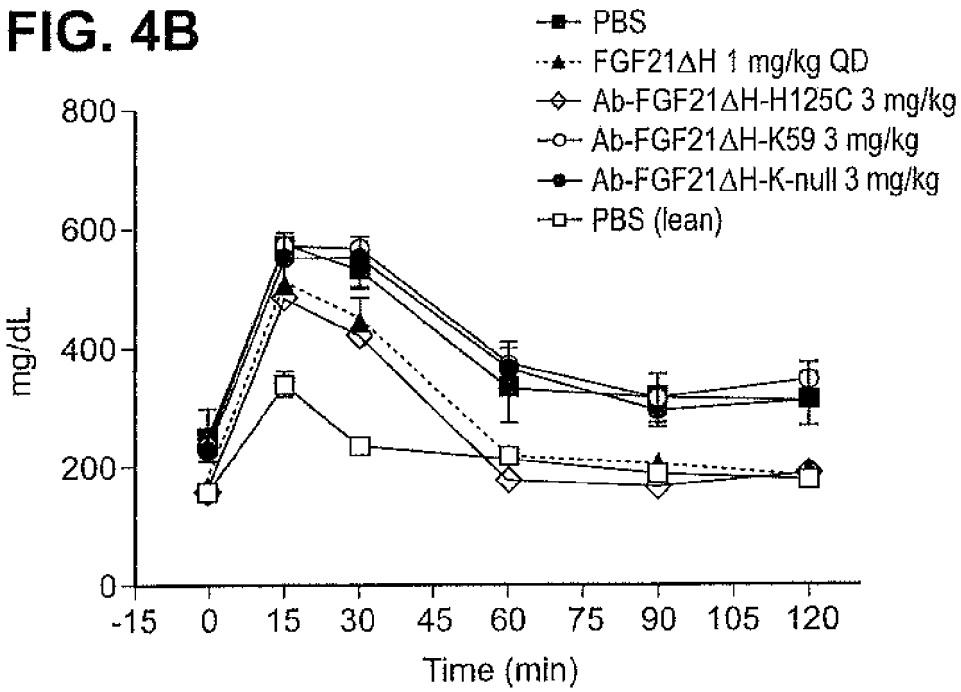

PBS
FGF21ΔH 1 mg/kg QD
Ab-FGF21ΔH-H125C 3 mg/kg
Ab-FGF21ΔH-K59 3 mg/kg
Ab-FGF21ΔH-K-null 3 mg/kg
PBS (lean)
800
600
400
200
0
mg/dL
-15
0
15
30
45
60
75
90
105
120
Time (min)

FIG. 5A

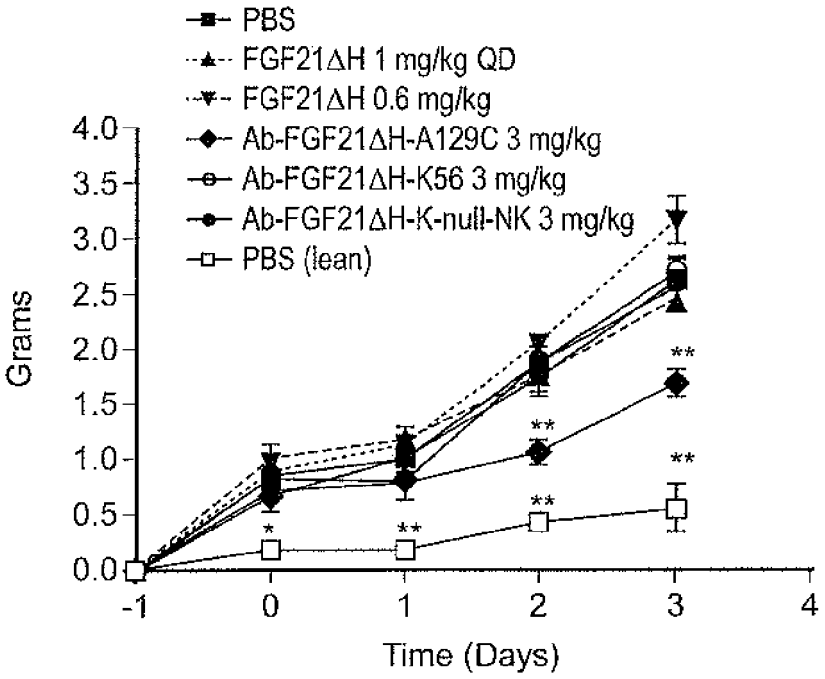

PBS
FGF21ΔH 1 mg/kg QD
FGF21ΔH 0.6 mg/kg
Ab-FGF21ΔH-A129C 3 mg/kg
Ab-FGF21ΔH-K56 3 mg/kg
Ab-FGF21ΔH-K-null-NK 3 mg/kg
PBS (lean)
Grams
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-1
0
1
2
3
4
Time (Days)
*
**
**
**
**

FIG. 5B

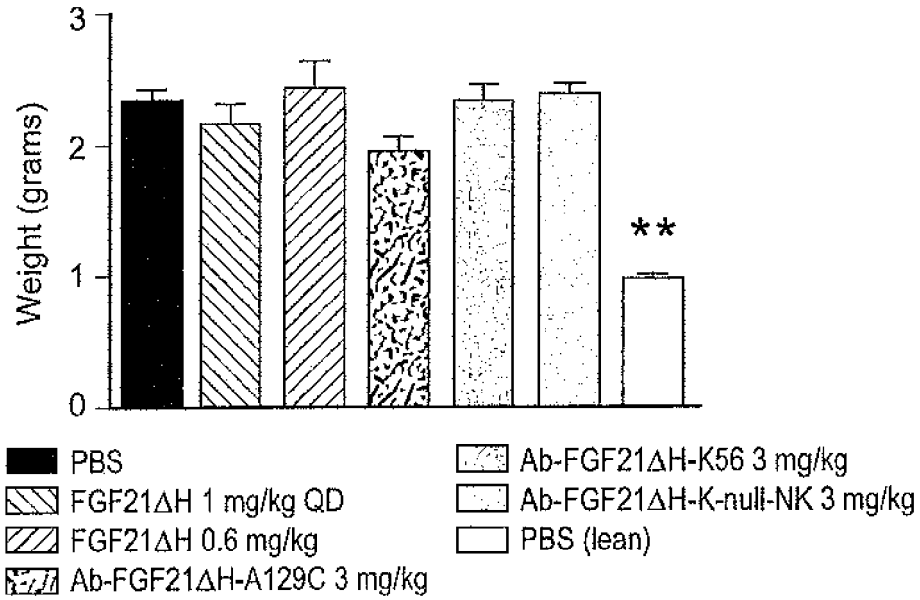

Weight (grams)
3
2
1
0
**
PBS
FGF21ΔH 1 mg/kg QD
FGF21ΔH 0.6 mg/kg
Ab-FGF21ΔH-A129C 3 mg/kg
Ab-FGF21ΔH-K56 3 mg/kg
Ab-FGF21ΔH-K-null-NK 3 mg/kg
PBS (lean)

FIG. 6A

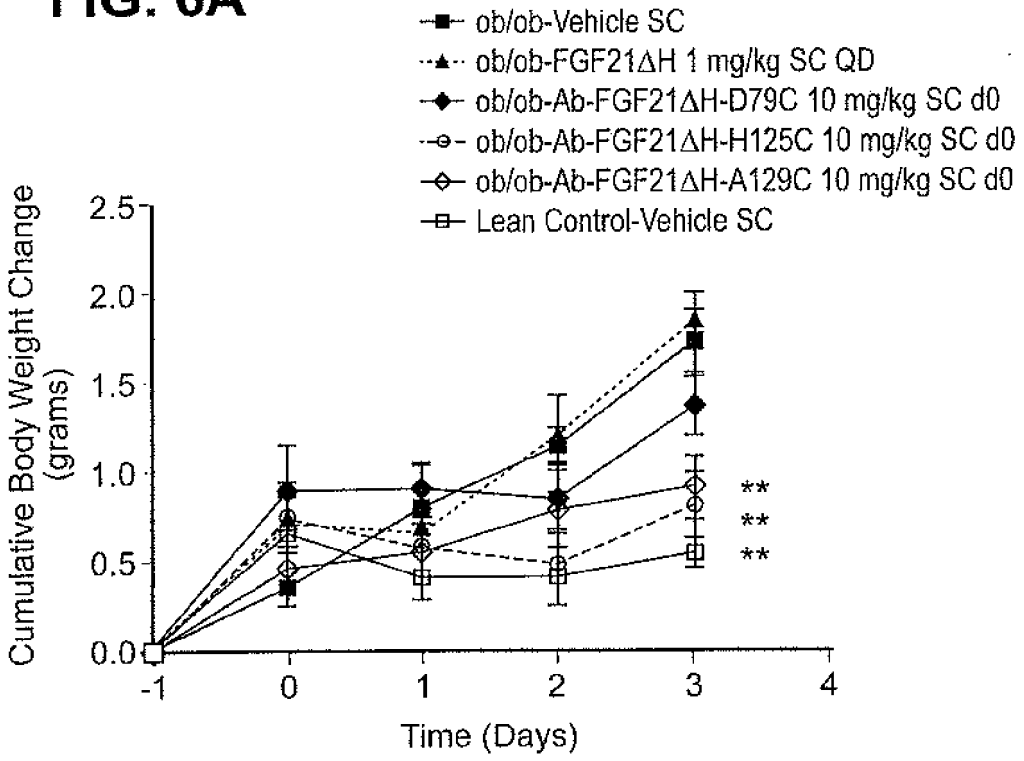

ob/ob-Vehicle SC
ob/ob-FGF21ΔH 1 mg/kg SC QD
ob/ob-Ab-FGF21ΔH-D79C 10 mg/kg SC d0
ob/ob-Ab-FGF21ΔH-H125C 10 mg/kg SC d0
ob/ob-Ab-FGF21ΔH-A129C 10 mg/kg SC d0
Lean Control-Vehicle SC
Cumulative Body Weight Change (grams)
2.5
2.0
1.5
1.0
0.5
0.0
-1
0
1
2
3
4
Time (Days)
**
**
**

FIG. 6B

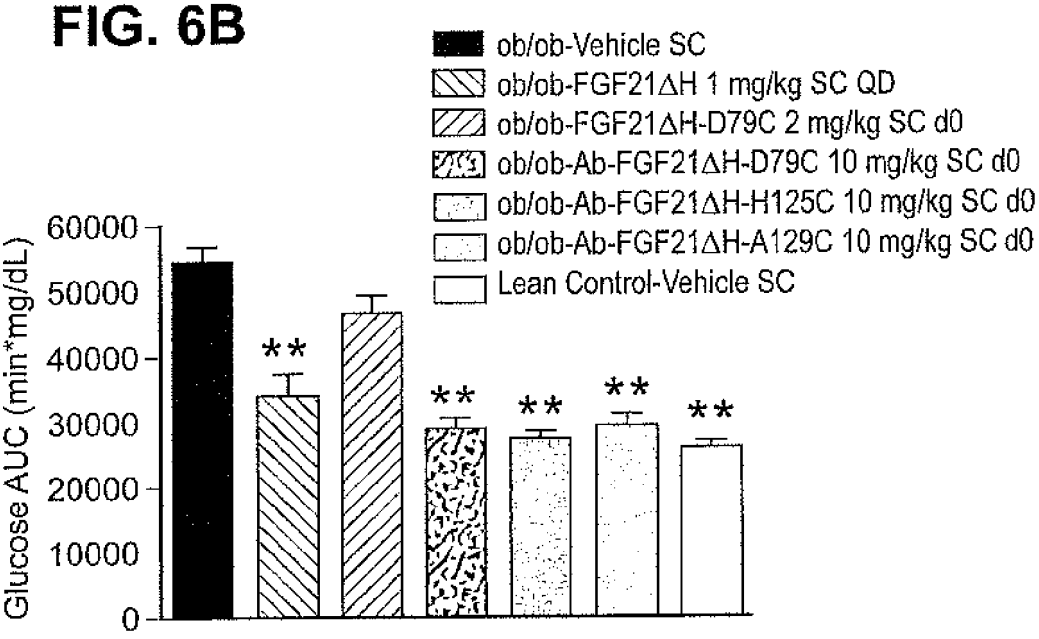

ob/ob-Vehicle SC
ob/ob-FGF21ΔH 1 mg/kg SC QD
ob/ob-FGF21ΔH-D79C 2 mg/kg SC d0
ob/ob-Ab-FGF21ΔH-D79C 10 mg/kg SC d0
ob/ob-Ab-FGF21ΔH-H125C 10 mg/kg SC d0
ob/ob-Ab-FGF21ΔH-A129C 10 mg/kg SC d0
Lean Control-Vehicle SC
Glucose AUC (min*mg/dL)
60000
50000
40000
30000
20000
10000
0
**
**
**
**
**

FIG. 6C

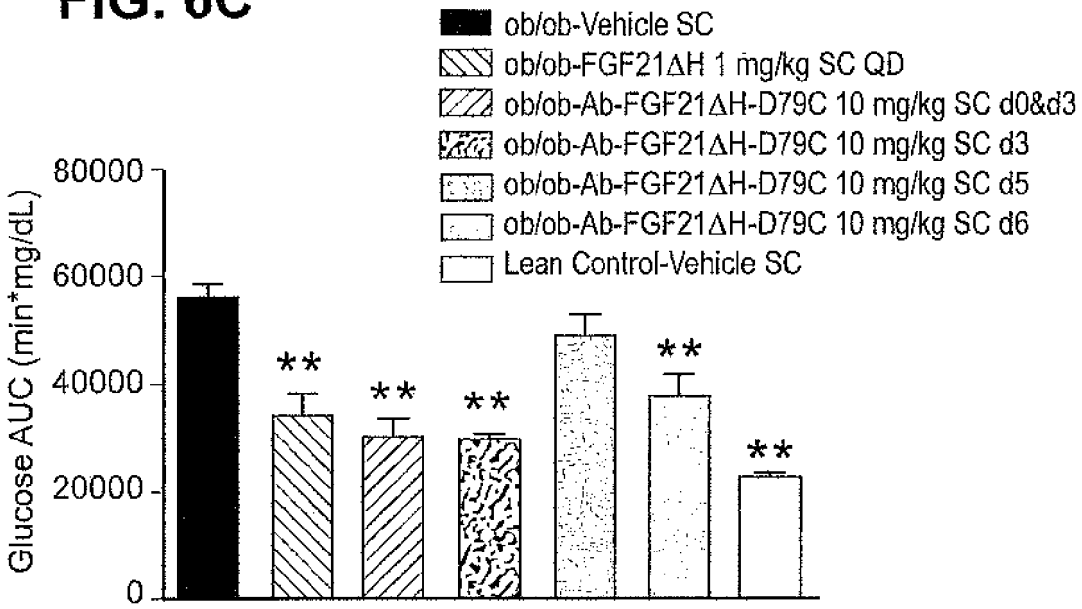

ob/ob-Vehicle SC
ob/ob-FGF21ΔH 1 mg/kg SC QD
ob/ob-Ab-FGF21ΔH-D79C 10 mg/kg SC d0&d3
ob/ob-Ab-FGF21ΔH-D79C 10 mg/kg SC d3
ob/ob-Ab-FGF21ΔH-D79C 10 mg/kg SC d5
ob/ob-Ab-FGF21ΔH-D79C 10 mg/kg SC d6
Lean Control-Vehicle SC
Glucose AUC (min*mg/dL)
80000
60000
40000
20000
0
**
**
**
**
**

FIG. 6D

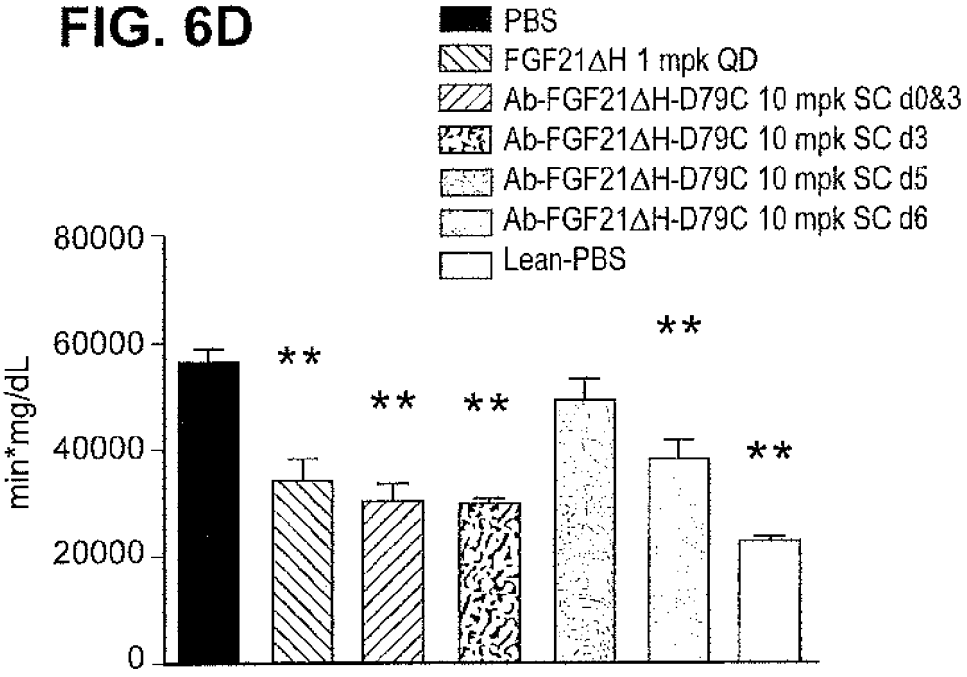

PBS
FGF21ΔH 1 mpk QD
Ab-FGF21ΔH-D79C 10 mpk SC d0&3
Ab-FGF21ΔH-D79C 10 mpk SC d3
Ab-FGF21ΔH-D79C 10 mpk SC d5
Ab-FGF21ΔH-D79C 10 mpk SC d6
Lean-PBS
min*mg/dL
80000
60000
40000
20000
0
**
**
**
**
**

FIG. 6E

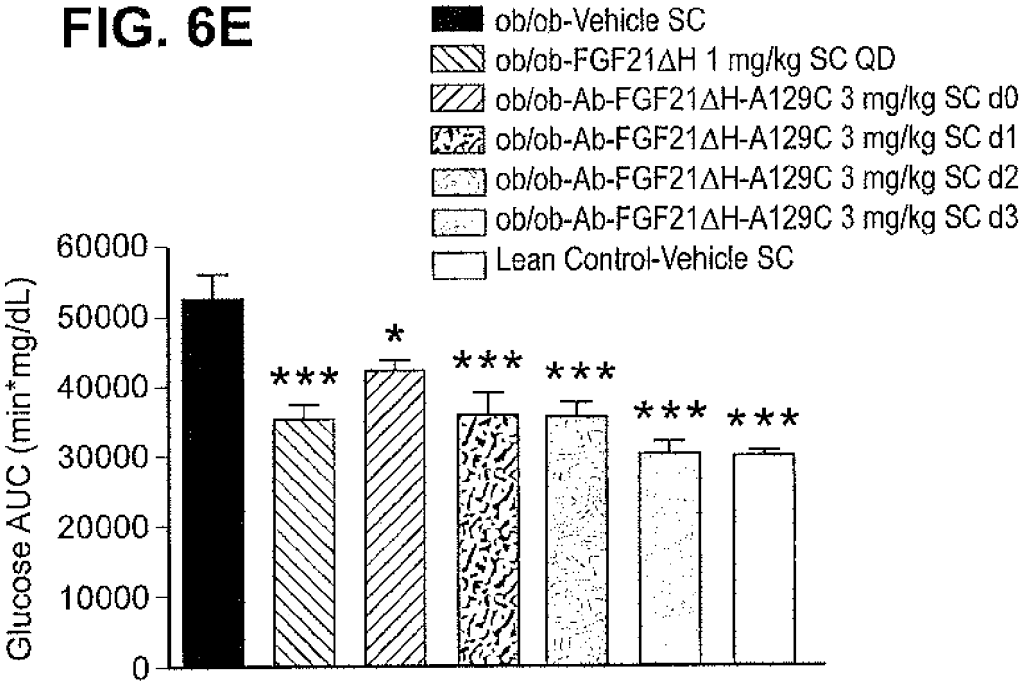

ob/ob-Vehicle SC
ob/ob-FGF21ΔH 1 mg/kg SC QD
ob/ob-Ab-FGF21ΔH-A129C 3 mg/kg SC d0
ob/ob-Ab-FGF21ΔH-A129C 3 mg/kg SC d1
ob/ob-Ab-FGF21ΔH-A129C 3 mg/kg SC d2
ob/ob-Ab-FGF21ΔH-A129C 3 mg/kg SC d3
Lean Control-Vehicle SC
Glucose AUC (min*mg/dL)
60000
50000
40000
30000
20000
10000
0
***
*
***
***
***
***

FIG. 6F

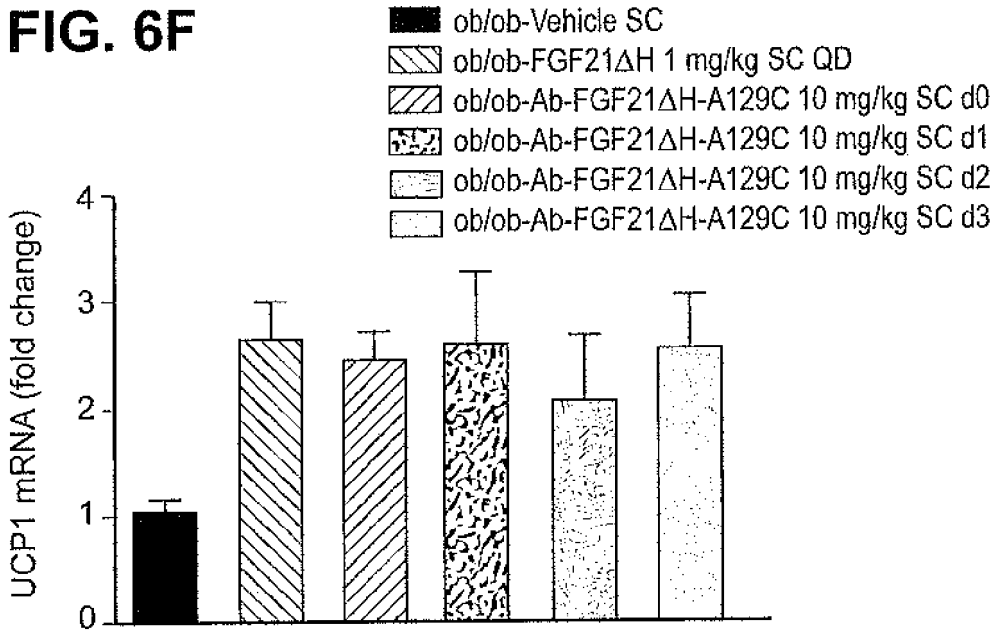

ob/ob-Vehicle SC
ob/ob-FGF21ΔH 1 mg/kg SC QD
ob/ob-Ab-FGF21ΔH-A129C 10 mg/kg SC d0
ob/ob-Ab-FGF21ΔH-A129C 10 mg/kg SC d1
ob/ob-Ab-FGF21ΔH-A129C 10 mg/kg SC d2
ob/ob-Ab-FGF21ΔH-A129C 10 mg/kg SC d3
UCP1 mRNA (fold change)
4
3
2
1
0

FIG. 6G

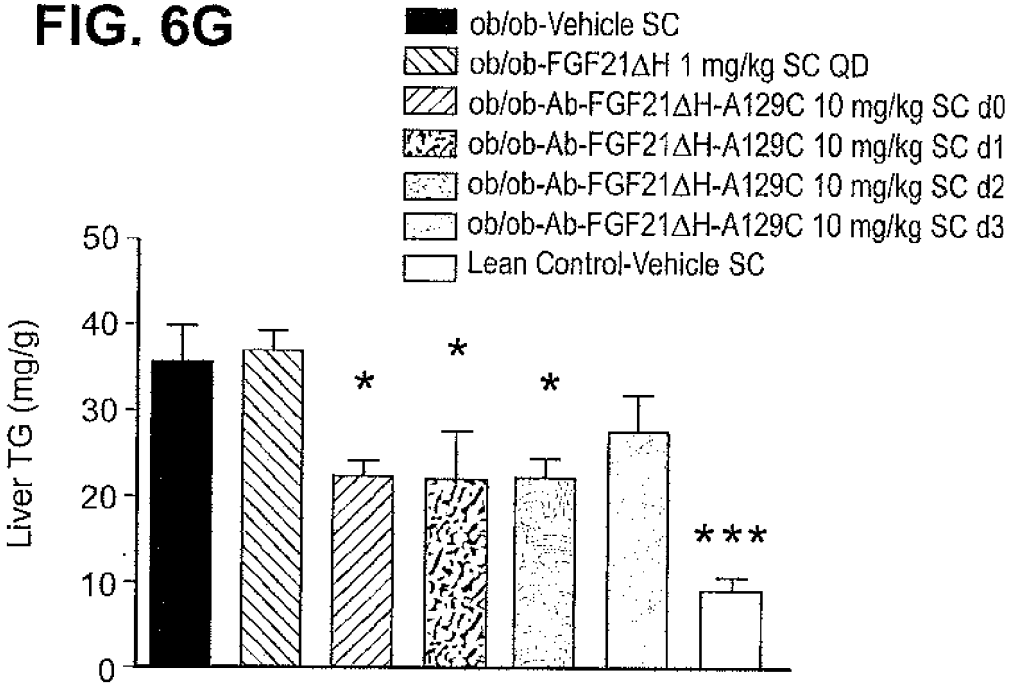

ob/ob-Vehicle SC
ob/ob-FGF21ΔH 1 mg/kg SC QD
ob/ob-Ab-FGF21ΔH-A129C 10 mg/kg SC d0
ob/ob-Ab-FGF21ΔH-A129C 10 mg/kg SC d1
ob/ob-Ab-FGF21ΔH-A129C 10 mg/kg SC d2
ob/ob-Ab-FGF21ΔH-A129C 10 mg/kg SC d3
Lean Control-Vehicle SC
Liver TG (mg/g)
50
40
30
20
10
0
*
*
*
***

FIG. 6H

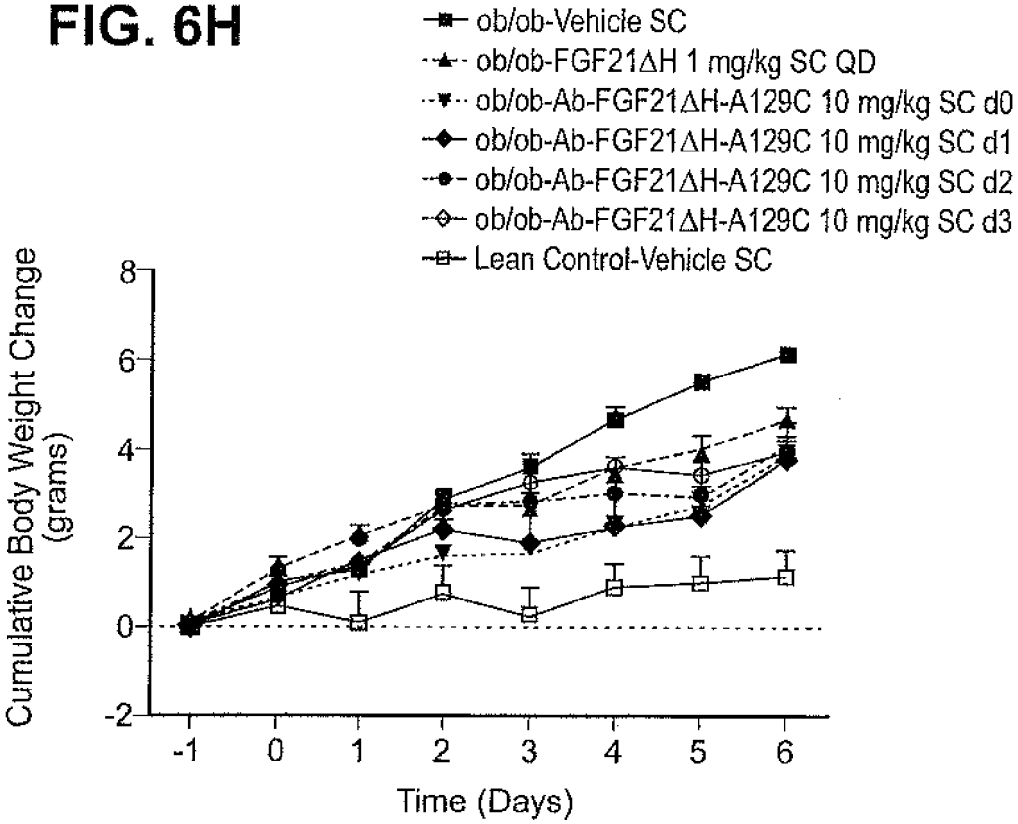

ob/ob-Vehicle SC
ob/ob-FGF21ΔH 1 mg/kg SC QD
ob/ob-Ab-FGF21ΔH-A129C 10 mg/kg SC d0
ob/ob-Ab-FGF21ΔH-A129C 10 mg/kg SC d1
ob/ob-Ab-FGF21ΔH-A129C 10 mg/kg SC d2
ob/ob-Ab-FGF21ΔH-A129C 10 mg/kg SC d3
Lean Control-Vehicle SC
Cumulative Body Weight Change (grams)
8
6
4
2
0
-2
-1
0
1
2
3
4
5
6
Time (Days)

FIG. 7A

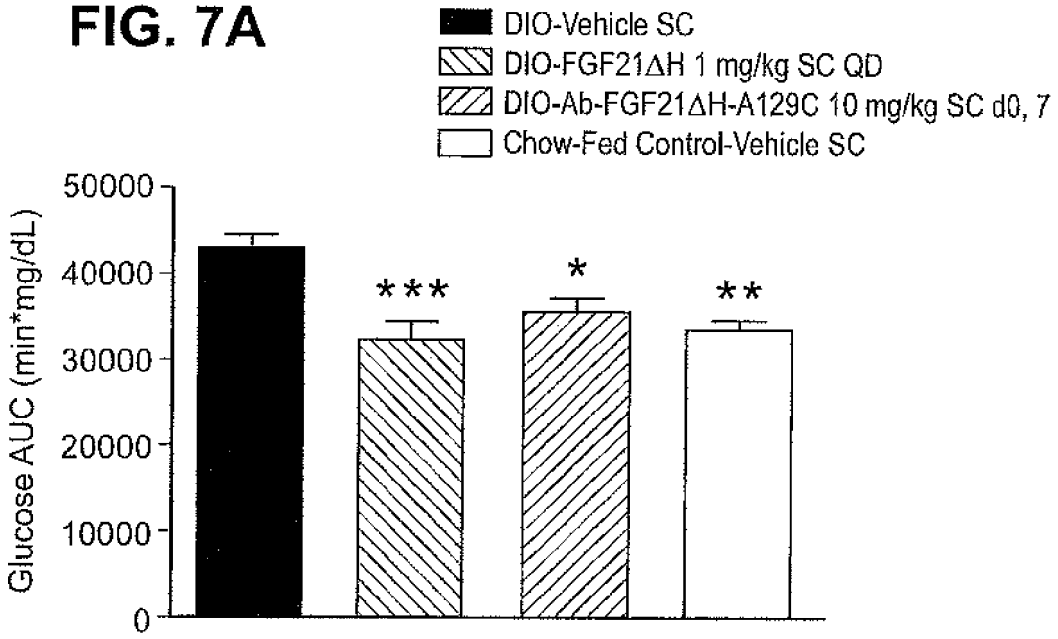

DIO-Vehicle SC
DIO-FGF21ΔH 1 mg/kg SC QD
DIO-Ab-FGF21ΔH-A129C 10 mg/kg SC d0, 7
Chow-Fed Control-Vehicle SC
Glucose AUC (min*mg/dL)
50000
40000
30000
20000
10000
0
***
*
**

FIG. 7B

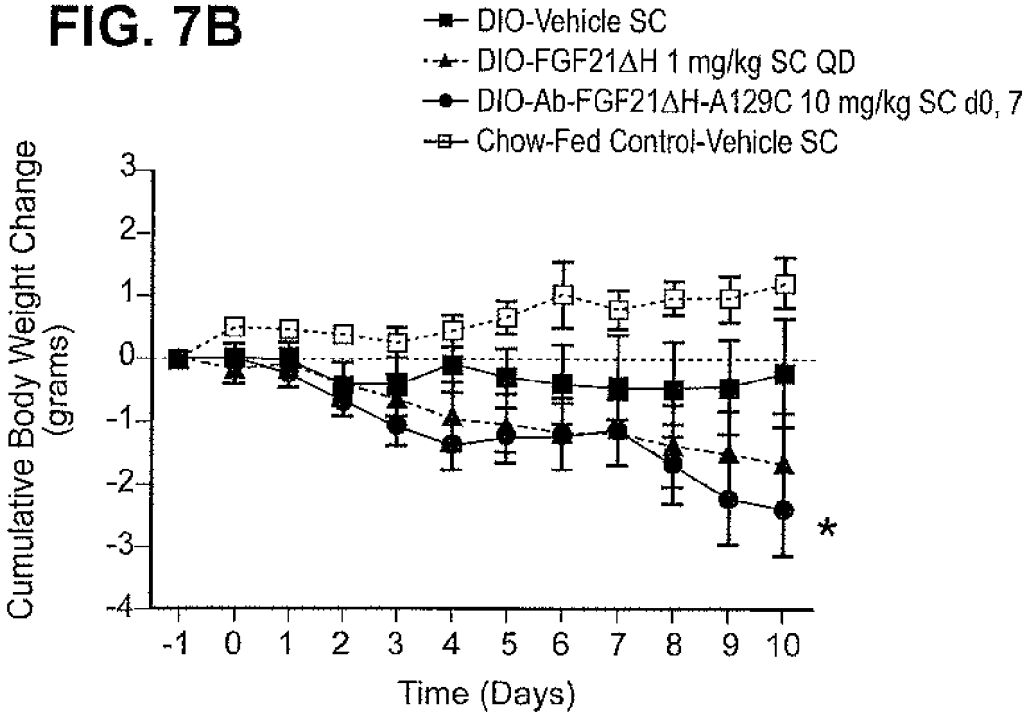

DIO-Vehicle SC
DIO-FGF21ΔH 1 mg/kg SC QD
DIO-Ab-FGF21ΔH-A129C 10 mg/kg SC d0, 7
Chow-Fed Control-Vehicle SC
Cumulative Body Weight Change (grams)
3
2
1
0
-1
-2
-3
-4
-1 0 1 2 3 4 5 6 7 8 9 10
Time (Days)
*

FIG. 7C

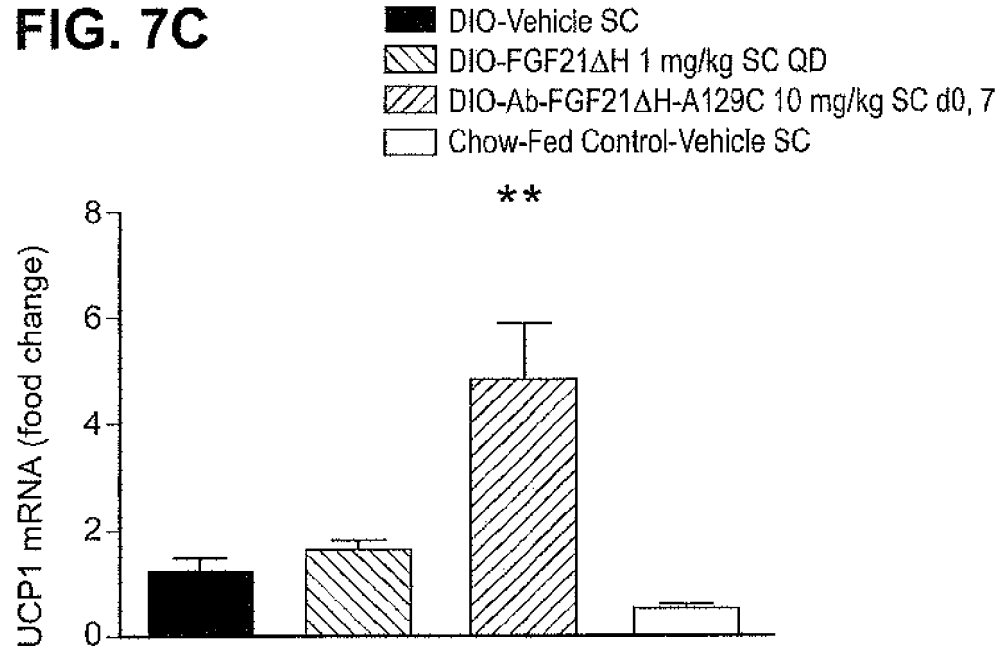

DIO-Vehicle SC
DIO-FGF21ΔH 1 mg/kg SC QD
DIO-Ab-FGF21ΔH-A129C 10 mg/kg SC d0, 7
Chow-Fed Control-Vehicle SC
UCP1 mRNA (food change)
0
2
4
6
8
**

FIG. 7D

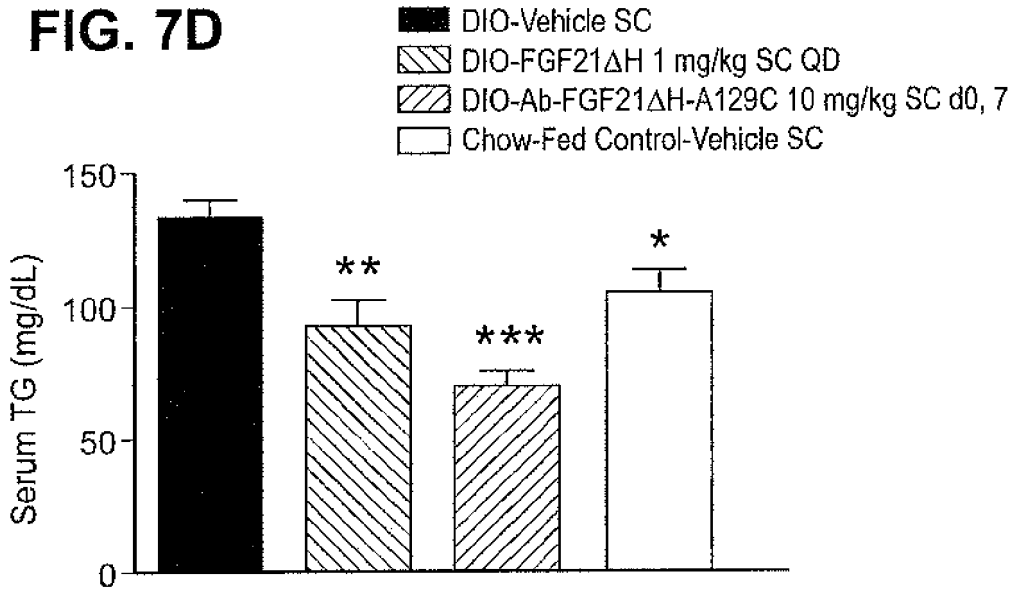

DIO-Vehicle SC
DIO-FGF21ΔH 1 mg/kg SC QD
DIO-Ab-FGF21ΔH-A129C 10 mg/kg SC d0, 7
Chow-Fed Control-Vehicle SC
Serum TG (mg/dL)
0
50
100
150
**
***
*

FIG. 7E

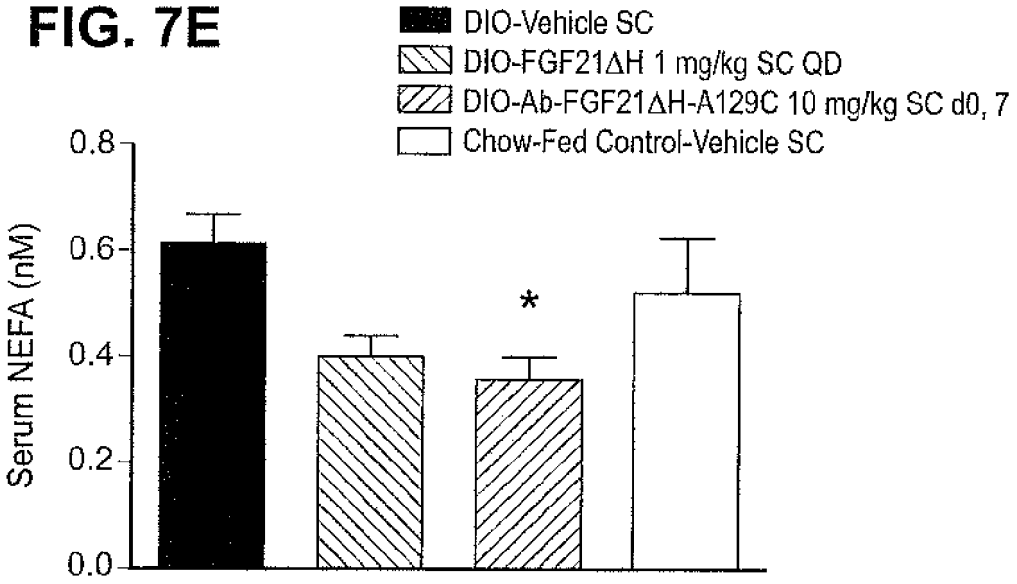

DIO-Vehicle SC
DIO-FGF21ΔH 1 mg/kg SC QD
DIO-Ab-FGF21ΔH-A129C 10 mg/kg SC d0, 7
Chow-Fed Control-Vehicle SC
Serum NEFA (nM)
0.8
0.6
0.4
0.2
0.0
*

FIG. 7F

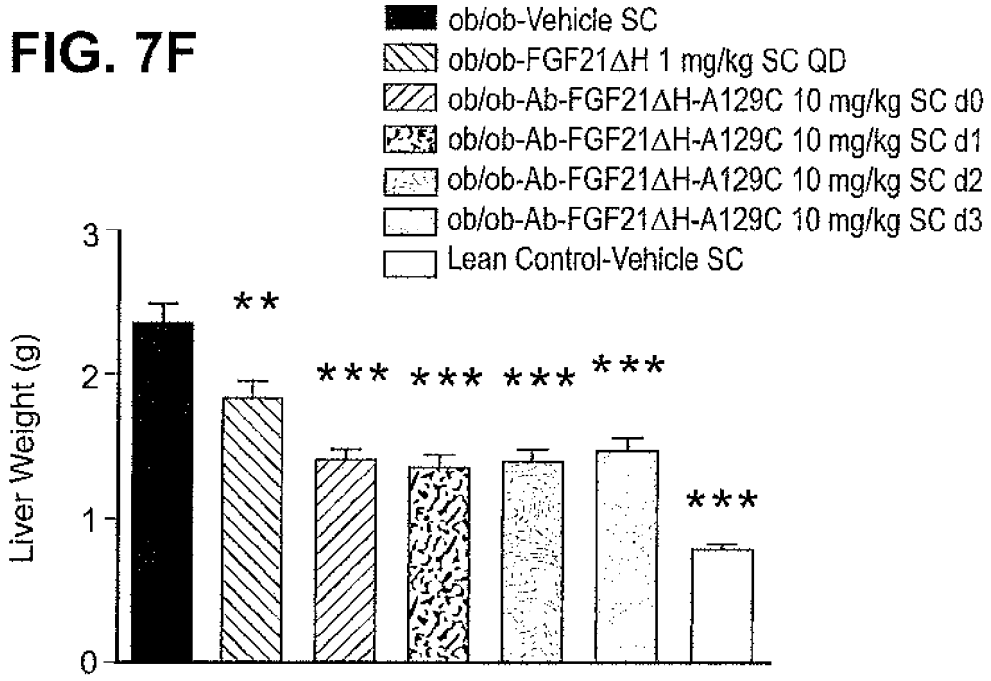

ob/ob-Vehicle SC
ob/ob-FGF21ΔH 1 mg/kg SC QD
ob/ob-Ab-FGF21ΔH-A129C 10 mg/kg SC d0
ob/ob-Ab-FGF21ΔH-A129C 10 mg/kg SC d1
ob/ob-Ab-FGF21ΔH-A129C 10 mg/kg SC d2
ob/ob-Ab-FGF21ΔH-A129C 10 mg/kg SC d3
Lean Control-Vehicle SC
Liver Weight (g)
3
2
1
0
**
*** *** *** ***
***

FIG. 7G

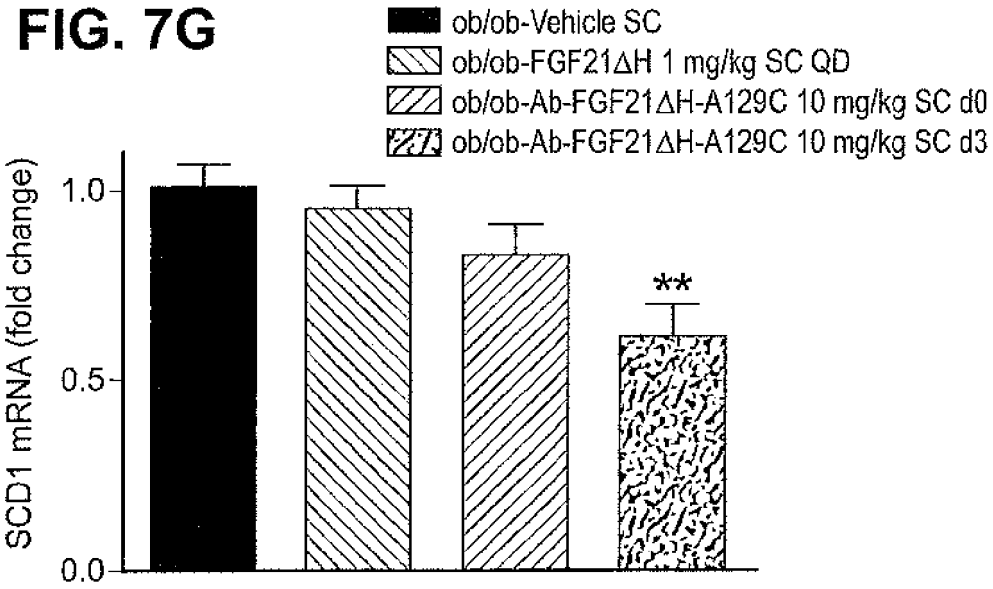

ob/ob-Vehicle SC
ob/ob-FGF21ΔH 1 mg/kg SC QD
ob/ob-Ab-FGF21ΔH-A129C 10 mg/kg SC d0
ob/ob-Ab-FGF21ΔH-A129C 10 mg/kg SC d3
SCD1 mRNA (fold change)
1.0
0.5
0.0
**

FIG. 7H

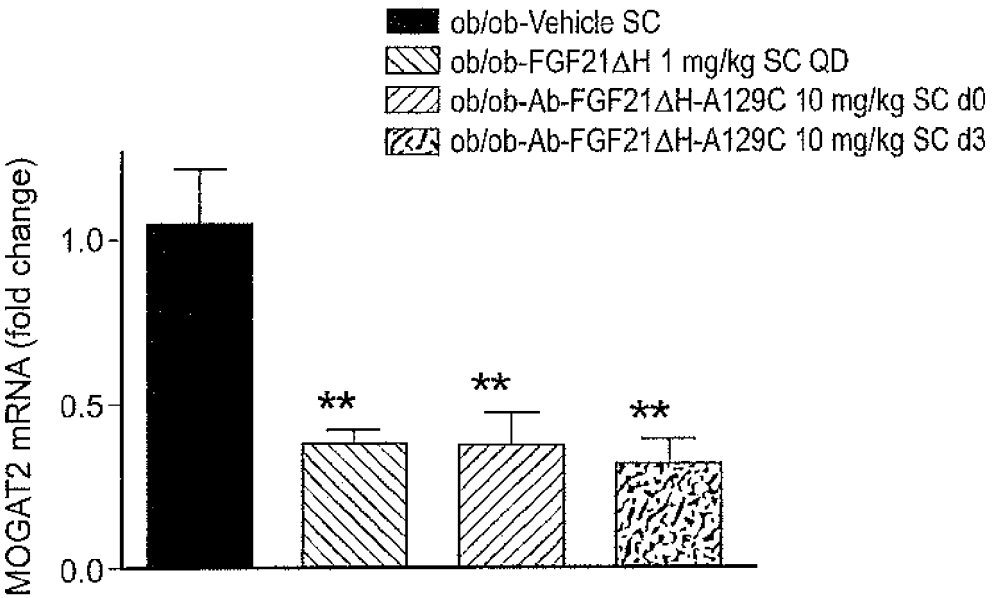

ob/ob-Vehicle SC
ob/ob-FGF21ΔH 1 mg/kg SC QD
ob/ob-Ab-FGF21ΔH-A129C 10 mg/kg SC d0
ob/ob-Ab-FGF21ΔH-A129C 10 mg/kg SC d3
MOGAT2 mRNA (fold change)
1.0
0.5
0.0
**
**
**

FIG. 7I

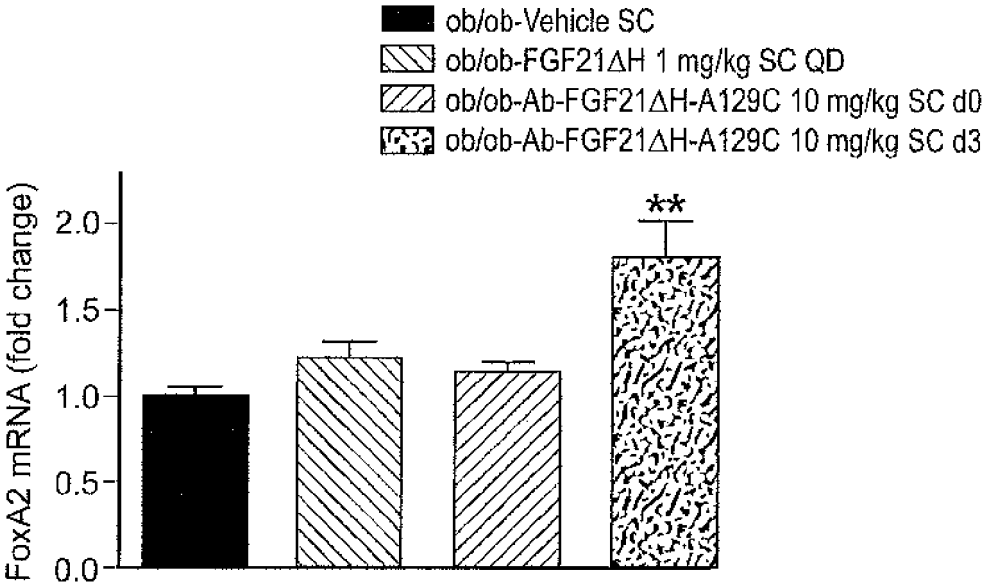
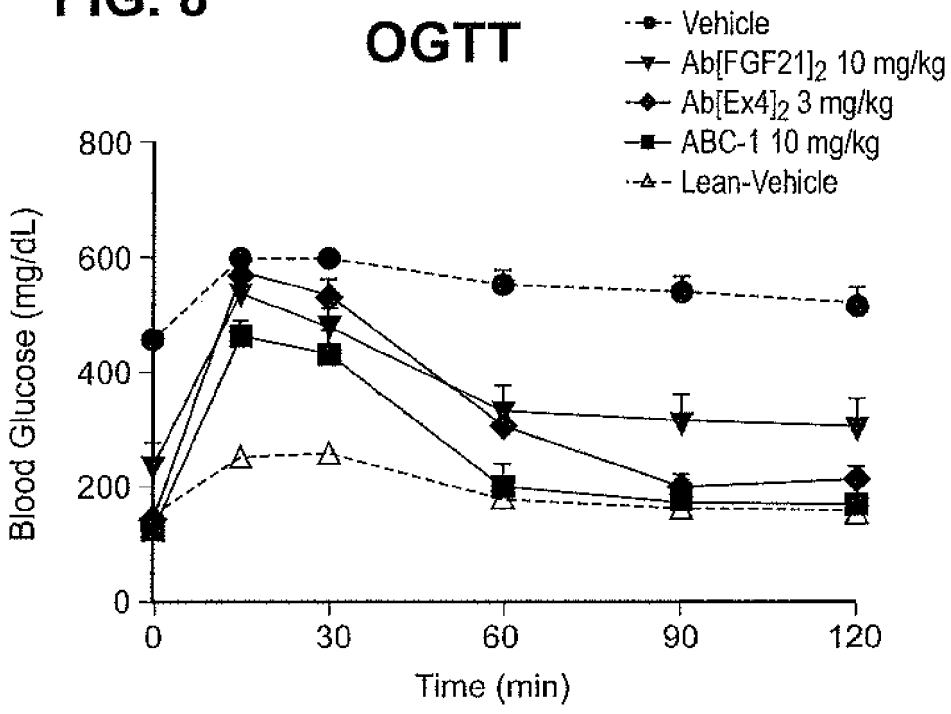

ob/ob-Vehicle SC
ob/ob-FGF21ΔH 1 mg/kg SC QD
ob/ob-Ab-FGF21ΔH-A129C 10 mg/kg SC d0
ob/ob-Ab-FGF21ΔH-A129C 10 mg/kg SC d3
FoxA2 mRNA (fold change)
0.0
0.5
1.0
1.5
2.0
**

FIG. 8


OGTT
Vehicle
Ab[FGF21]2 10 mg/kg
Ab[Ex4]2 3 mg/kg
ABC-1 10 mg/kg
Lean-Vehicle
Blood Glucose (mg/dL)
0
200
400
600
800
0
30
60
90
120
Time (min)