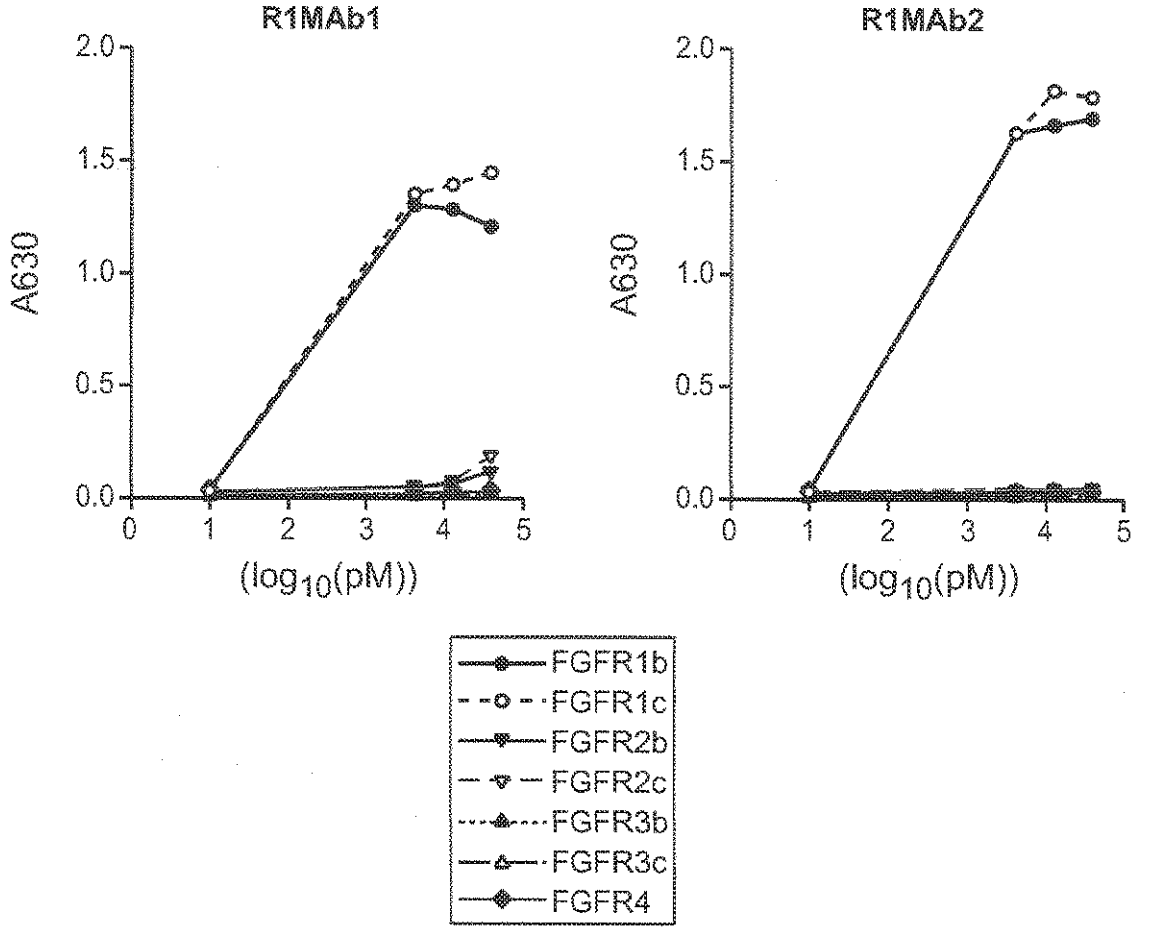


FIG. 1A

		k_{on} ($M^{-1}s^{-1}$)	k_{off} (s^{-1})	KD (M)
R1MAb1	FGFR1b	2.7×10^{6}	1.6×10^{-3}	5.9×10^{-10}
	FGFR1c	3.2×10^{6}	2.2×10^{-3}	6.7×10^{-10}
R1MAb2	FGFR1b	1.9×10^{6}	8.2×10^{-4}	4.4×10^{-10}
	FGFR1c	1.9×10^{6}	8.7×10^{-4}	4.6×10^{-10}

FIG. 1B

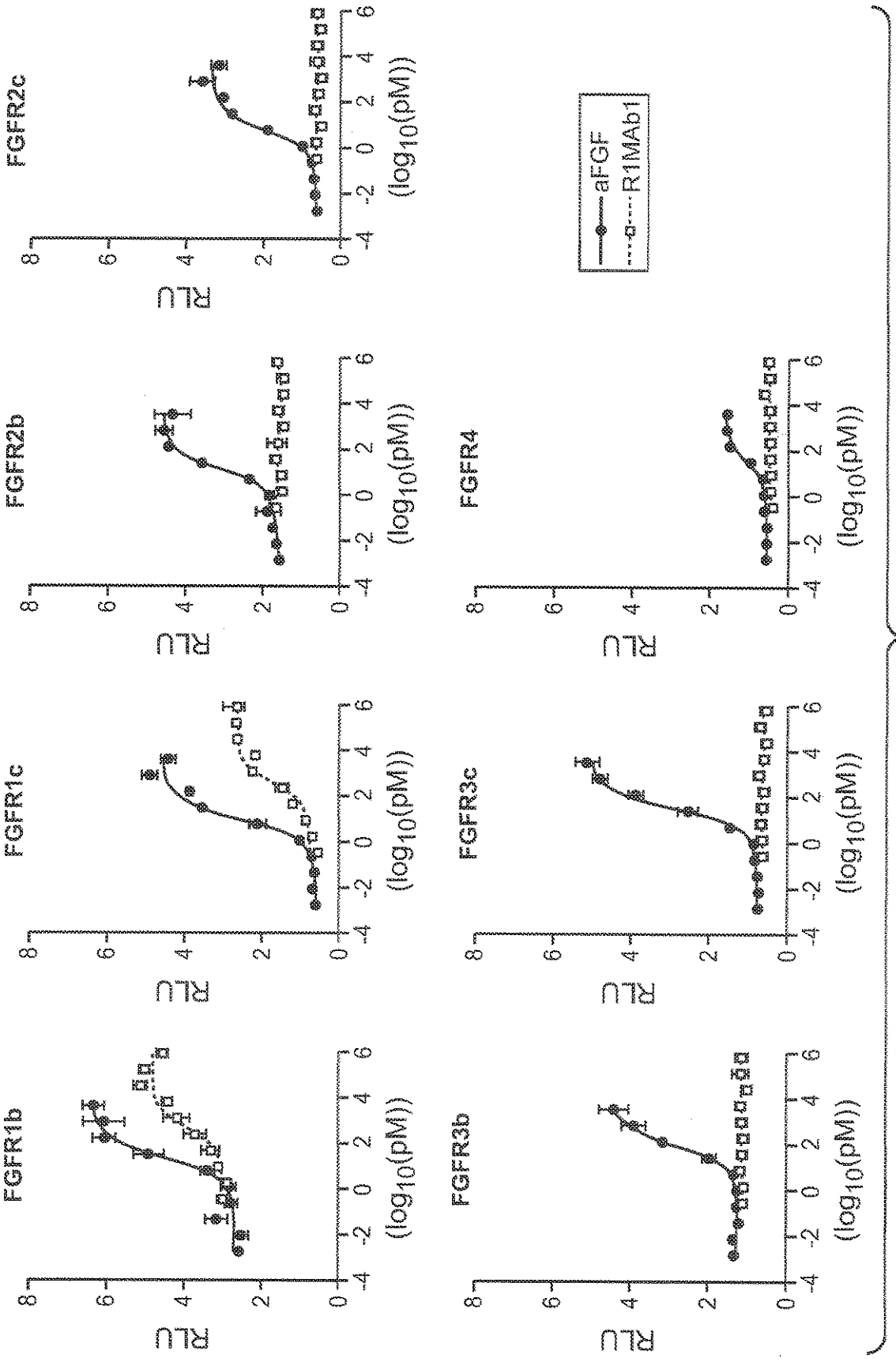

FGFR1b
FGFR1c
FGFR2b
FGFR2c
FGFR3b
FGFR3c
FGFR4
RLU
(log10(pM))
aFGF
R1MAb1

FIG. 1C-1

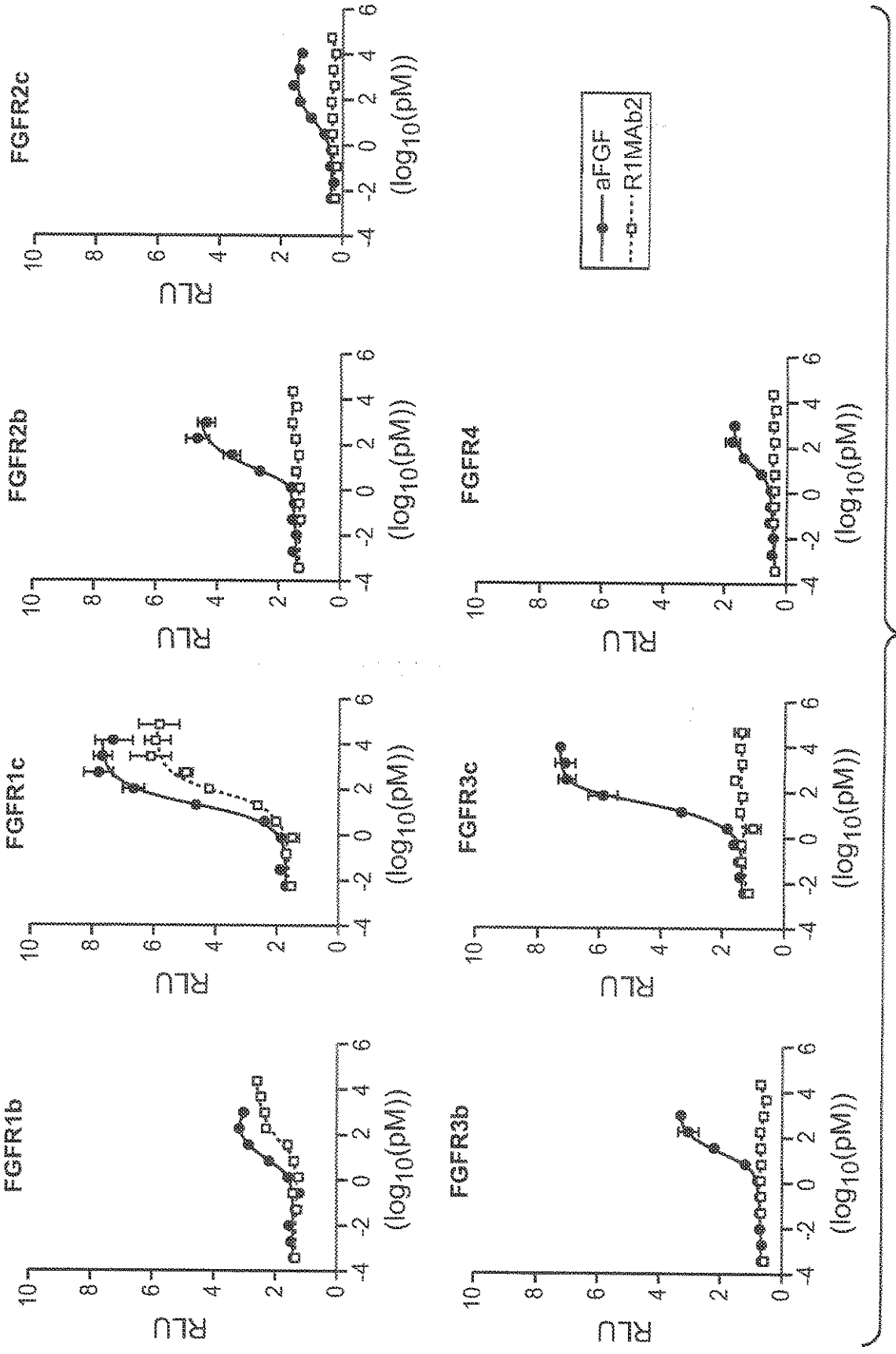

FGFR1b
FGFR1c
FGFR2b
FGFR2c
FGFR3b
FGFR3c
FGFR4
RLU
(log10(pM))
aFGF
R1MAb2

FIG. 1C-2

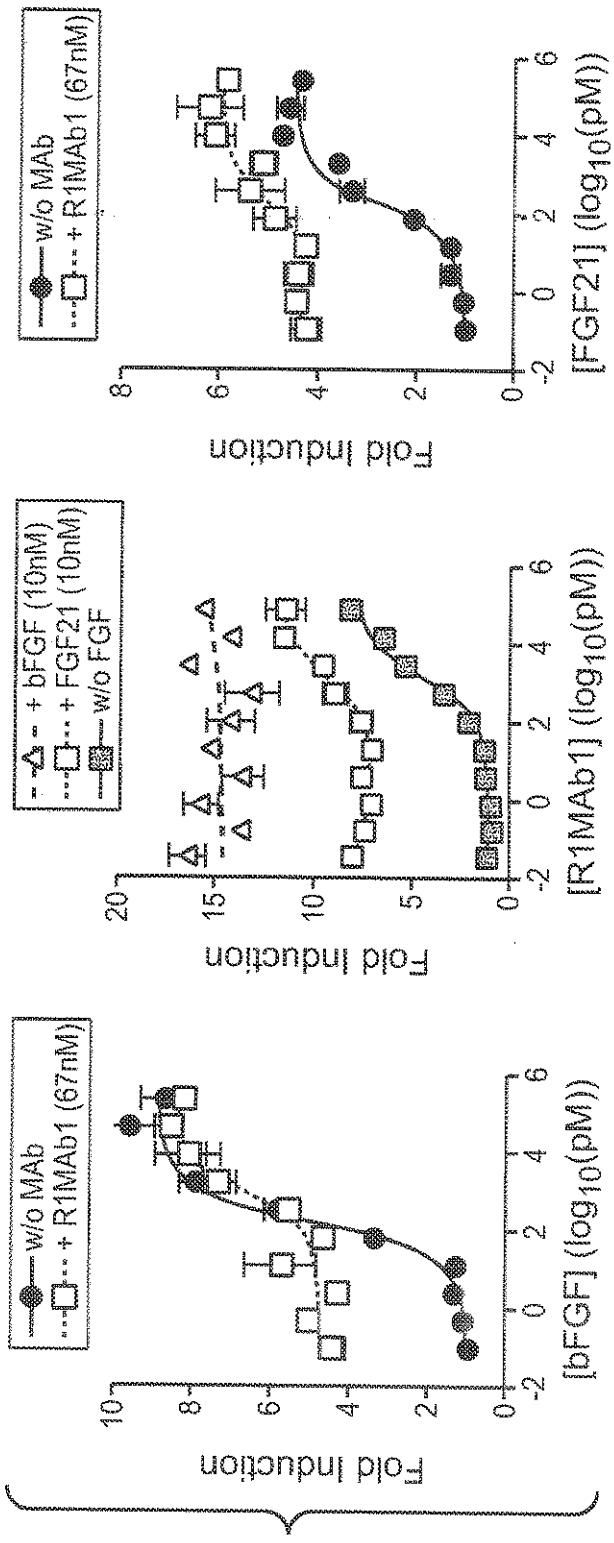

w/o MAb
+ R1MAb1 (67nM)
Fold Induction
[bFGF] (log10(pM))
+ bFGF (10nM)
+ FGF21 (10nM)
w/o FGF
[R1MAb1] (log10(pM))
[FGF21] (log10(pM))

FIG. 1D

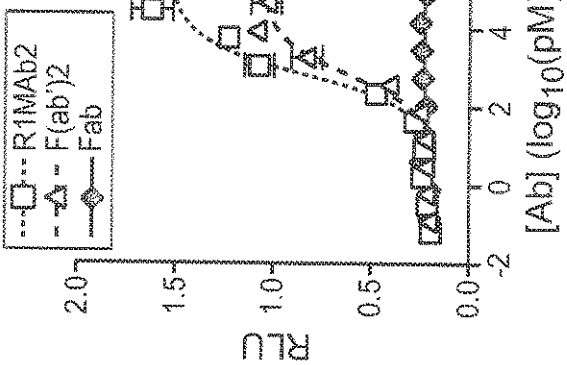

R1MAb2
F(ab')2
Fab
RLU
[Ab] (log10(pM))

FIG. 1E

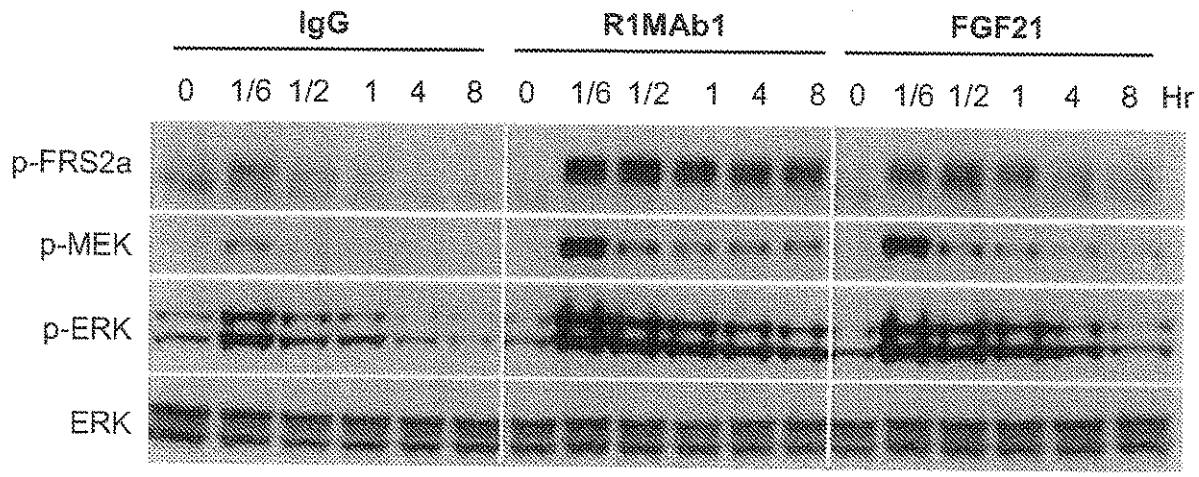

IgG
R1MAb1
FGF21
0 1/6 1/2 1 4 8 0 1/6 1/2 1 4 8 0 1/6 1/2 1 4 8 Hr
p-FRS2a
p-MEK
p-ERK
ERK

FIG. 1F

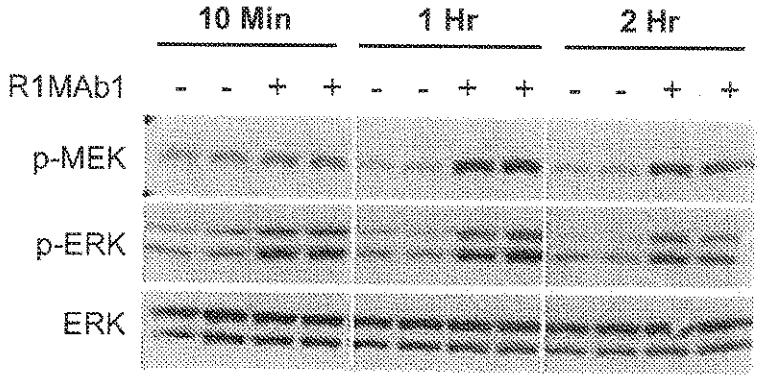

10 Min
1 Hr
2 Hr
R1MAb1 - - + + - - + + - - + +
p-MEK
p-ERK
ERK

FIG. 1G

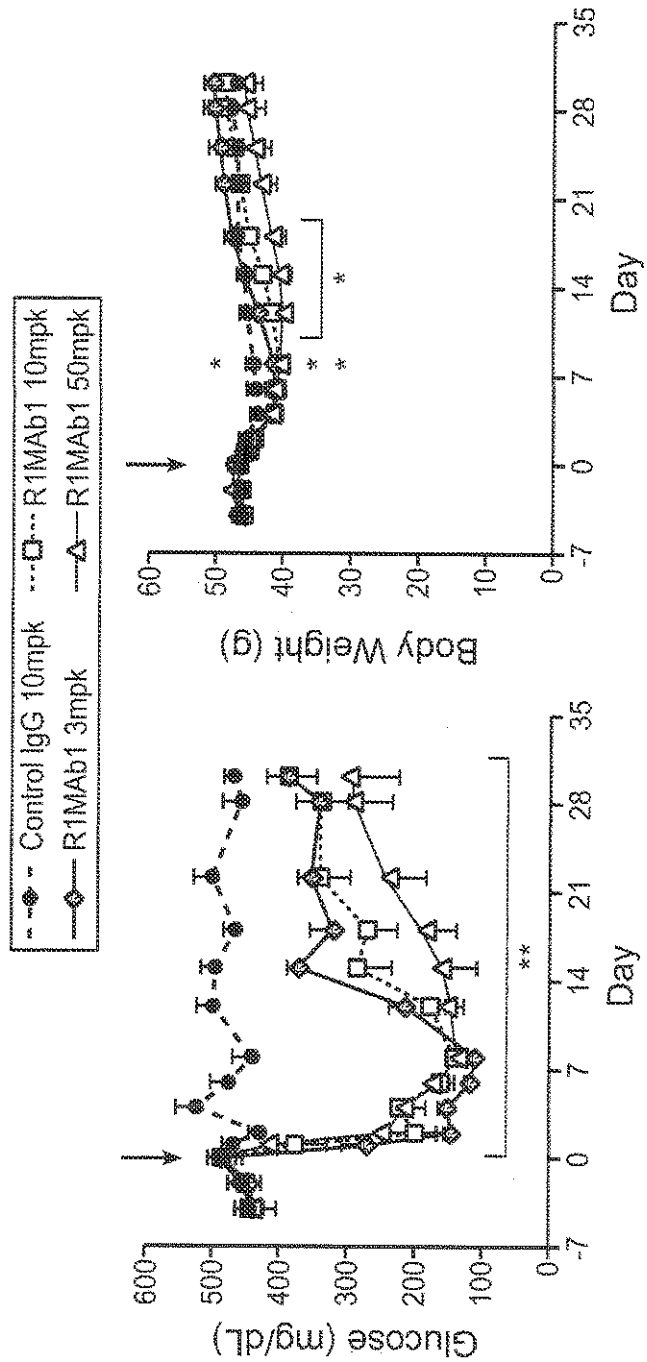

Control IgG 10mpk
R1MAb1 10mpk
R1MAb1 3mpk
R1MAb1 50mpk
Glucose (mg/dL)
Day
Body Weight (g)
Day

FIG. 2A

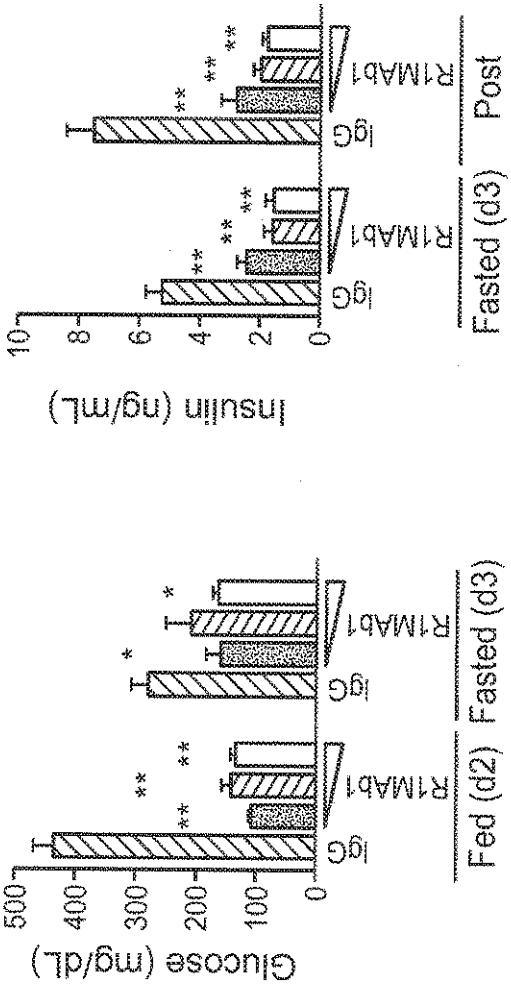

Glucose (mg/dL)
IgG
R1MAb1
Fed (d2)
Fasted (d3)
Insulin (ng/mL)
Fasted (d3)
Post

FIG. 2B

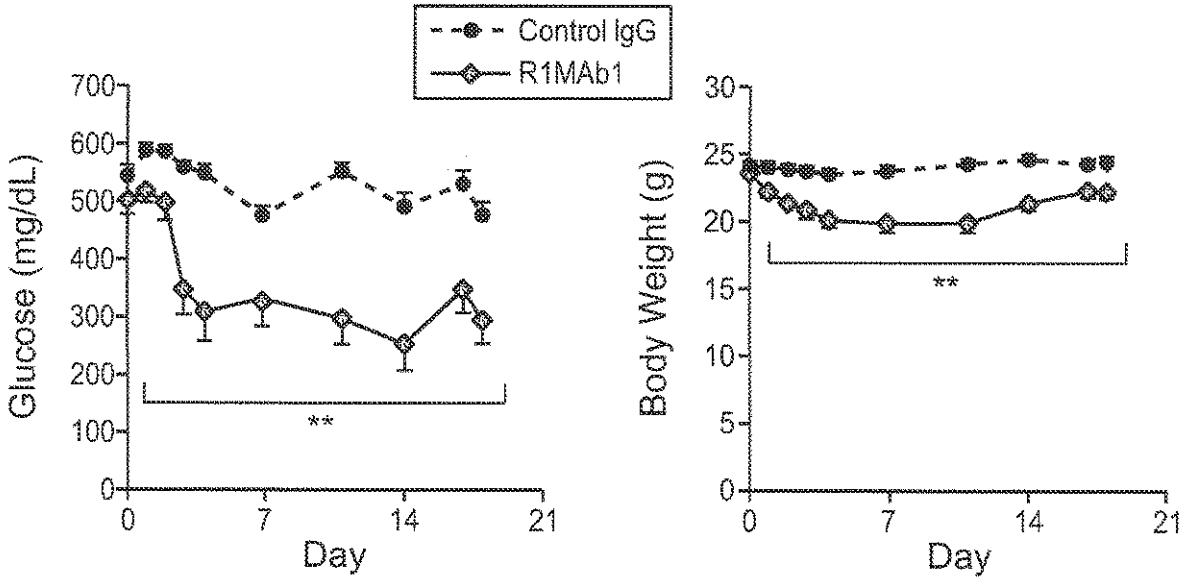

Control IgG
R1MAb1
Glucose (mg/dL)
Body Weight (g)
Day
**
**

FIG. 2C

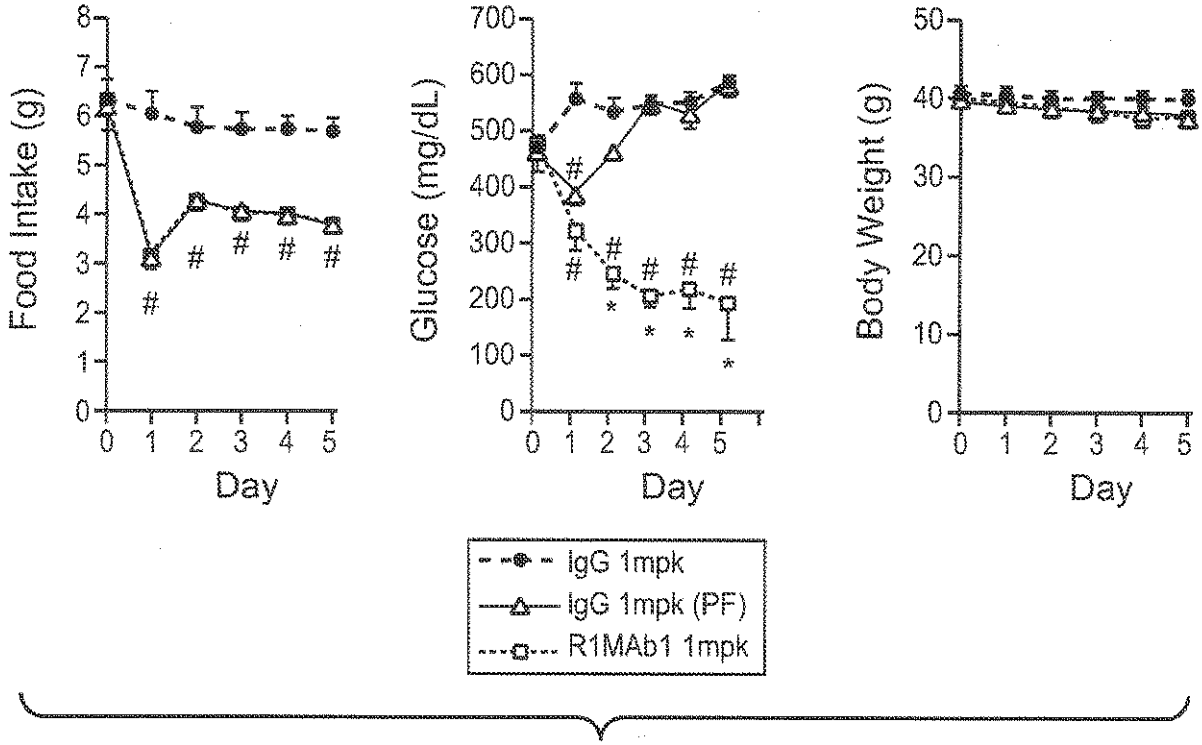

Food Intake (g)
Glucose (mg/dL)
Body Weight (g)
Day
IgG 1mpk
IgG 1mpk (PF)
R1MAb1 1mpk

FIG. 2D

FIG. 2E

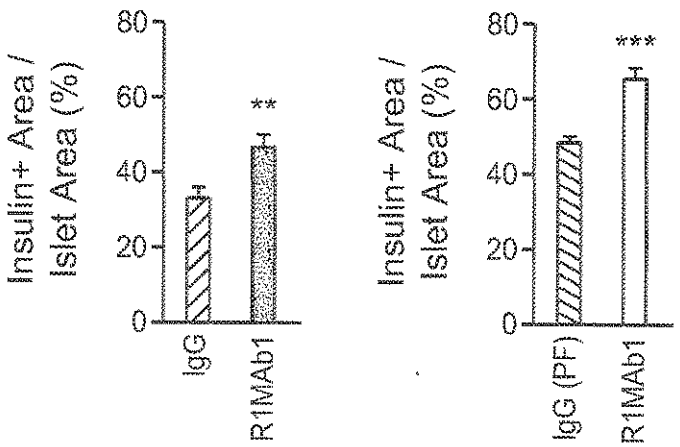
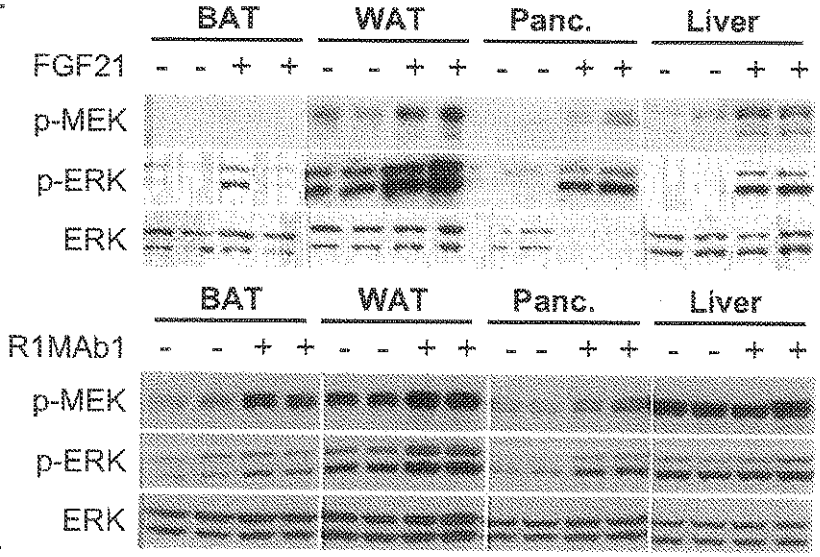


FIG. 3A



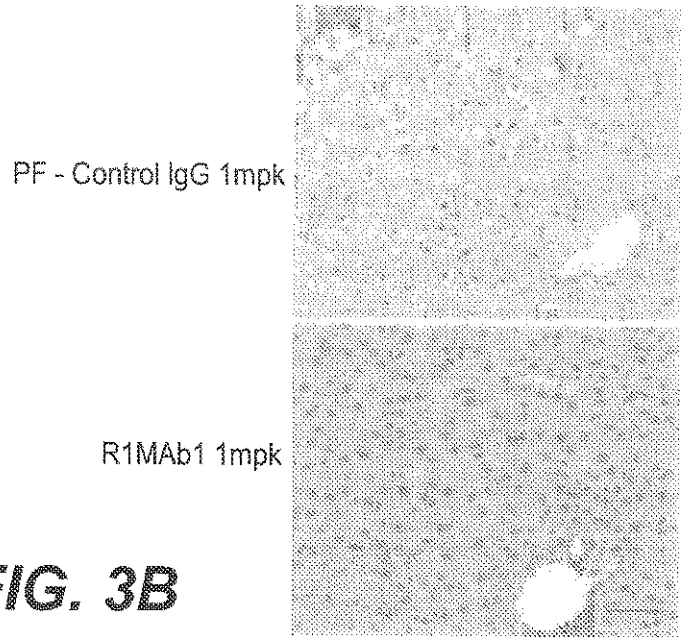


FIG. 3B

FIG. 3C

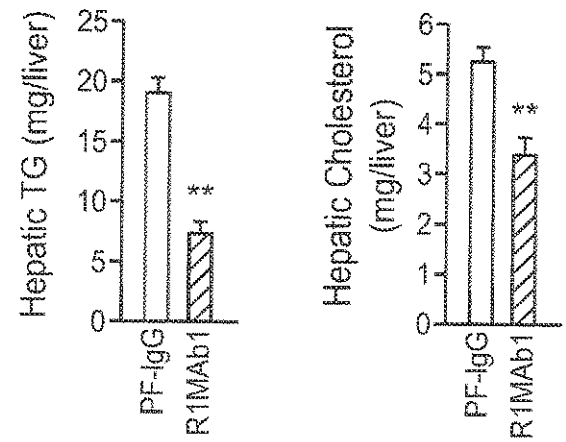


FIG. 3D

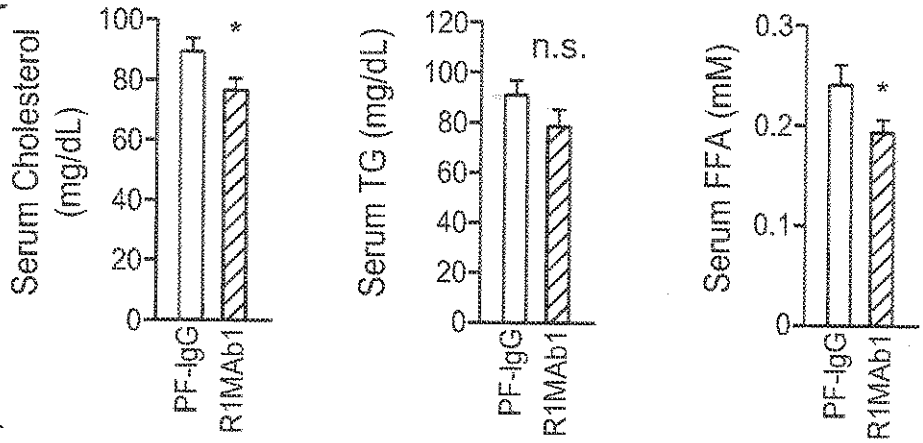
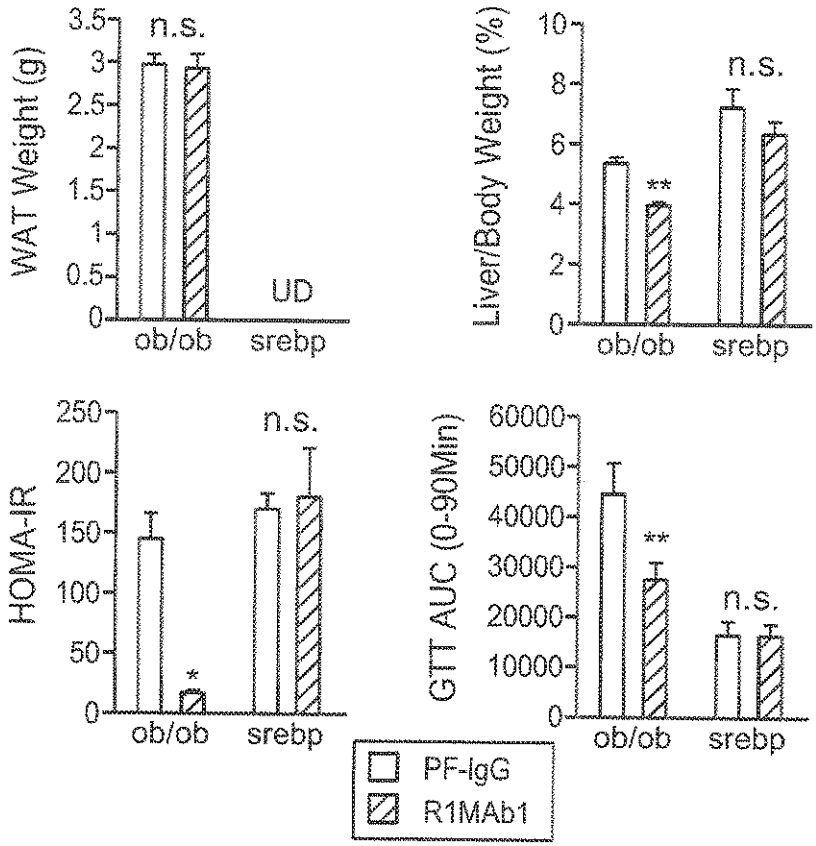


FIG. 3E



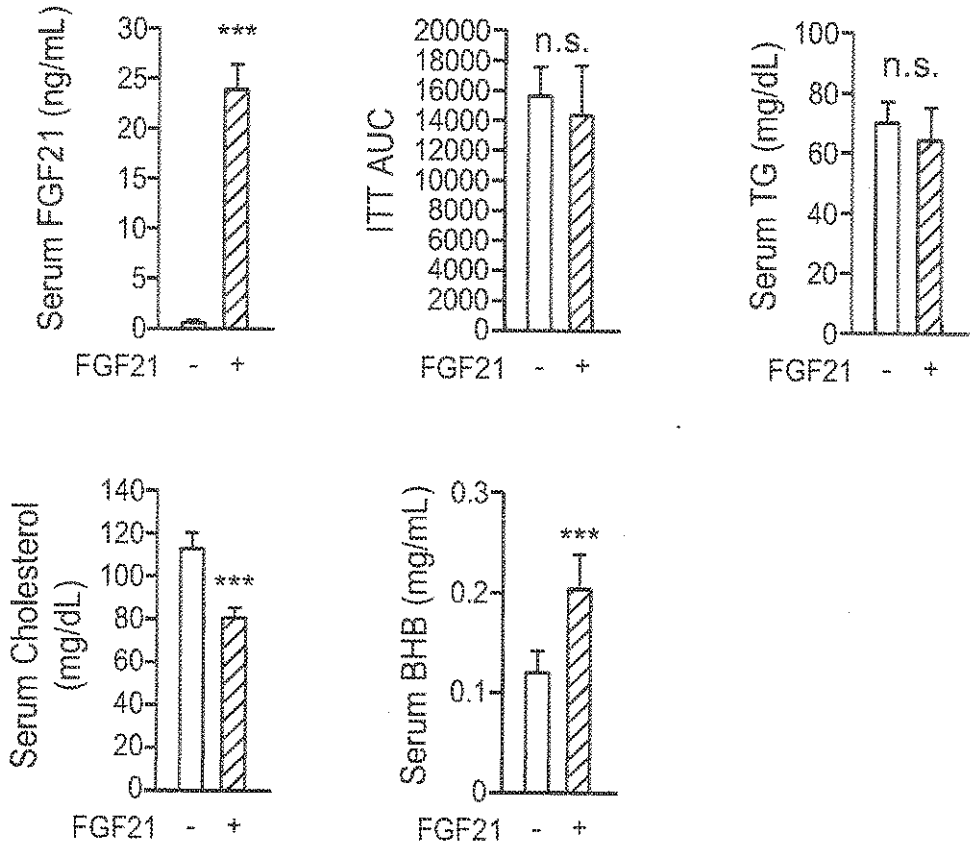

Serum FGF21 (ng/mL)
30
25
20
15
10
5
0
***
FGF21 - +
ITT AUC
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
n.s.
FGF21 - +
Serum TG (mg/dL)
100
80
60
40
20
0
n.s.
FGF21 - +
Serum Cholesterol (mg/dL)
140
120
100
80
60
40
20
0
***
FGF21 - +
Serum BHB (mg/mL)
0.3
0.2
0.1
0
***
FGF21 - +

FIG. 3F

FIG. 4A

FIG. 4A-1 FIG. 4A-2

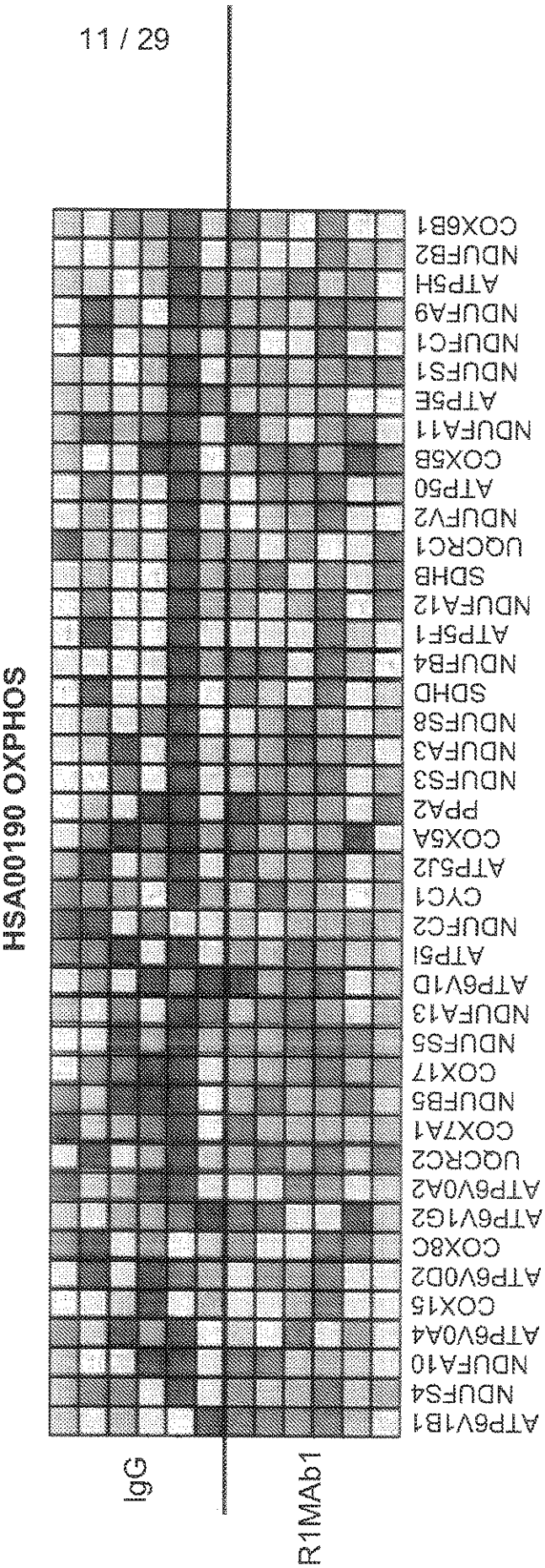


FIG. 4A-1

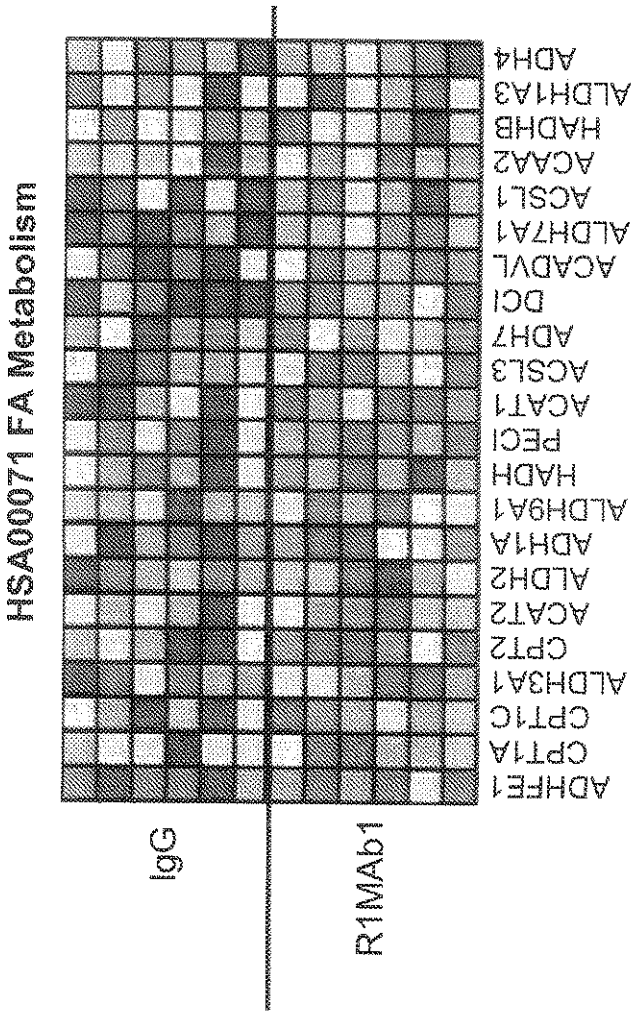

HSA00071 FA Metabolism
IgG
R1MAb1
ADHFE1
CPT1A
CPT1C
ALDH3A1
CPT2
ACAT2
ALDH2
ADH1A
ALDH9A1
HADH
PECI
ACAT1
ACSL3
ADH7
DCI
ACADVL
ALDH7A1
ACSL1
ACAA2
HADHB
ALDH1A3
ADH4

FIG. 4A-2

FIG. 4B

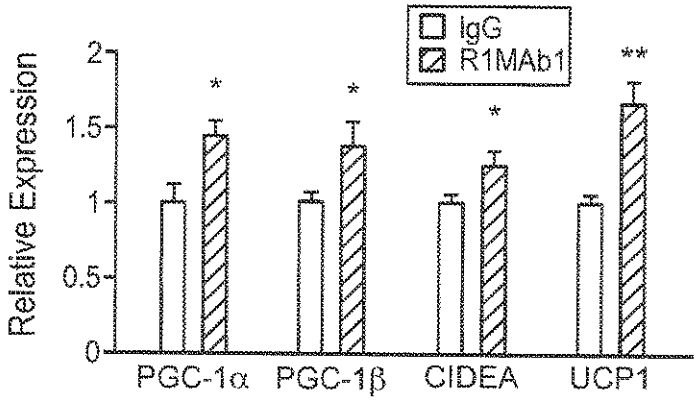
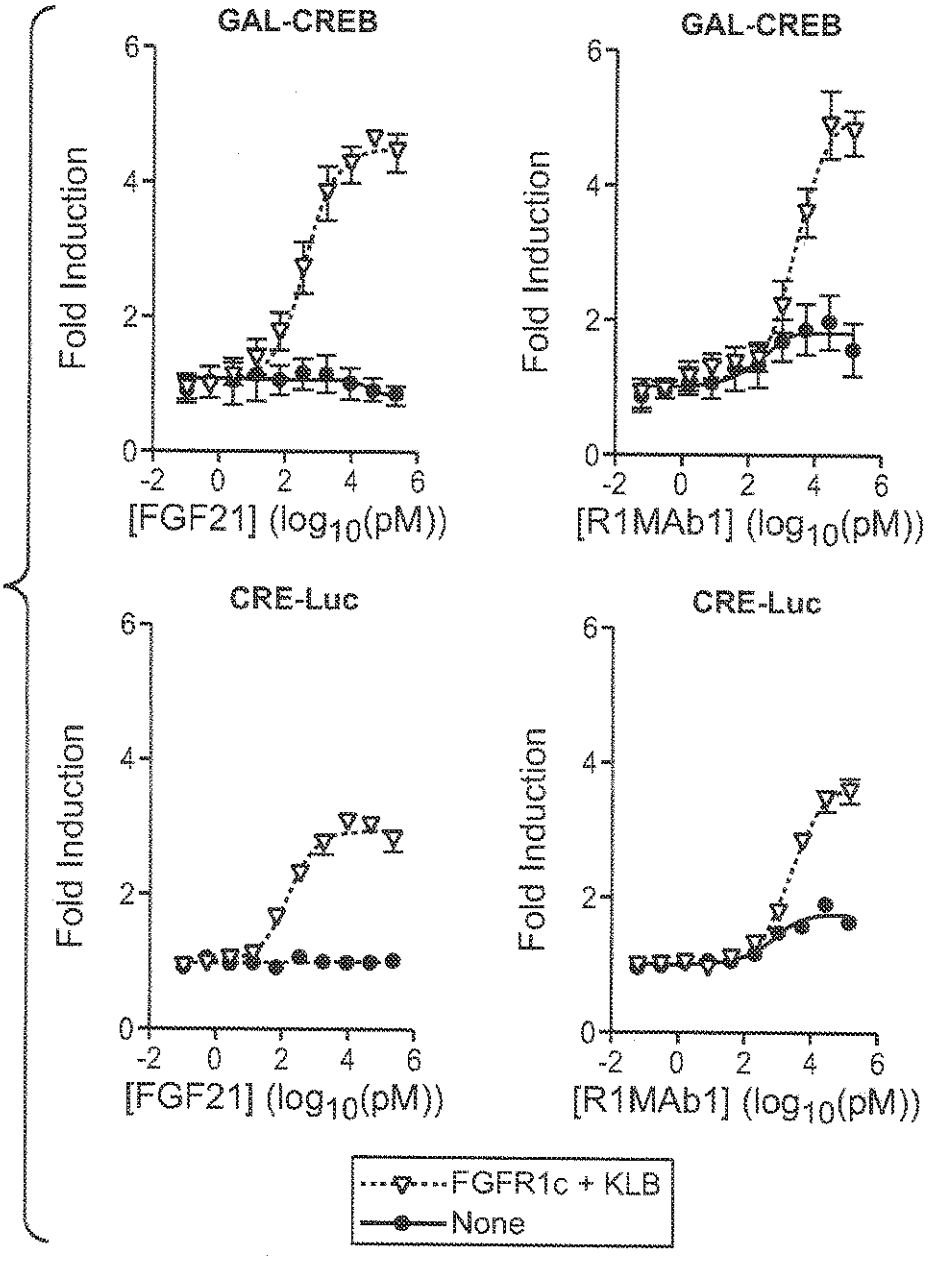

IgG
R1MAb1
Relative Expression
2
1.5
1
0.5
0
*
*
*
**
PGC-1α
PGC-1β
CIDEA
UCP1

FIG. 4C


GAL-CREB
Fold Induction
[FGF21] (log10(pM))
GAL-CREB
Fold Induction
[R1MAb1] (log10(pM))
CRE-Luc
Fold Induction
[FGF21] (log10(pM))
CRE-Luc
Fold Induction
[R1MAb1] (log10(pM))
FGFR1c + KLB
None

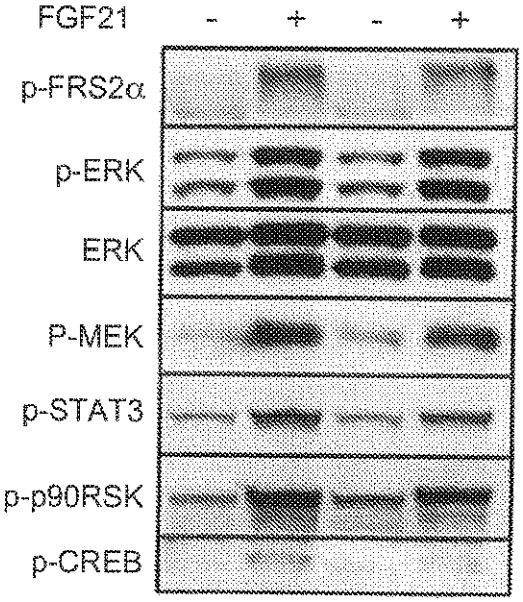


FIG. 4D

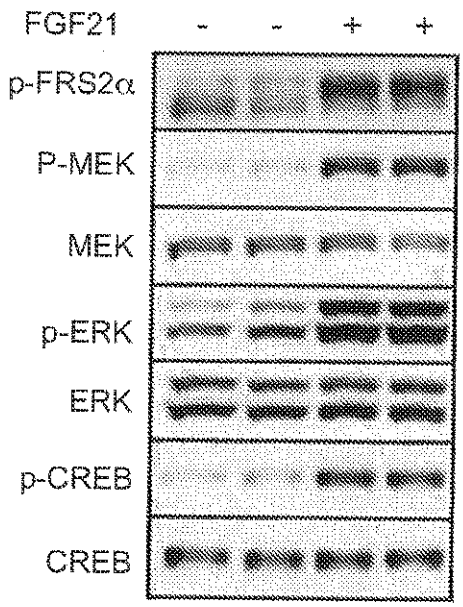


FIG. 4E

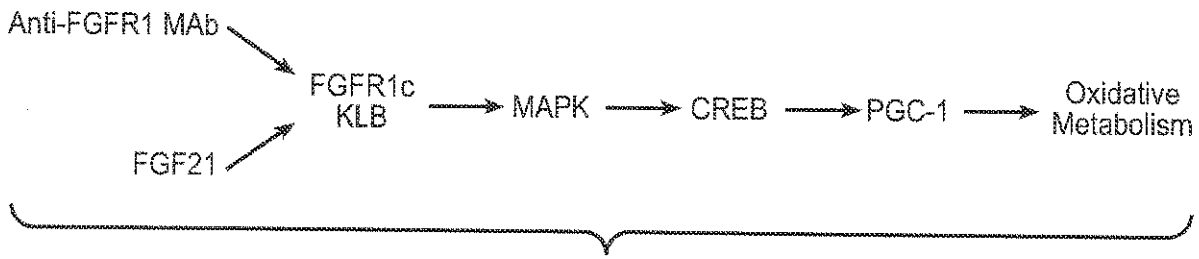


FIG. 4F

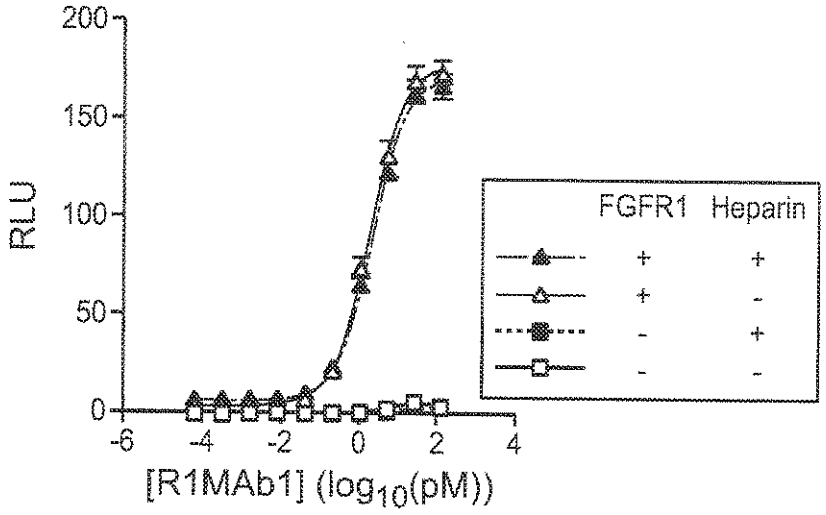
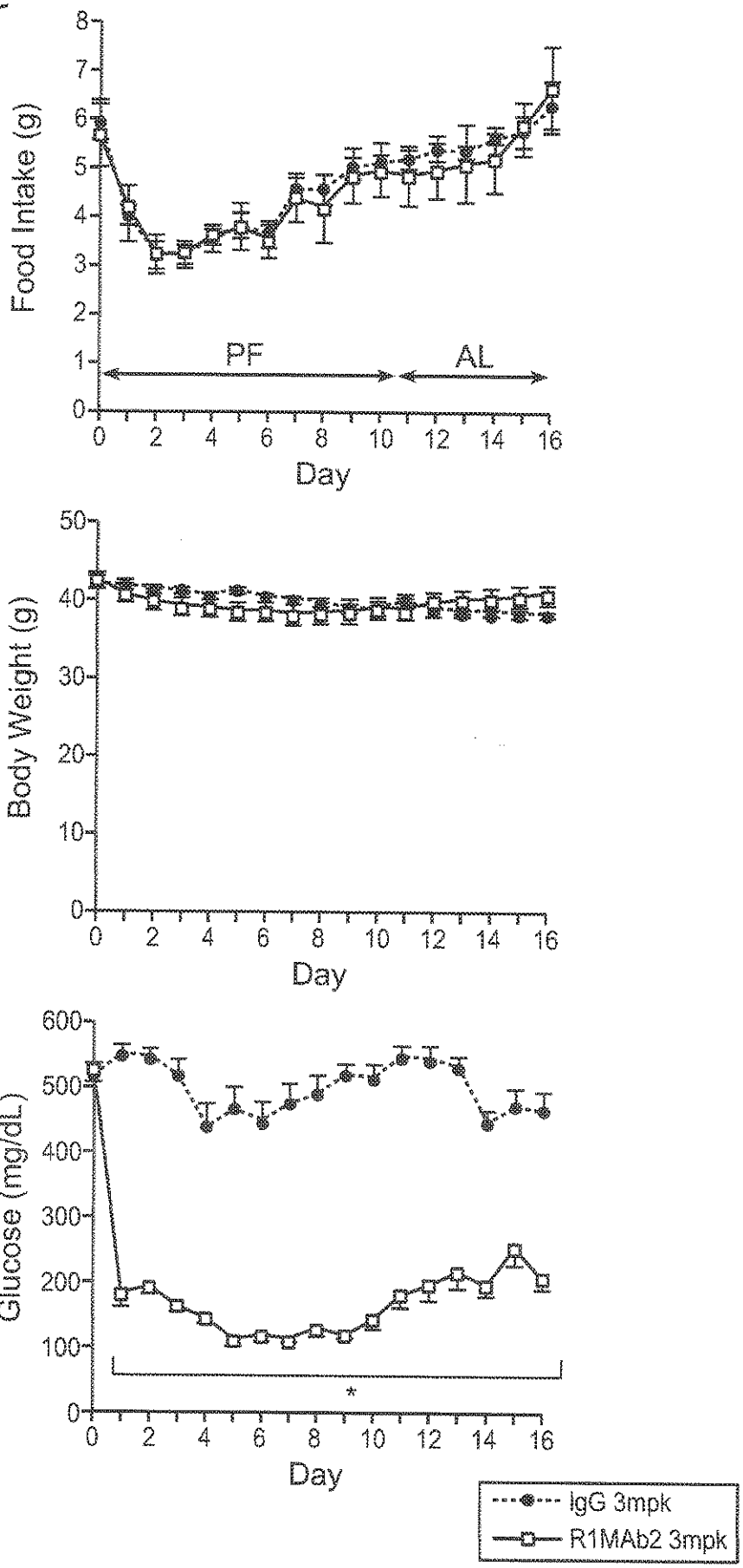


FIG. 5

FIG. 6A


Food Intake (g)
PF
AL
Day
Body Weight (g)
Day
Glucose (mg/dL)
*
Day
IgG 3mpk
R1MAb2 3mpk

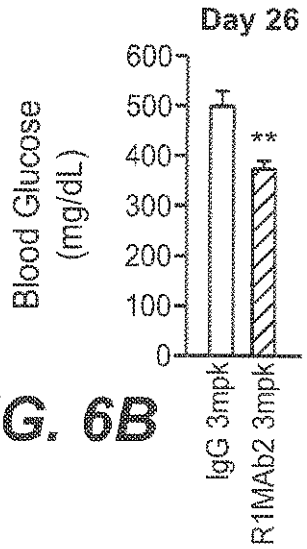


FIG. 6B

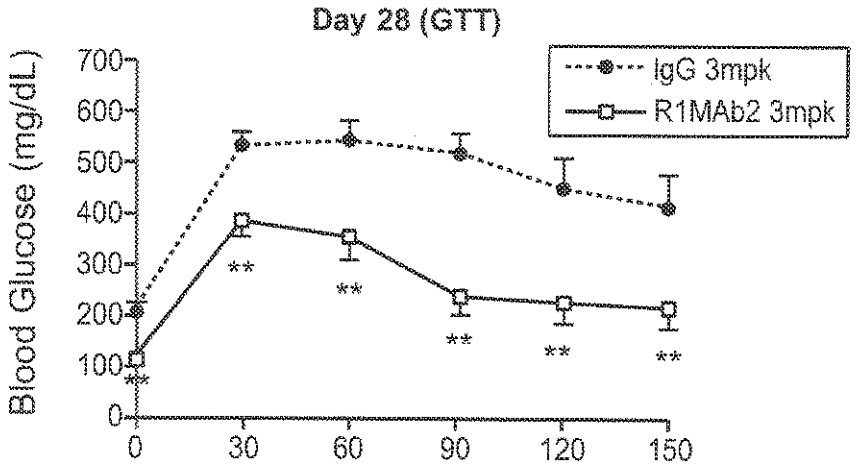


FIG. 6C

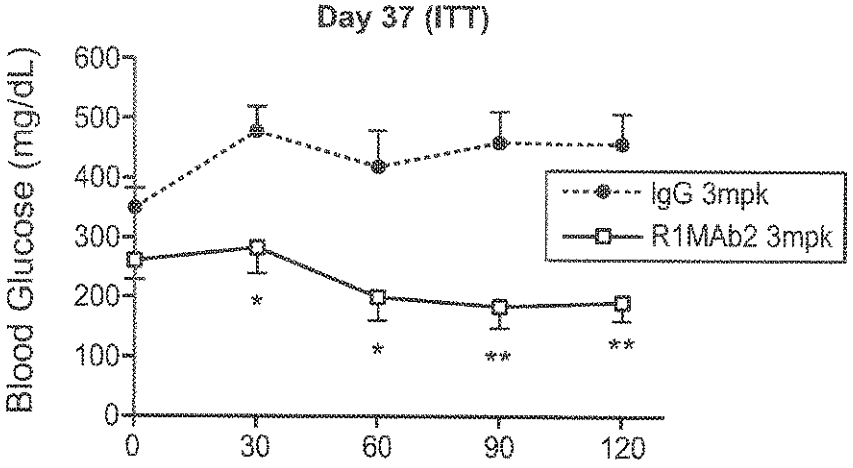


FIG. 6D

FIG. 7A

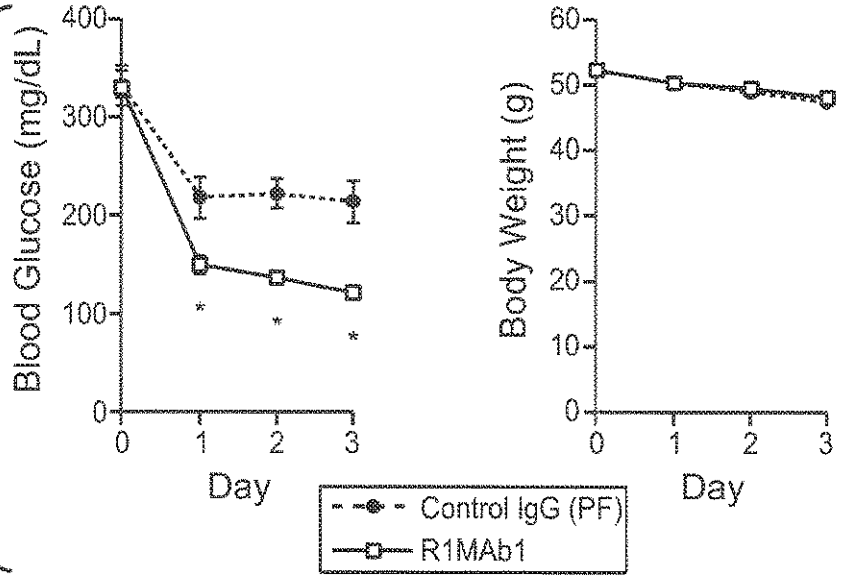


FIG. 7B

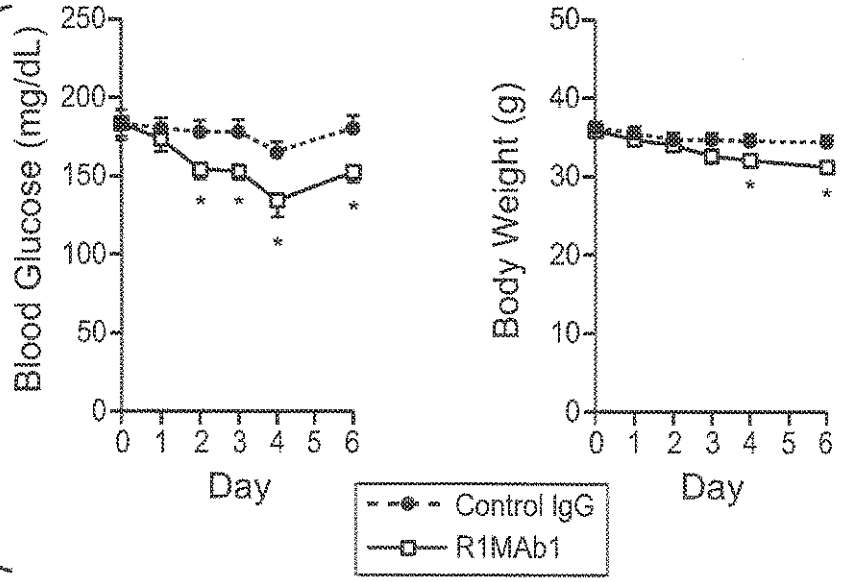


FIG. 7C

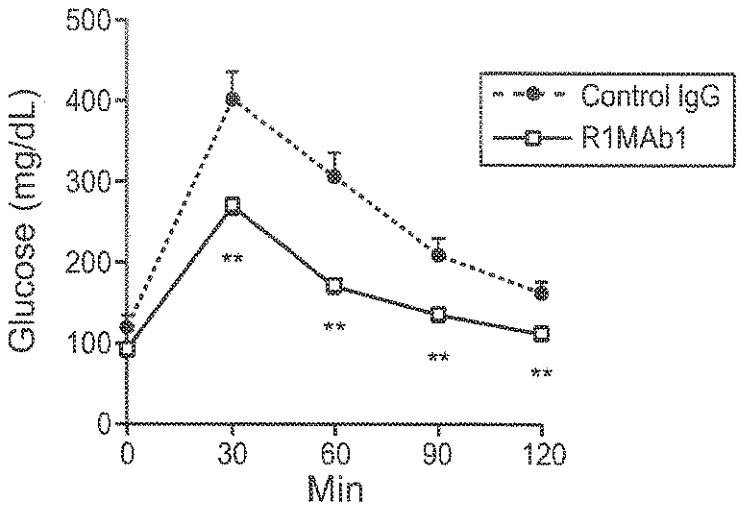


FIG. 7D

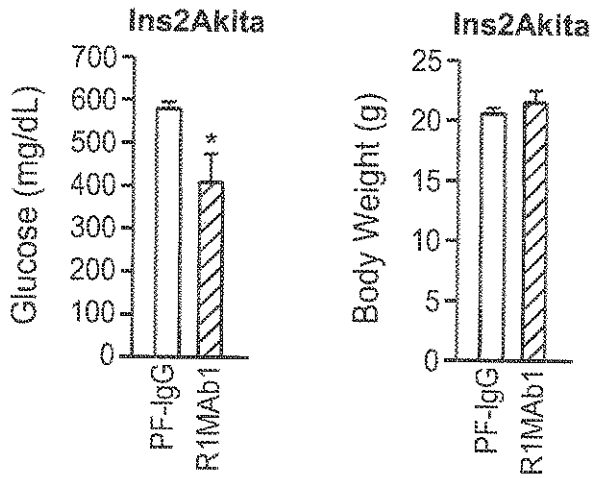


FIG. 8A

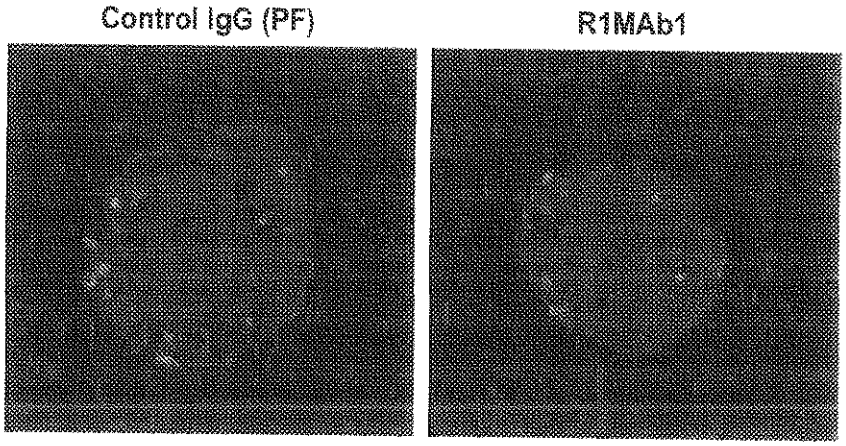
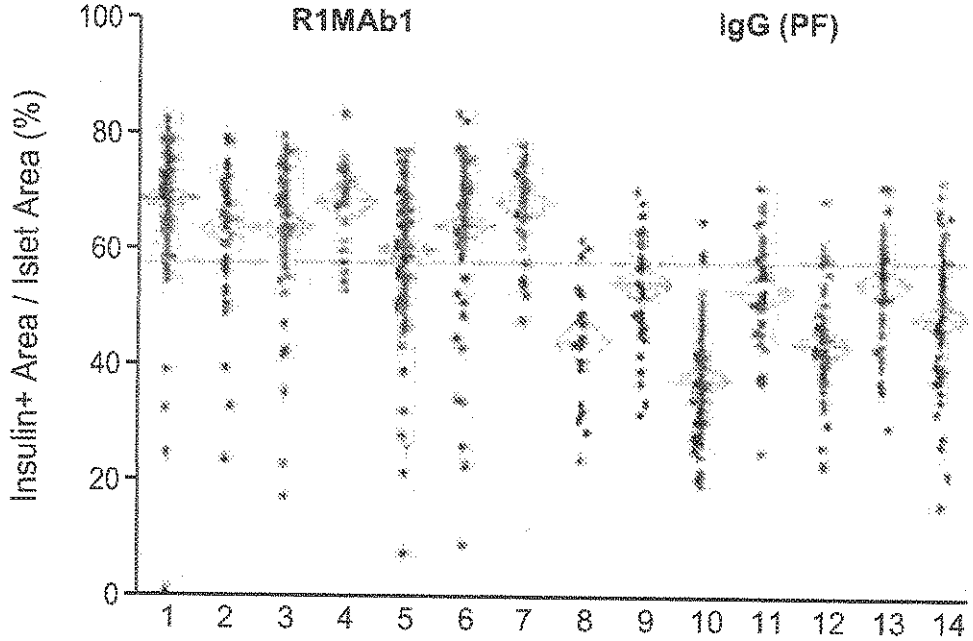


FIG. 8B



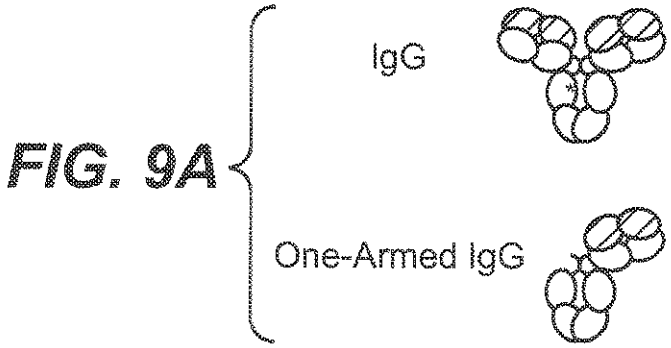


FIG. 9A

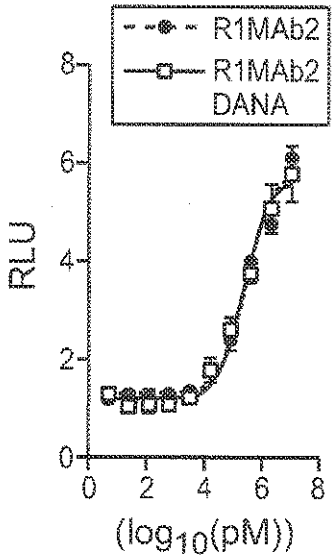


FIG. 9B

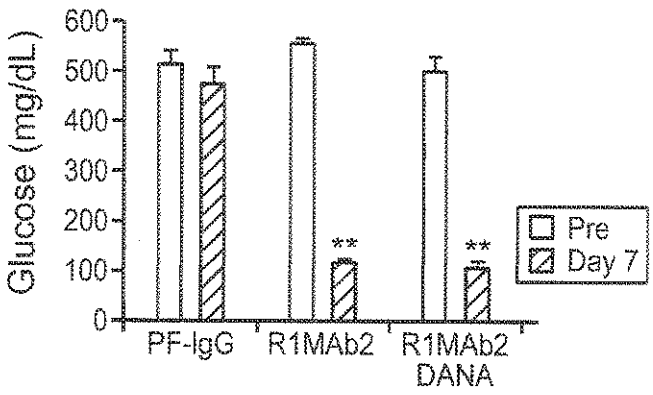


FIG. 9C

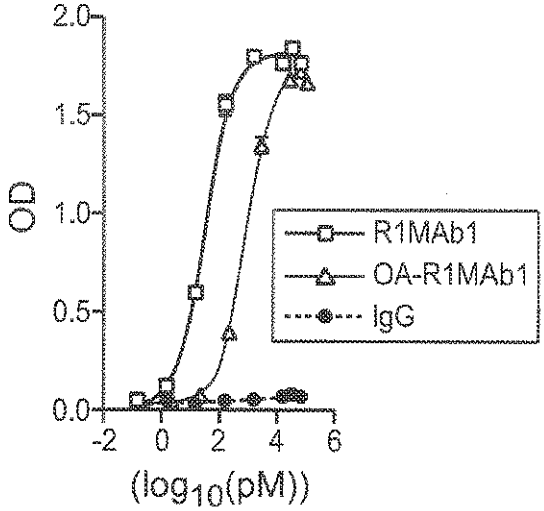


FIG. 9D

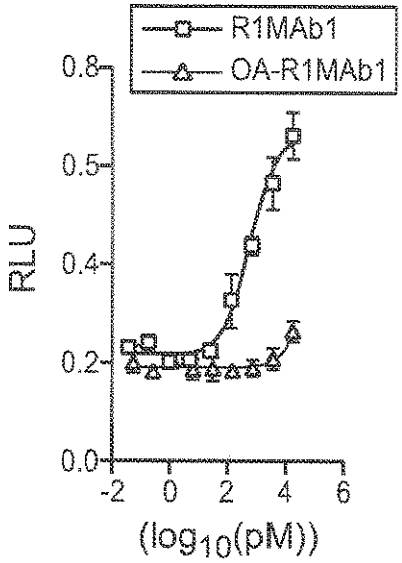


FIG. 9E

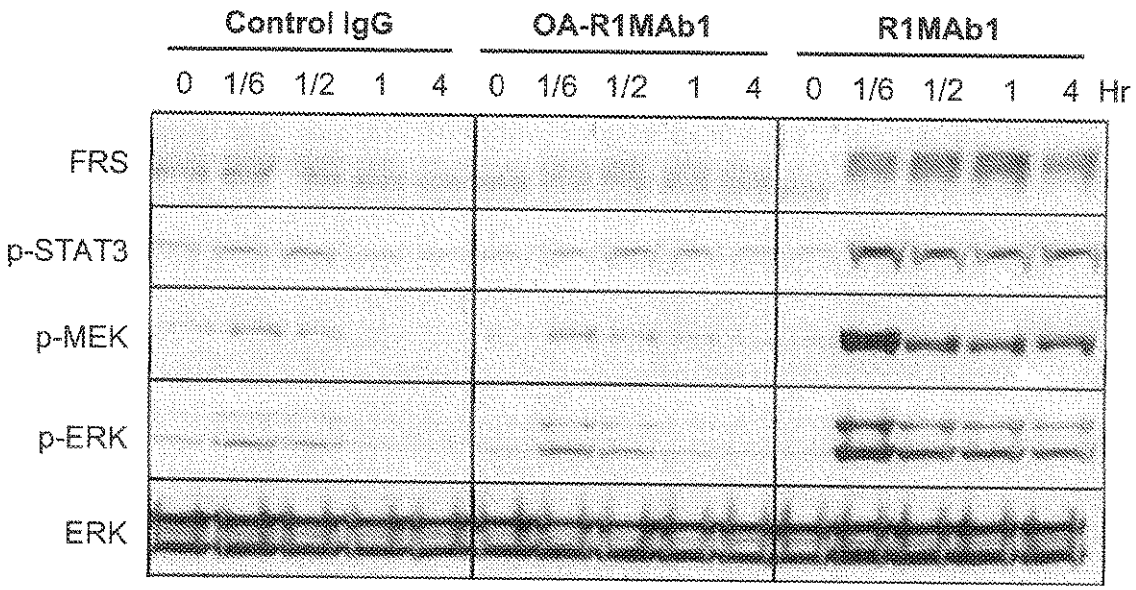
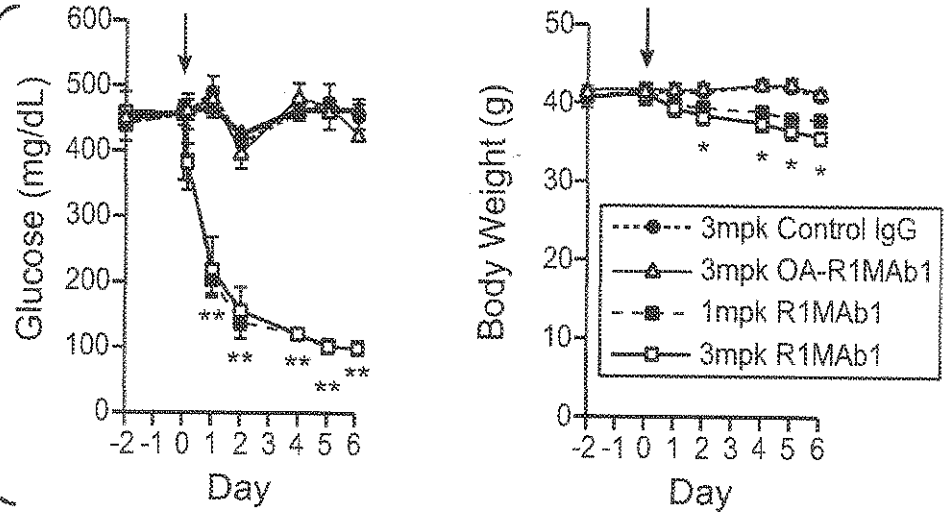


FIG. 9F

FIG. 9G



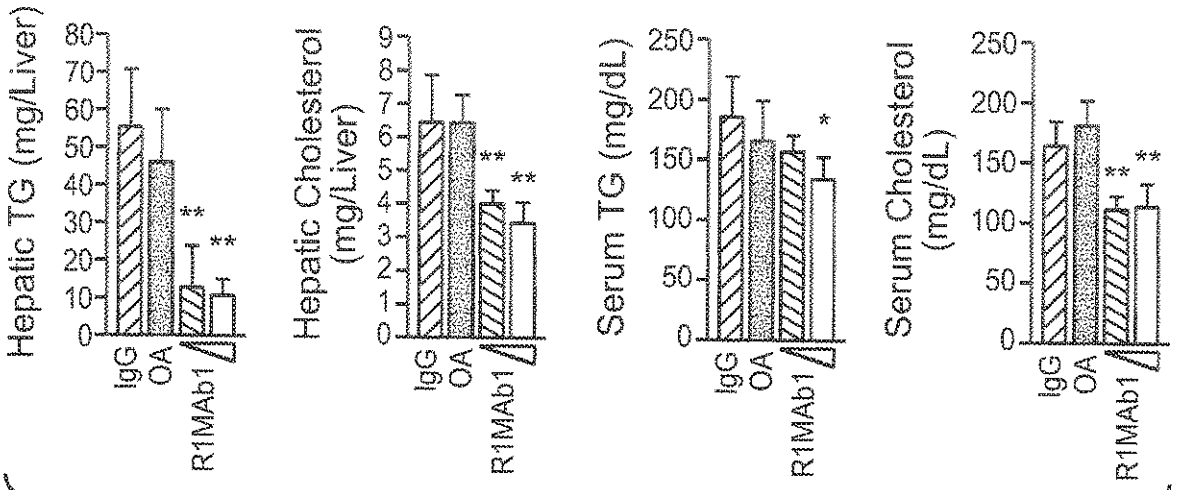


FIG. 9H

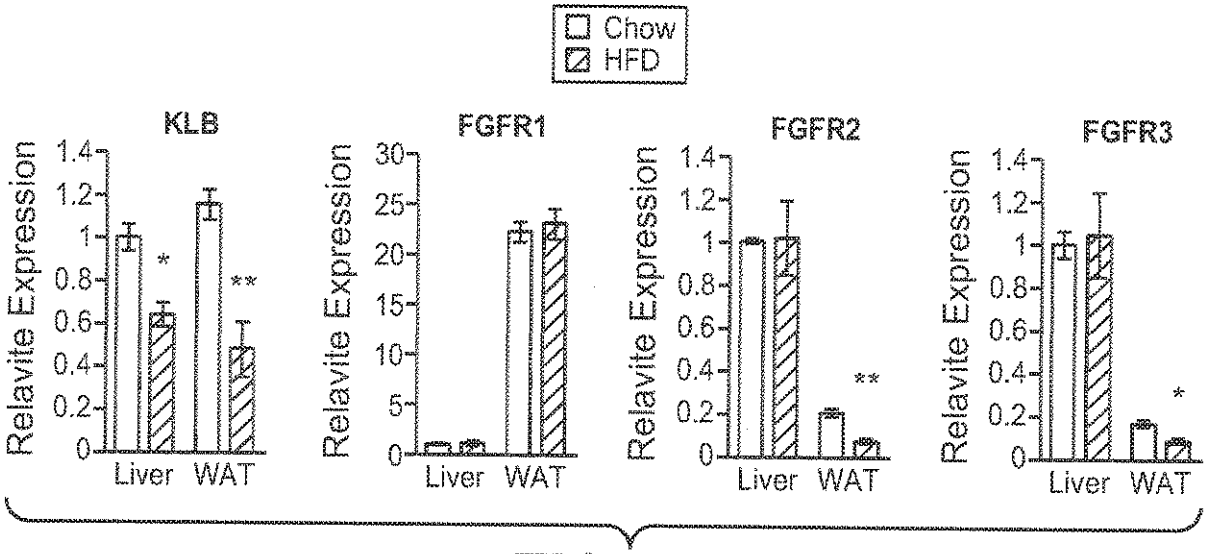

Chow
HFD
KLB
FGFR1
FGFR2
FGFR3
Relavite Expression
Liver
WAT

FIG. 10

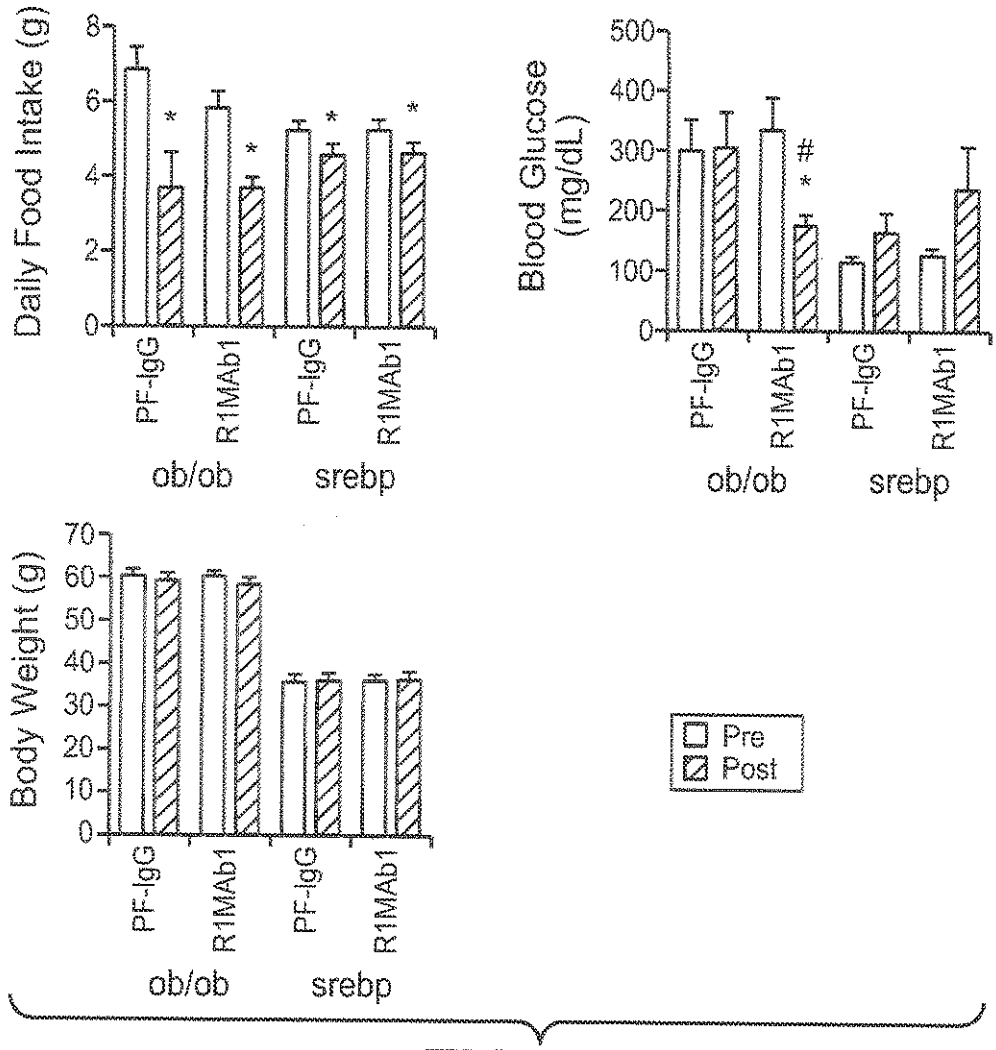

Daily Food Intake (g)
Blood Glucose (mg/dL)
Body Weight (g)
PF-IgG
R1MAb1
ob/ob
srebp
Pre
Post

FIG. 11

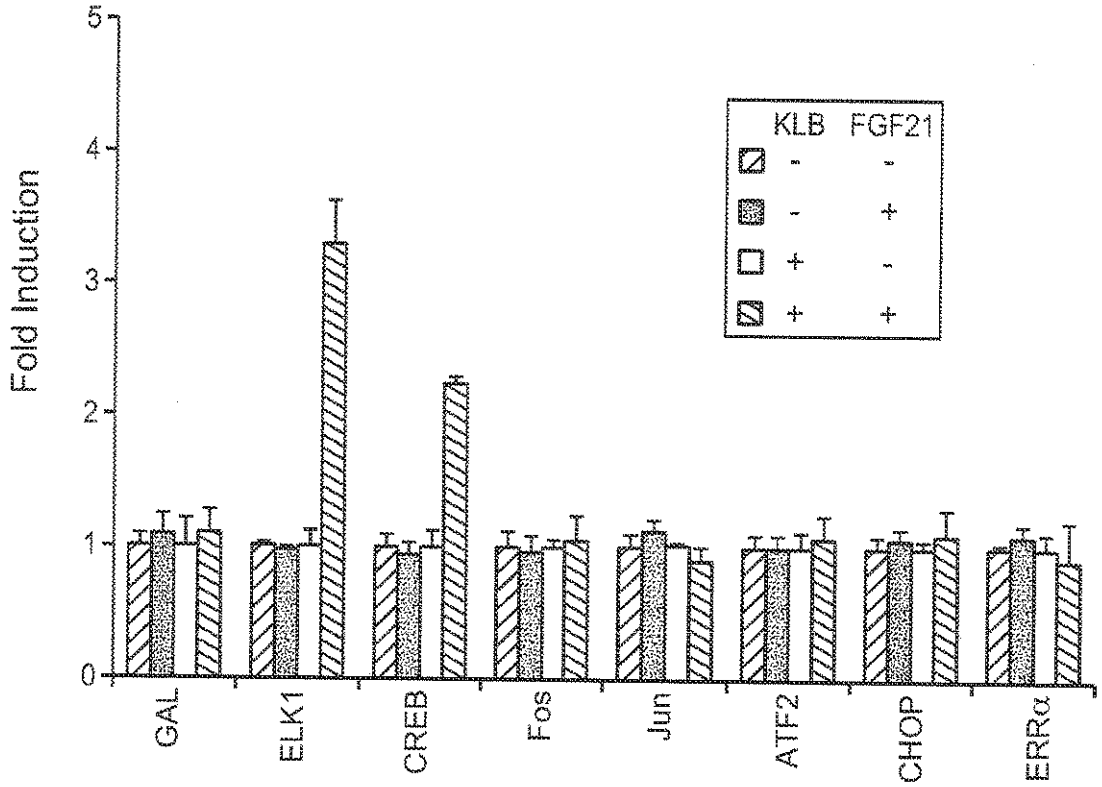


FIG. 12A

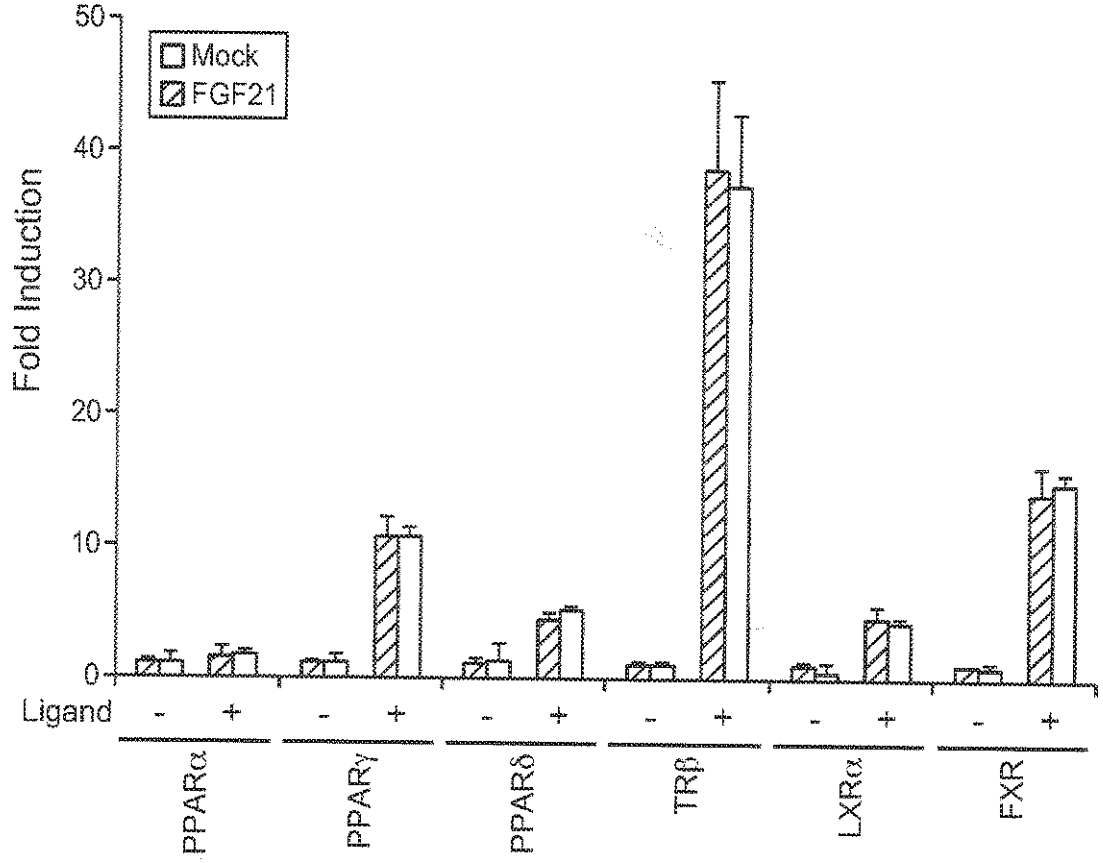


FIG. 12B

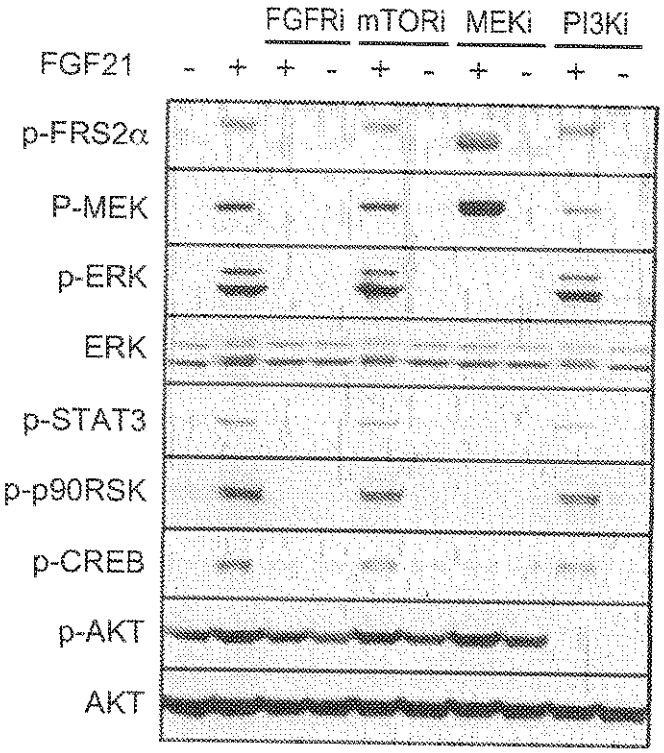


FIG. 12C

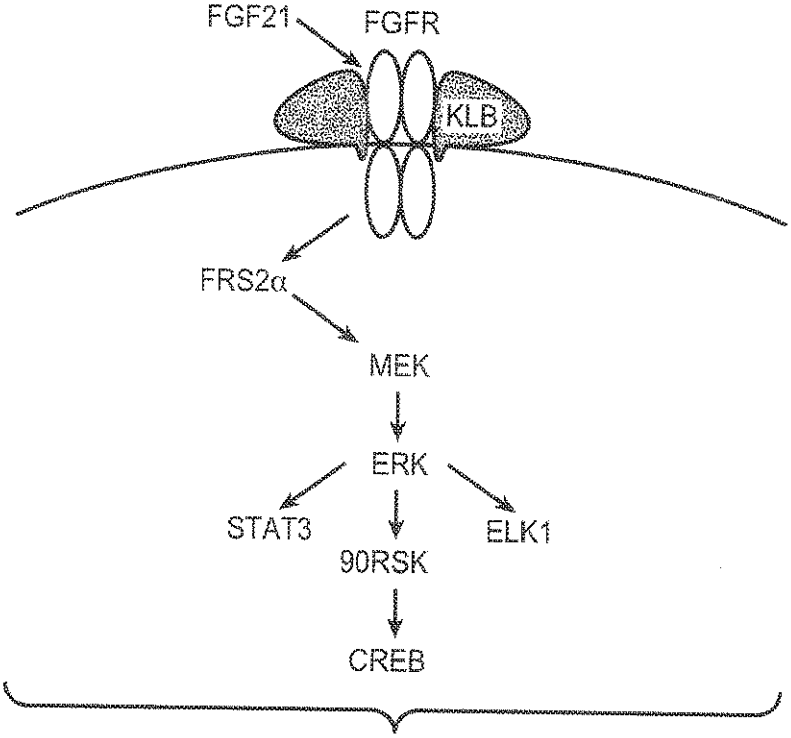
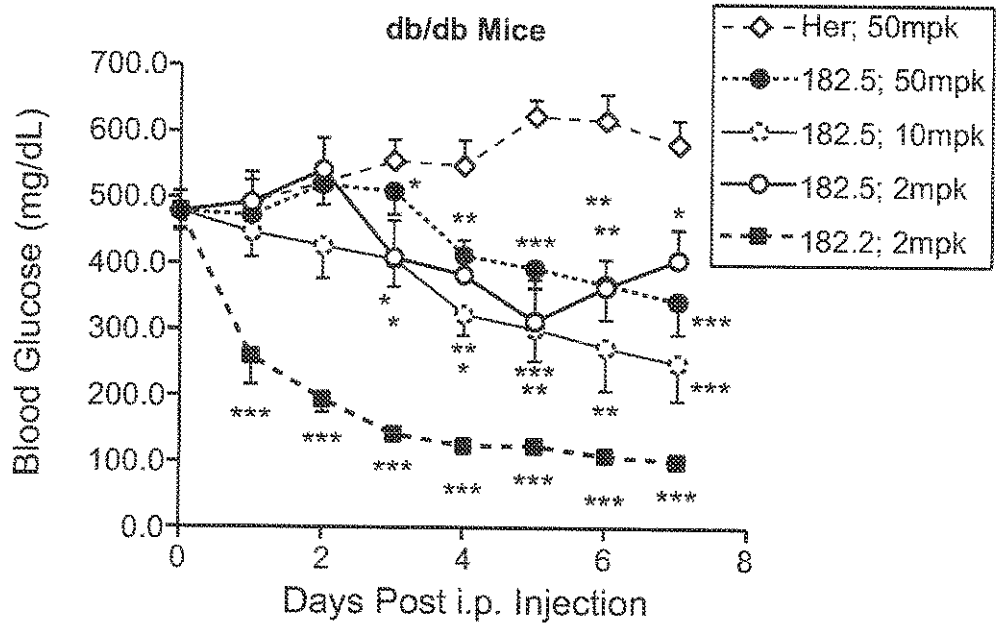
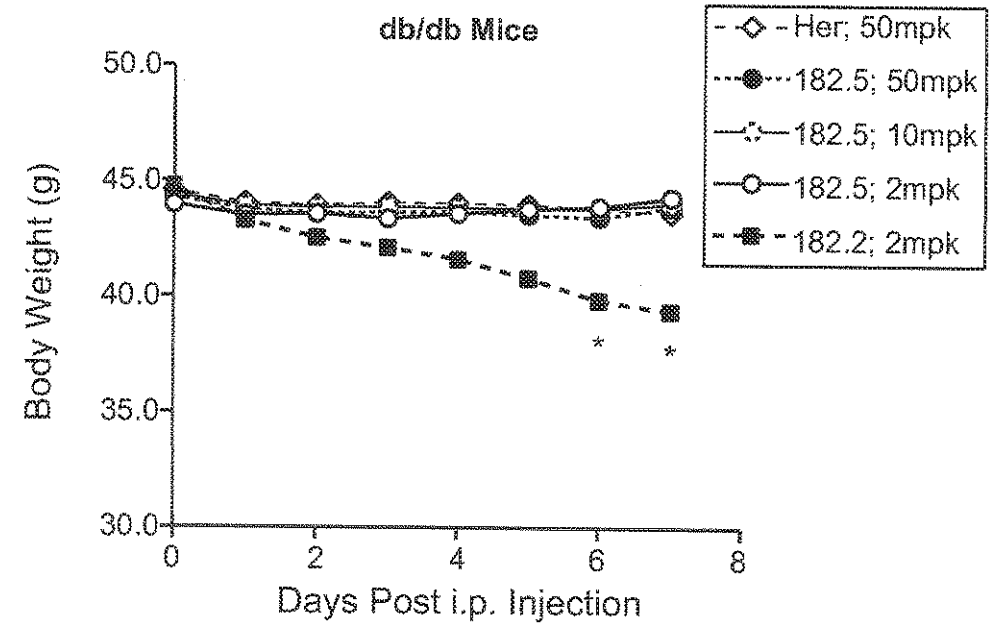


FIG. 12D





* p<0.05
** p<0.005
*** p<0.0005

FIG. 13

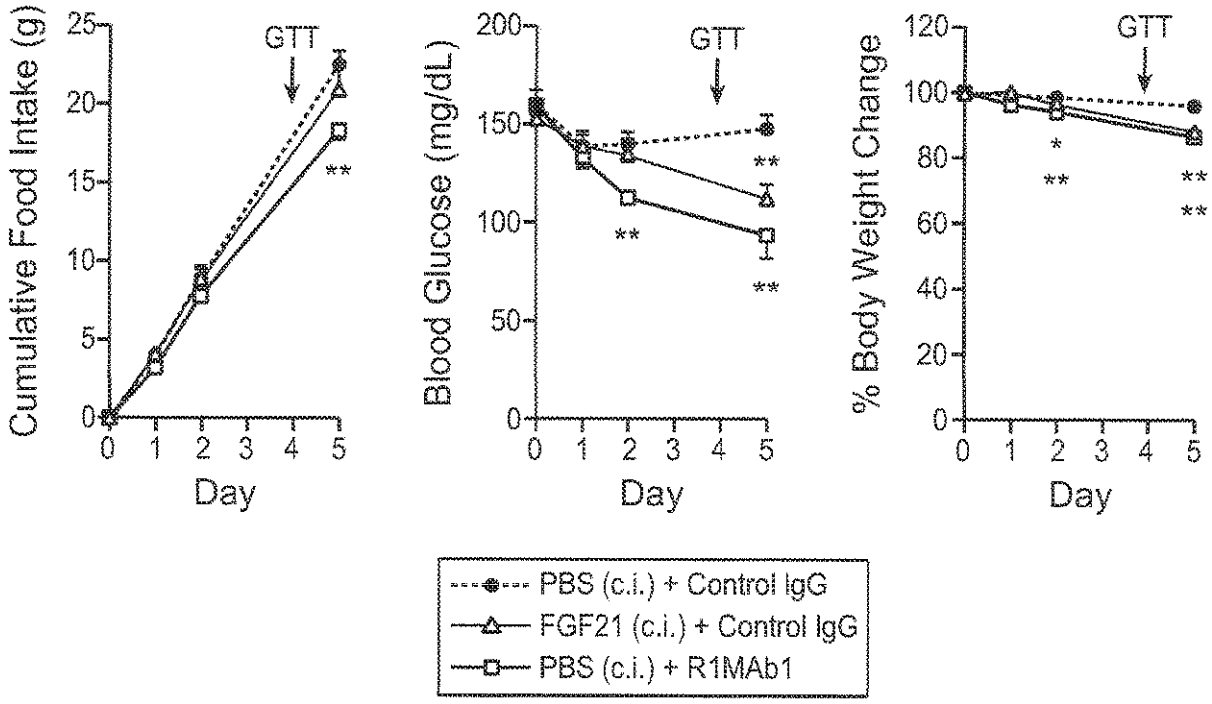


FIG. 14A

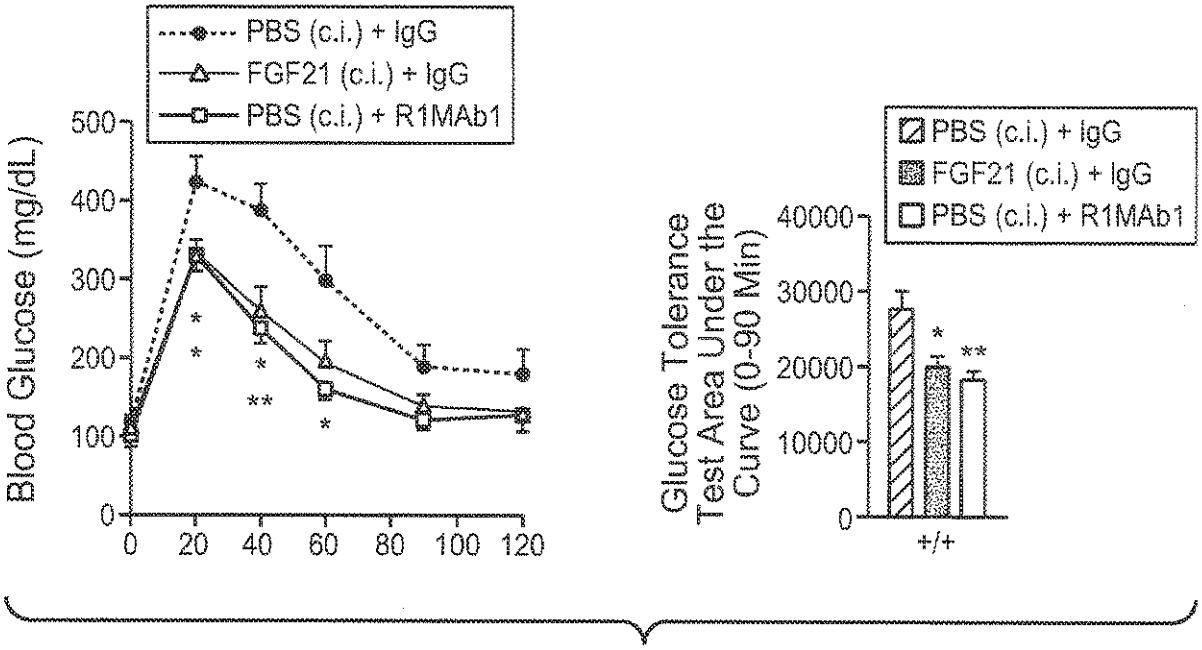


FIG. 14B

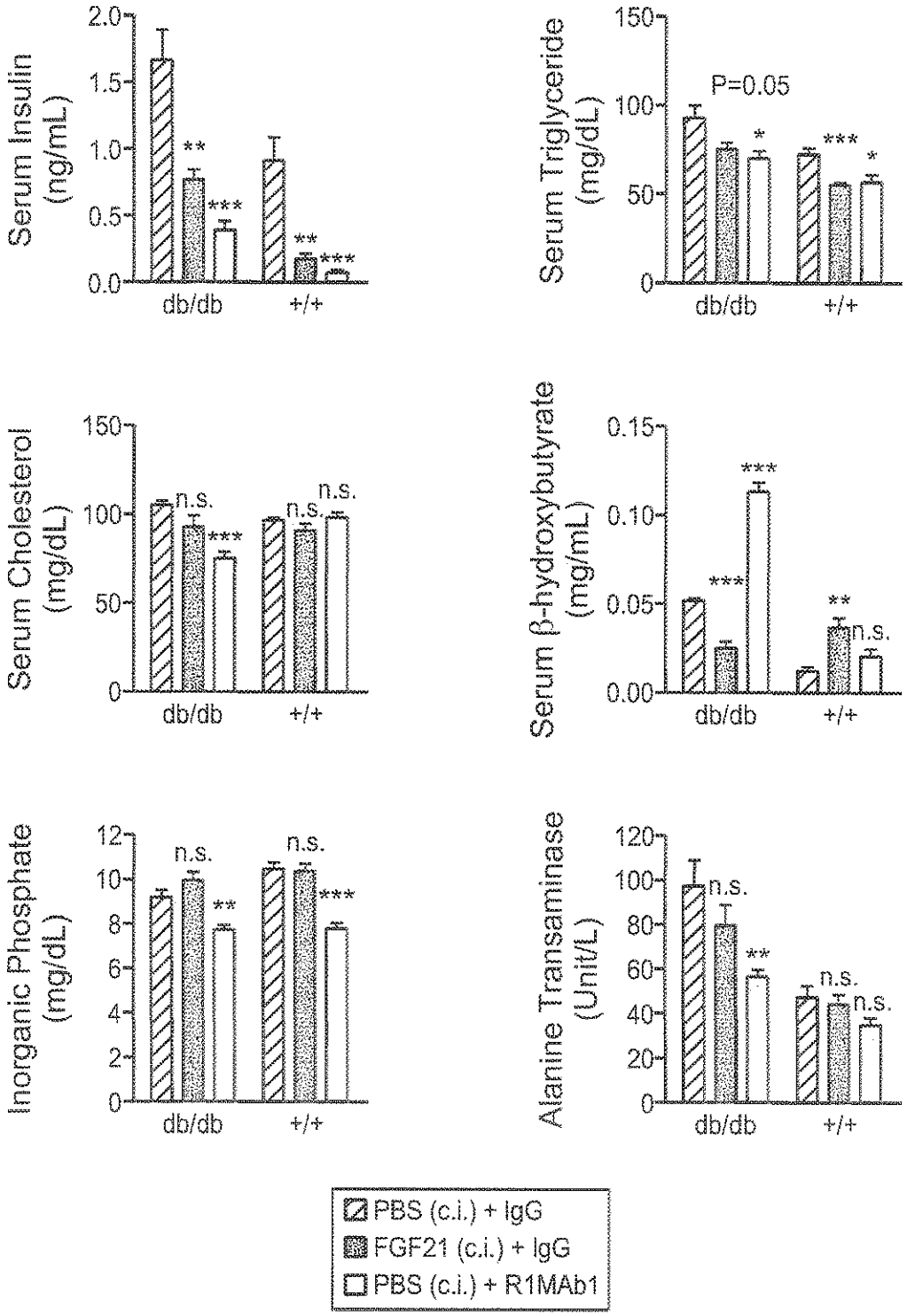

Serum Insulin (ng/mL)
2.0
1.5
1.0
0.5
0.0
**
***
**
***
db/db
+/+
Serum Triglyceride (mg/dL)
150
100
50
0
P=0.05
*
***
*
db/db
+/+
Serum Cholesterol (mg/dL)
150
100
50
0
n.s.
***
n.s.
n.s.
db/db
+/+
Serum β-hydroxybutyrate (mg/mL)
0.15
0.10
0.05
0.00
***
***
**
n.s.
db/db
+/+
Inorganic Phosphate (mg/dL)
12
10
8
6
4
2
0
n.s.
**
n.s.
***
db/db
+/+
Alanine Transaminase (Unit/L)
120
100
80
60
40
20
0
n.s.
**
n.s.
n.s.
db/db
+/+
PBS (c.i.) + IgG
FGF21 (c.i.) + IgG
PBS (c.i.) + R1MAb1

FIG. 14C

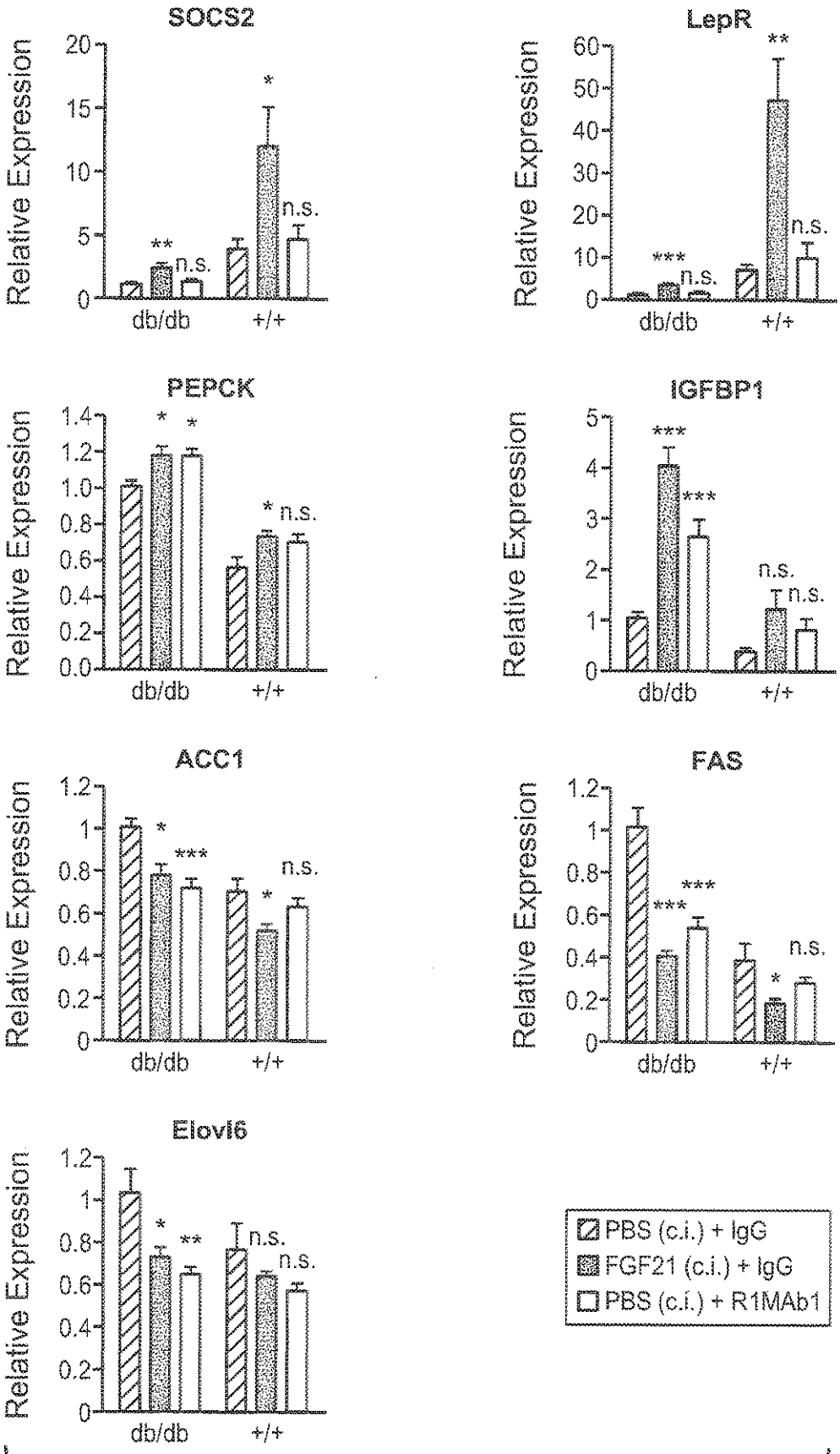

SOCS2
LepR
PEPCK
IGFBP1
ACC1
FAS
Elovl6
Relative Expression
db/db
+/+
n.s.
PBS (c.i.) + IgG
FGF21 (c.i.) + IgG
PBS (c.i.) + R1MAb1

FIG. 15

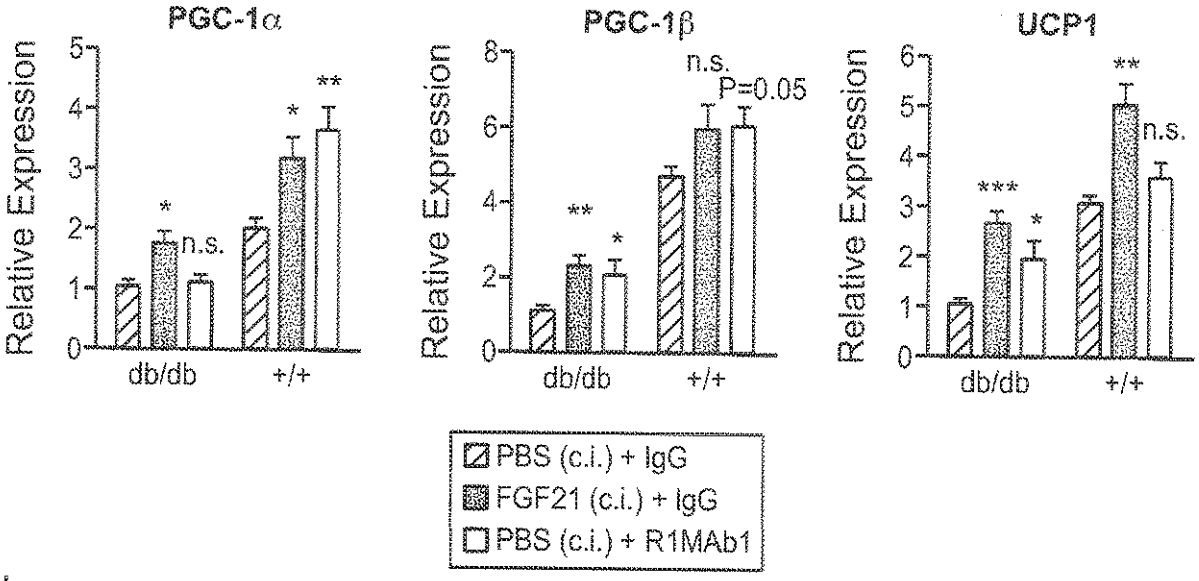


FIG. 16

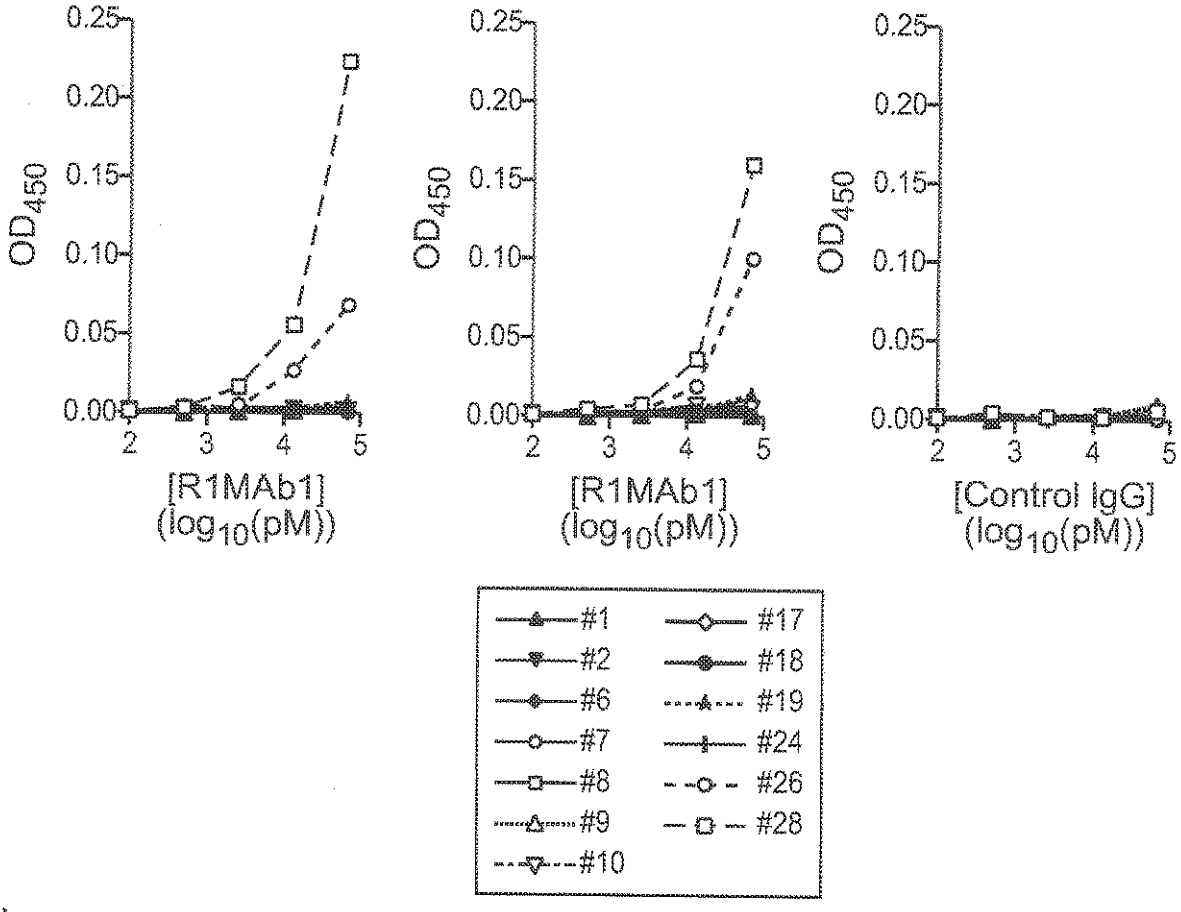


FIG. 17A

161 212

...MEKKLHAVPAAKTVKFKCPSSGTPNPTLRWLKNGKEFKPDHRIGGYKVRYATW...

FGFR1:KLHAVPAAKTVKFKCP(#26) FKPDHRIGGYKVRY(#28)

FGFR2:RLHAVPAANTVKFRCP FKQEHRIGGYKVRN

FGFR3:KLLAVPAANTVRFRCP FRGEHRIGGIKLRH

FGFR4:KLHAVPAGNTVKFRCP FHGENRIGGIRLRH

FIG. 17B

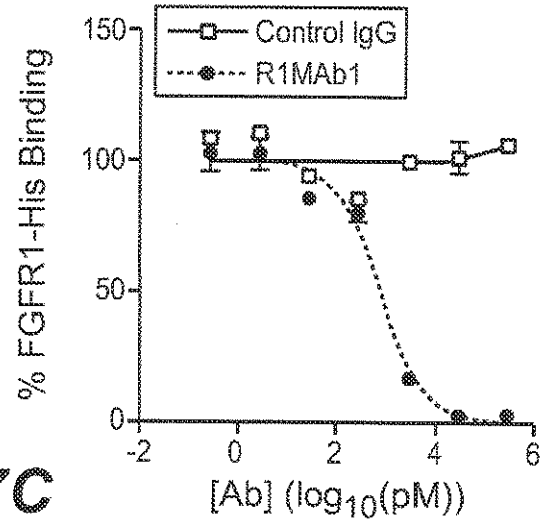


FIG. 17C

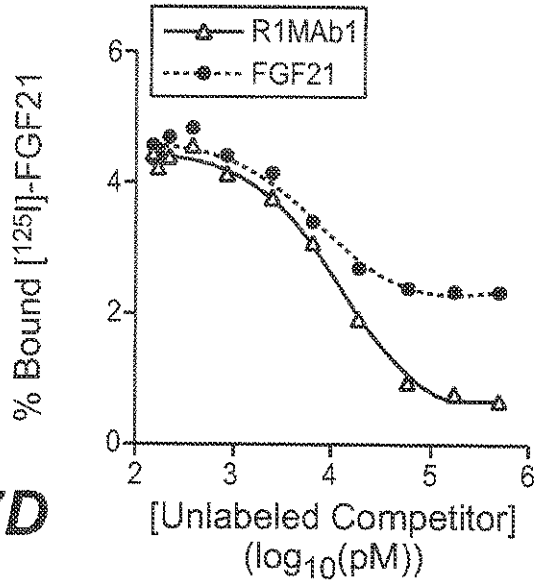


FIG. 17D