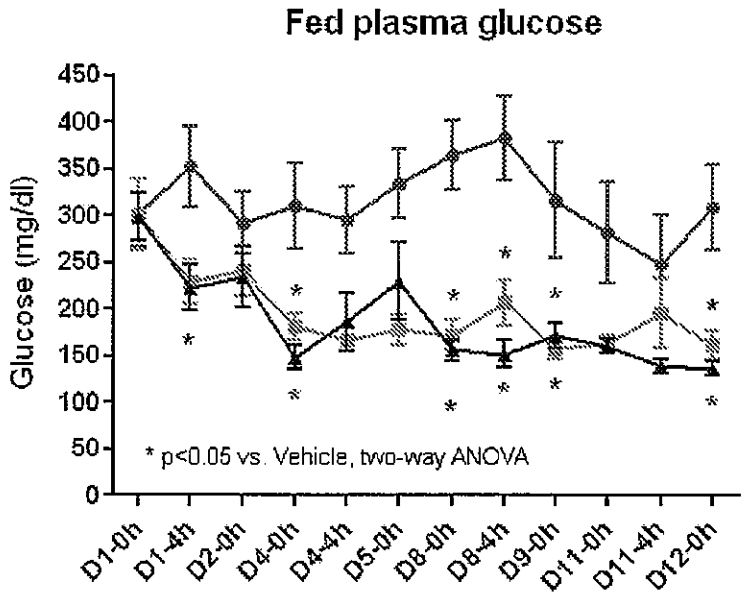

Fed plasma glucose
Glucose (mg/dl)
450
400
350
300
250
200
150
100
50
0
* p<0.05 vs. Vehicle, two-way ANOVA
D1-0h
D1-4h
D2-0h
D4-0h
D4-4h
D5-0h
D8-0h
D8-4h
D9-0h
D11-0h
D11-4h
D12-0h

FIG 1A

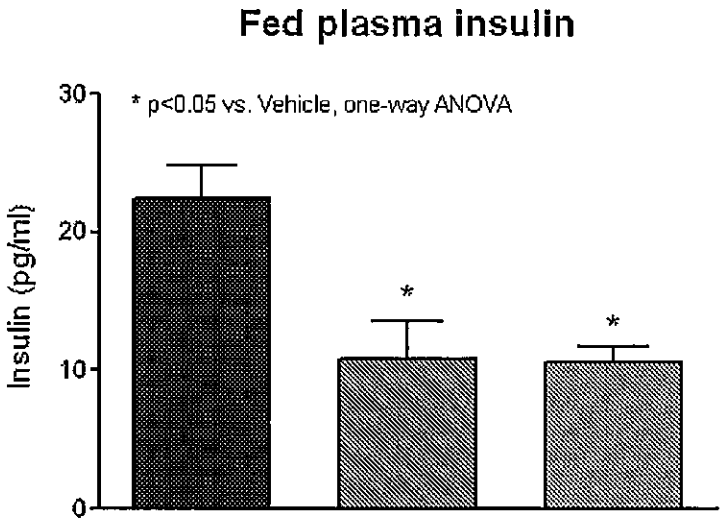

Fed plasma insulin
* p<0.05 vs. Vehicle, one-way ANOVA
Insulin (pg/ml)
30
20
10
0

FIG 1B

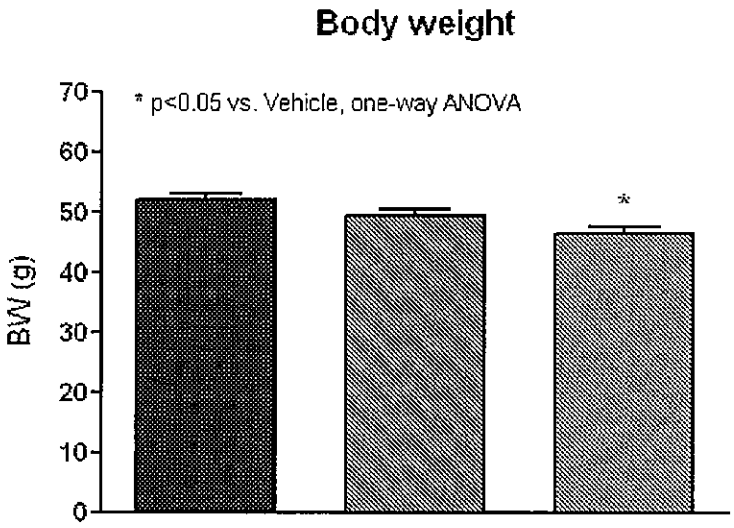

Body weight
* p<0.05 vs. Vehicle, one-way ANOVA
BW (g)
70
60
50
40
30
20
10
0
*

FIG 1C

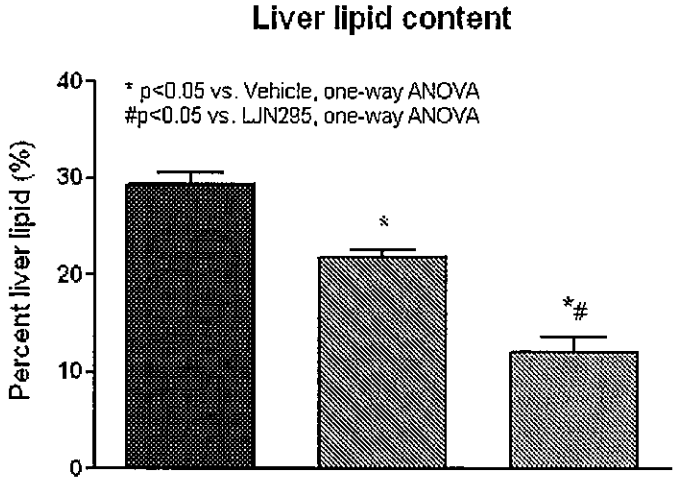

Liver lipid content
* p<0.05 vs. Vehicle, one-way ANOVA
#p<0.05 vs. LJN285, one-way ANOVA
Percent liver lipid (%)
40
30
20
10
0
*
*#

FIG 1D

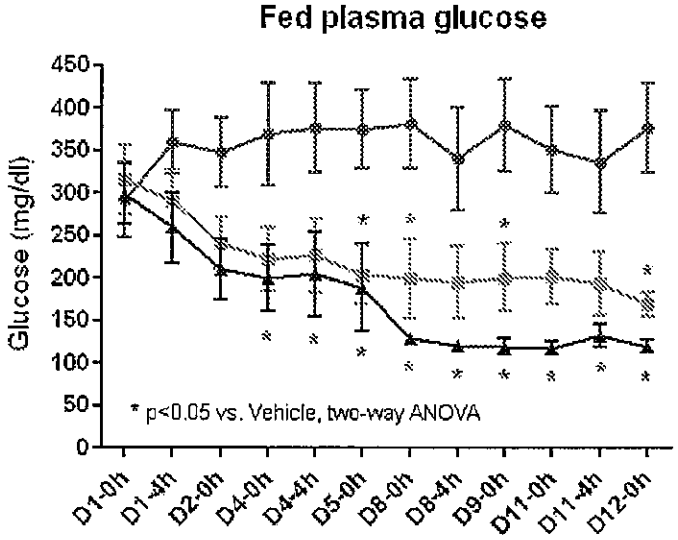

Fed plasma glucose
Glucose (mg/dl)
450
400
350
300
250
200
150
100
50
0
* p<0.05 vs. Vehicle, two-way ANOVA
D1-0h
D1-4h
D2-0h
D4-0h
D4-4h
D5-0h
D8-0h
D8-4h
D9-0h
D11-0h
D11-4h
D12-0h

FIG 2A

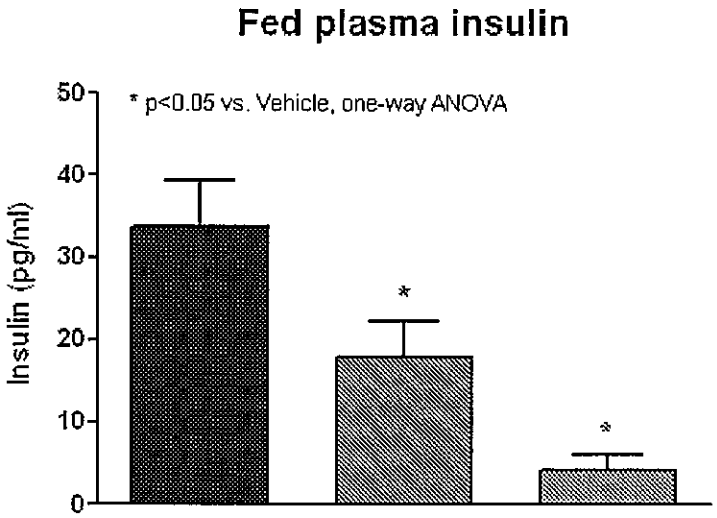

Fed plasma insulin
* p<0.05 vs. Vehicle, one-way ANOVA
Insulin (pg/ml)
50
40
30
20
10
0

FIG 2B

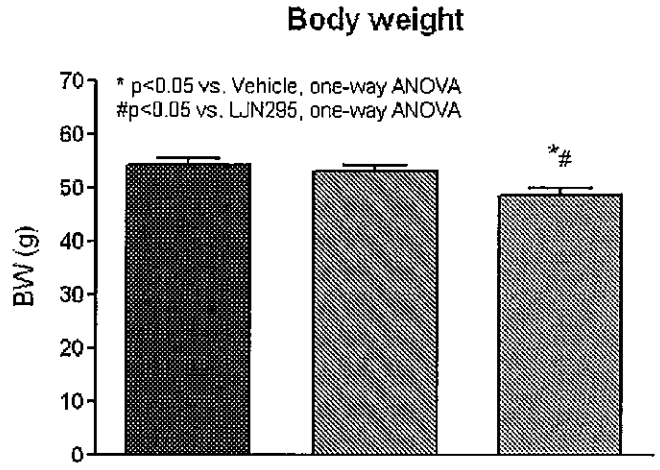

Body weight
* p<0.05 vs. Vehicle, one-way ANOVA
#p<0.05 vs. LJN295, one-way ANOVA
BW (g)
70
60
50
40
30
20
10
0
*#

FIG 2C

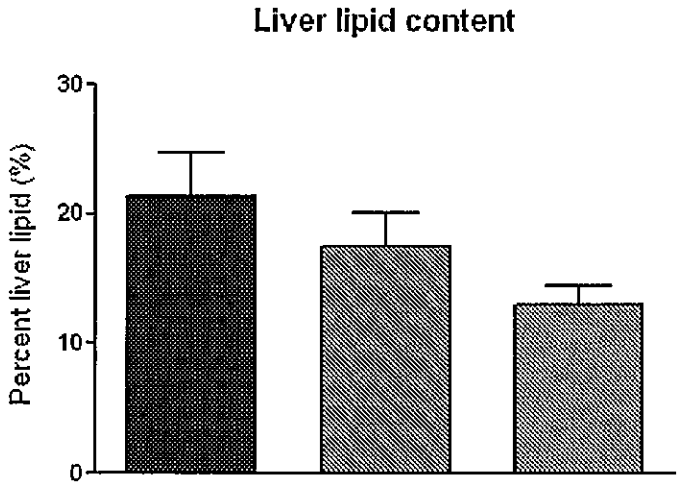

Liver lipid content
Percent liver lipid (%)
30
20
10
0

FIG 2D

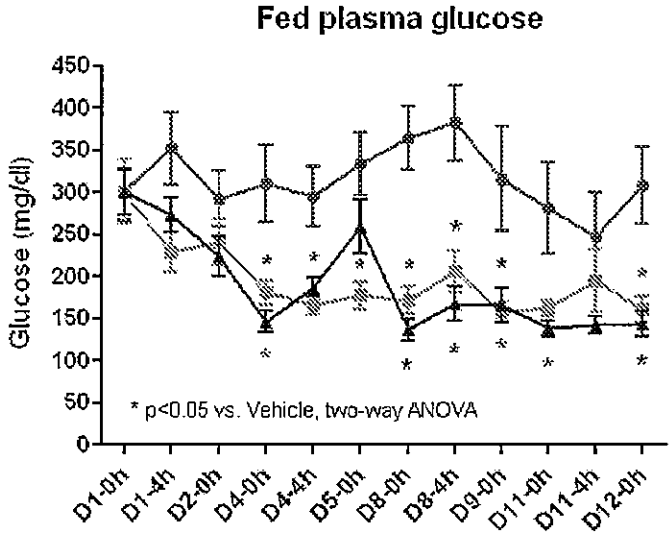

Fed plasma glucose
Glucose (mg/dl)
450
400
350
300
250
200
150
100
50
0
* p<0.05 vs. Vehicle, two-way ANOVA
D1-0h
D1-4h
D2-0h
D4-0h
D4-4h
D5-0h
D8-0h
D8-4h
D9-0h
D11-0h
D11-4h
D12-0h

FIG 3A

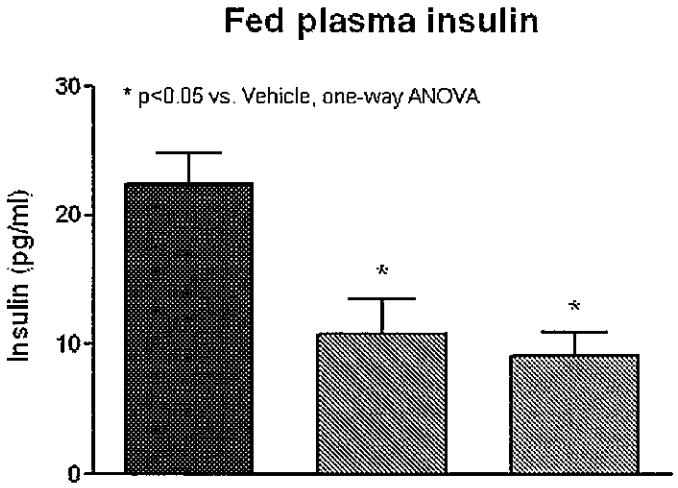

Fed plasma insulin
* p<0.05 vs. Vehicle, one-way ANOVA
Insulin (pg/ml)
30
20
10
0

FIG 3B

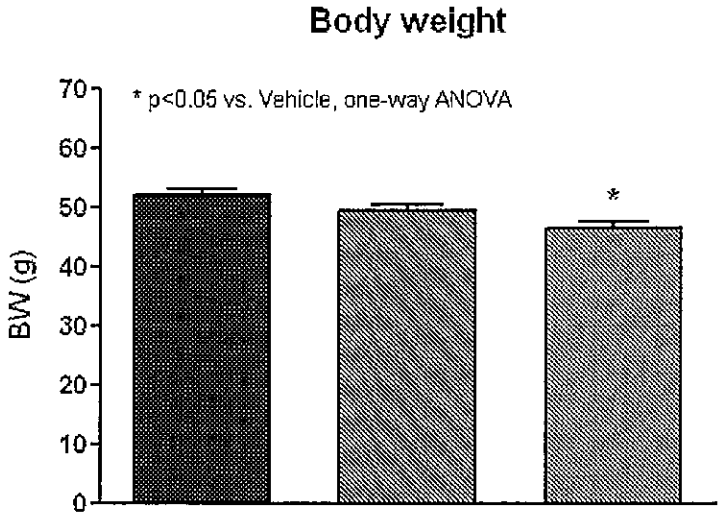

Body weight
* p<0.05 vs. Vehicle, one-way ANOVA
BW (g)
70
60
50
40
30
20
10
0
*

FIG 3C

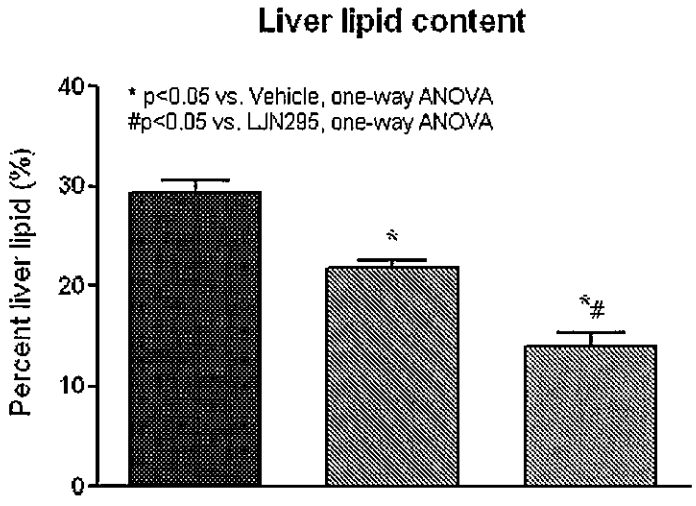

Liver lipid content
* p<0.05 vs. Vehicle, one-way ANOVA
#p<0.05 vs. LJN295, one-way ANOVA
Percent liver lipid (%)
40
30
20
10
0
*
*#

FIG 3D

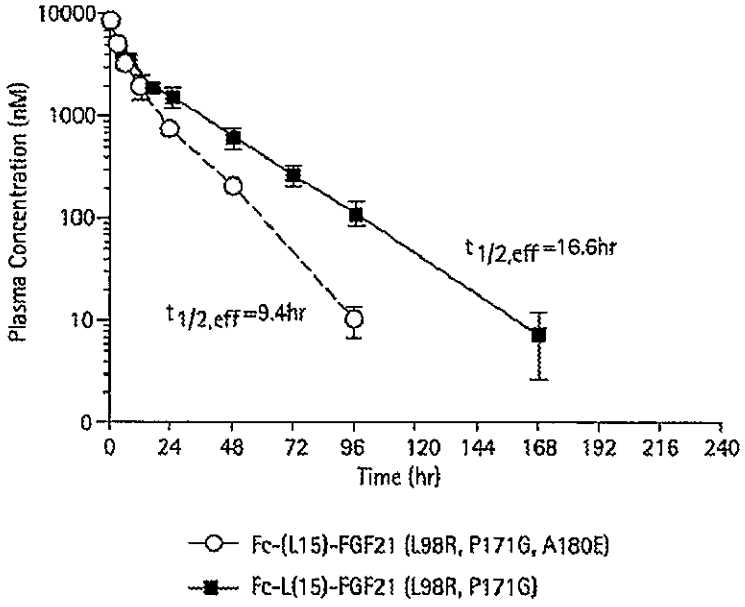

10000
1000
100
10
0
Plasma Concentration (nM)
0
24
48
72
96
120
144
168
192
216
240
Time (hr)
t 1/2,eff =16.6hr
t 1/2,eff =9.4hr
Fc-(L15)-FGF21 (L98R, P171G, A180E)
Fc-L(15)-FGF21 (L98R, P171G)

FIG 4A

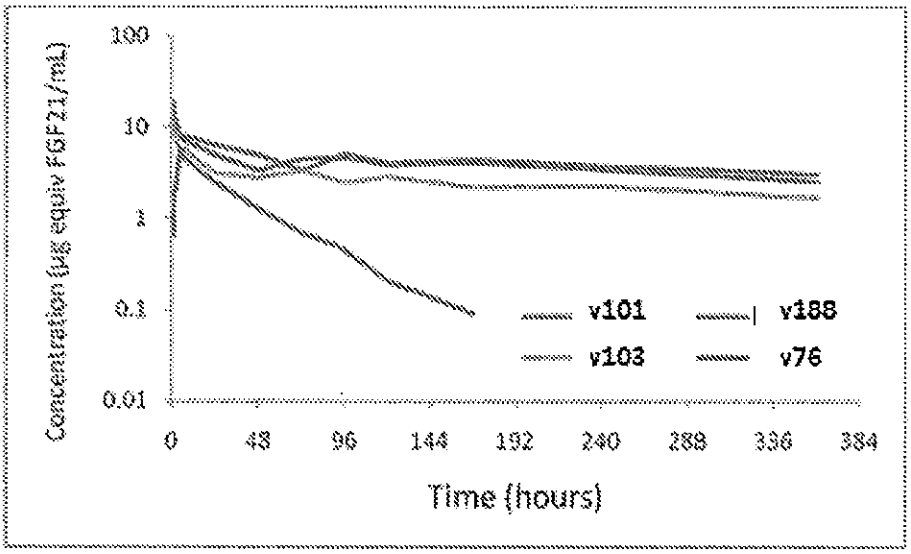

Single dose mouse PK IV 1 mg/kg
Concentration (µg equiv FGF21/mL)
100
10
1
0.1
0.01
0
48
96
144
192
240
288
336
384
Time (hours)
v101
v188
v103
v76

FIG 4B

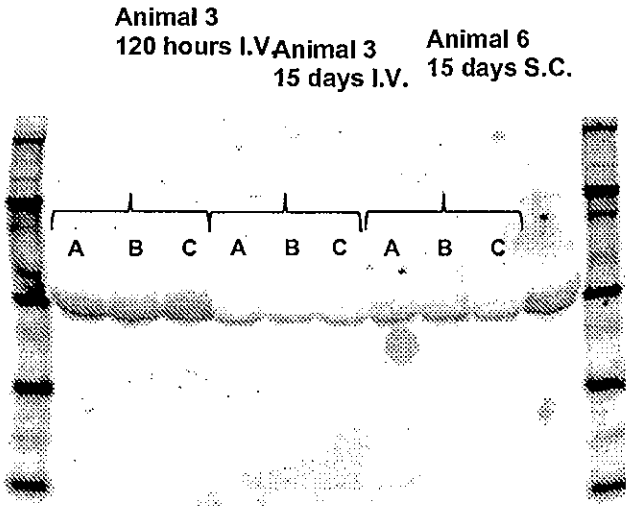

Animal 3
120 hours I.V
Animal 3
15 days I.V.
Animal 6
15 days S.C.
A B C A B C A B C

FIG 4C

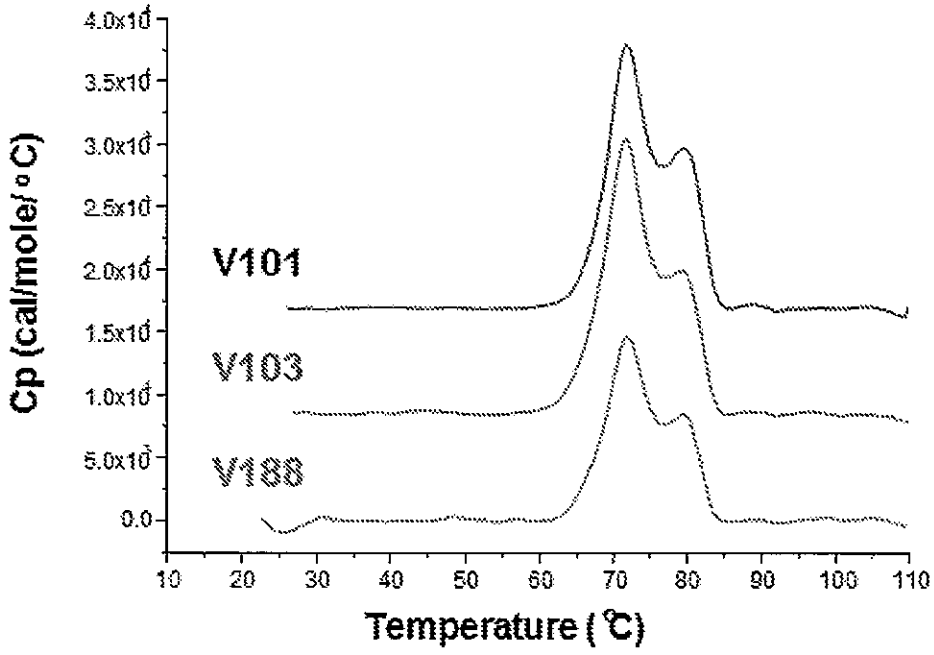

Cp (cal/mole/°C)
4.0x10
3.5x10
3.0x10
2.5x10
2.0x10
1.5x10
1.0x10
5.0x10
0.0
V101
V103
V188
10 20 30 40 50 60 70 80 90 100 110
Temperature (°C)

FIG4D