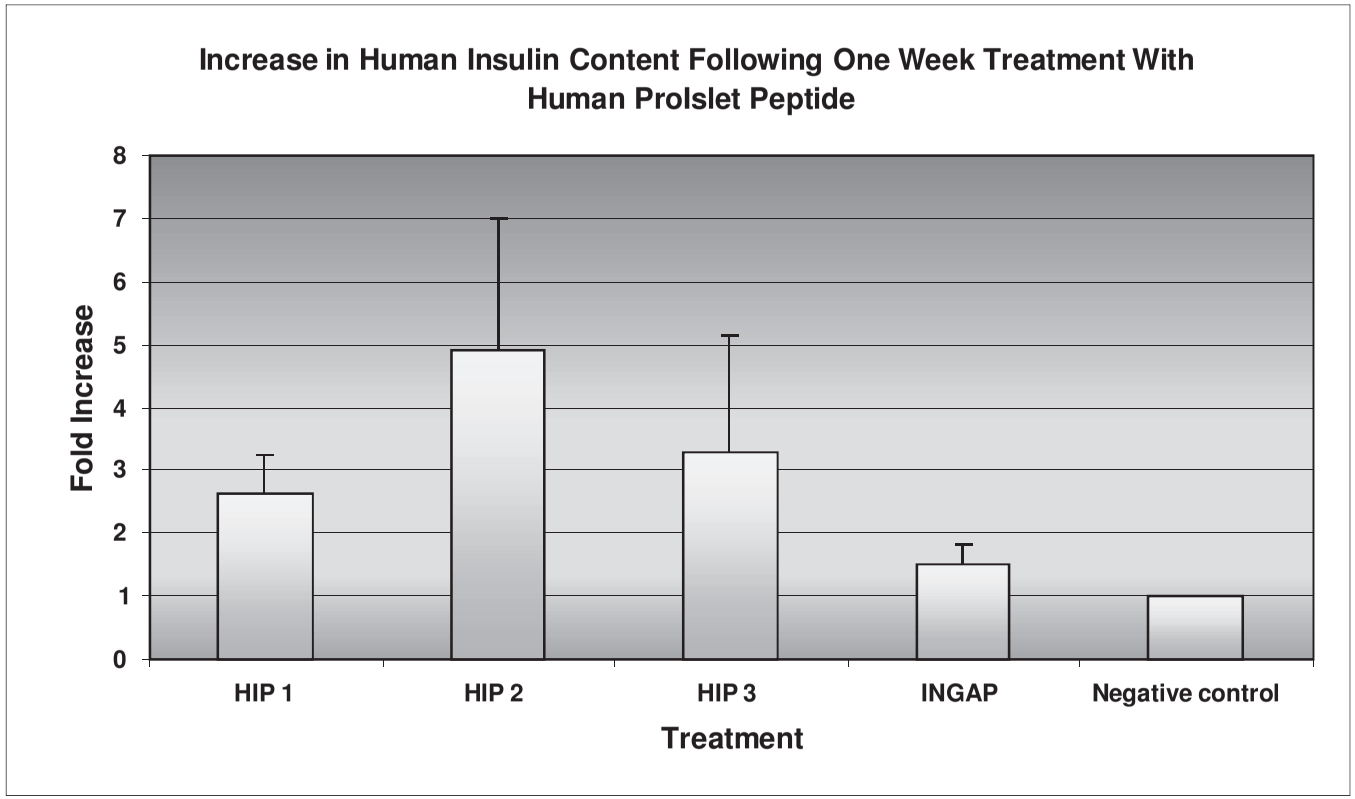

Increase in Human Insulin Content Following One Week Treatment With Human Prolslet Peptide
Fold Increase
8
7
6
5
4
3
2
1
0
HIP 1
HIP 2
HIP 3
INGAP
Negative control
Treatment

Fig. 1

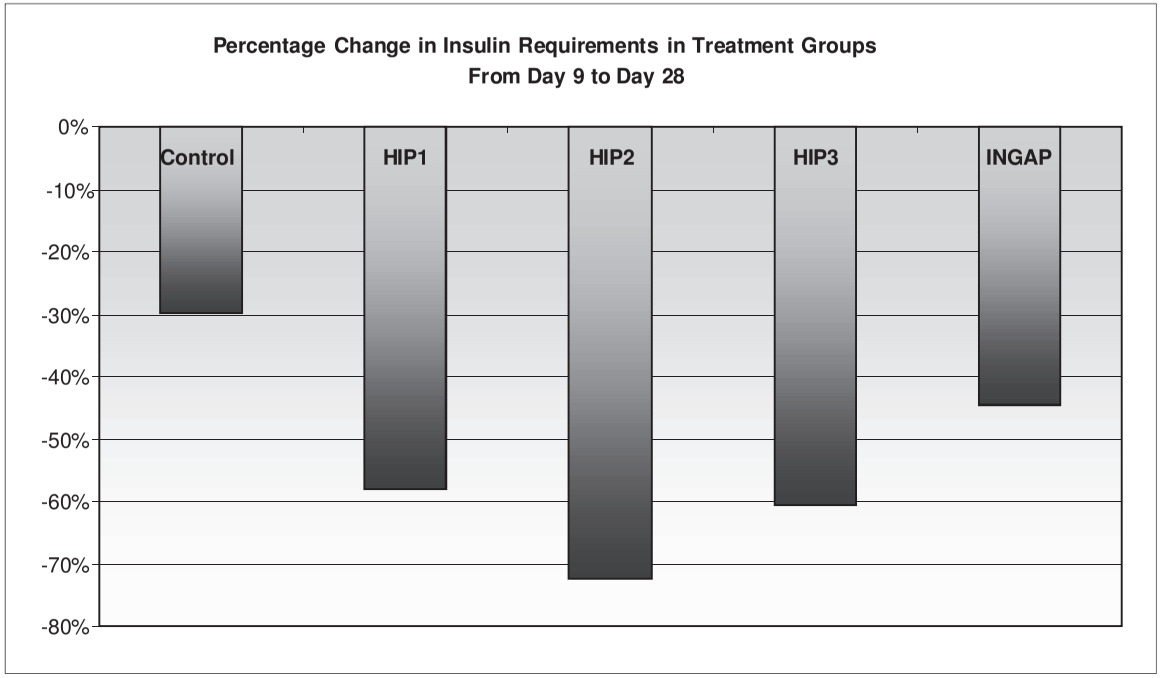

Percentage Change in Insulin Requirements in Treatment Groups
From Day 9 to Day 28
0%
-10%
-20%
-30%
-40%
-50%
-60%
-70%
-80%
Control
HIP1
HIP2
HIP3
INGAP

Fig. 2

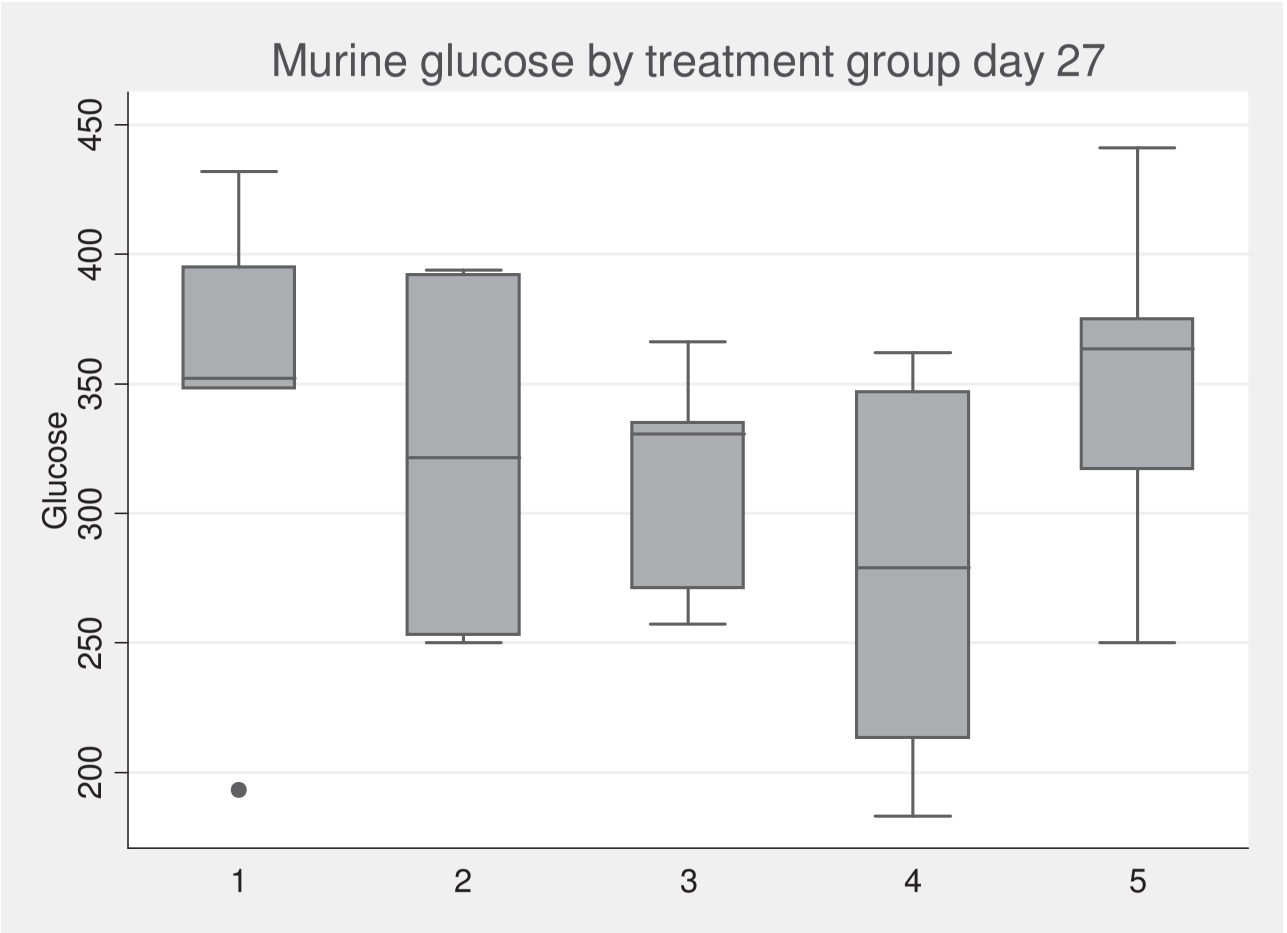

Murine glucose by treatment group day 27
Glucose
200
250
300
350
400
450
1
2
3
4
5

Fig. 3

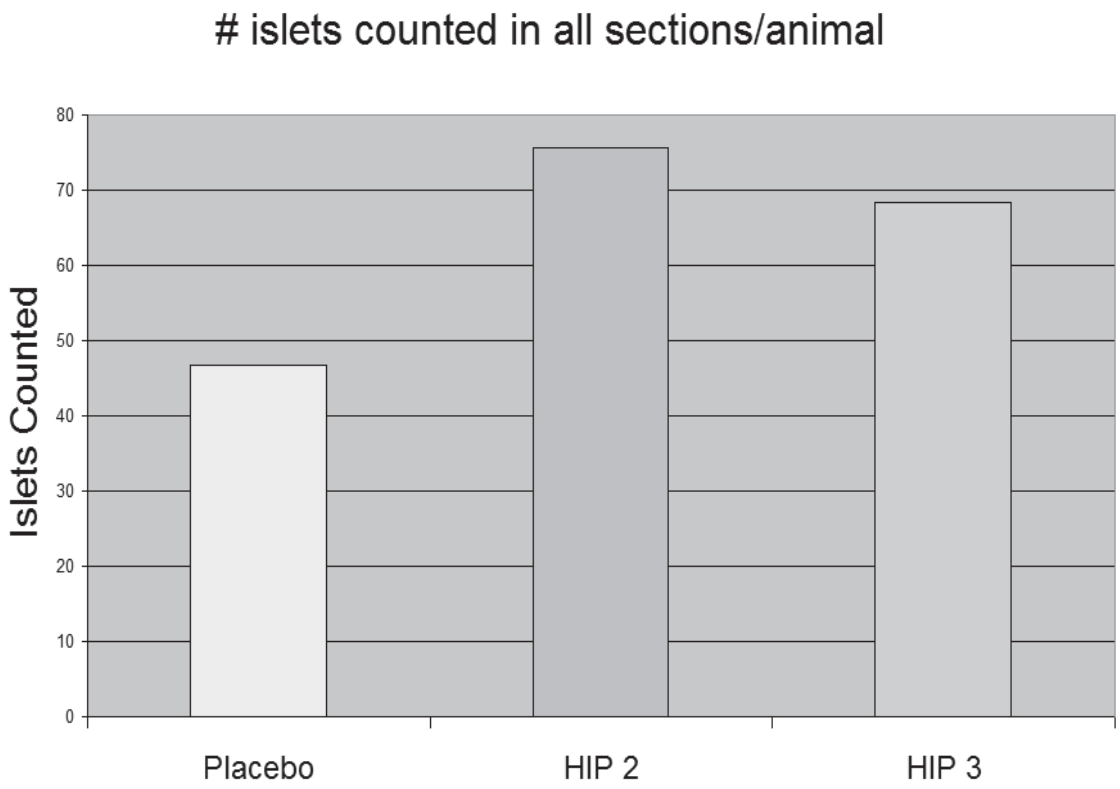

islets counted in all sections/animal
Islets Counted
80
70
60
50
40
30
20
10
0
Placebo
HIP 2
HIP 3

Fig. 4A

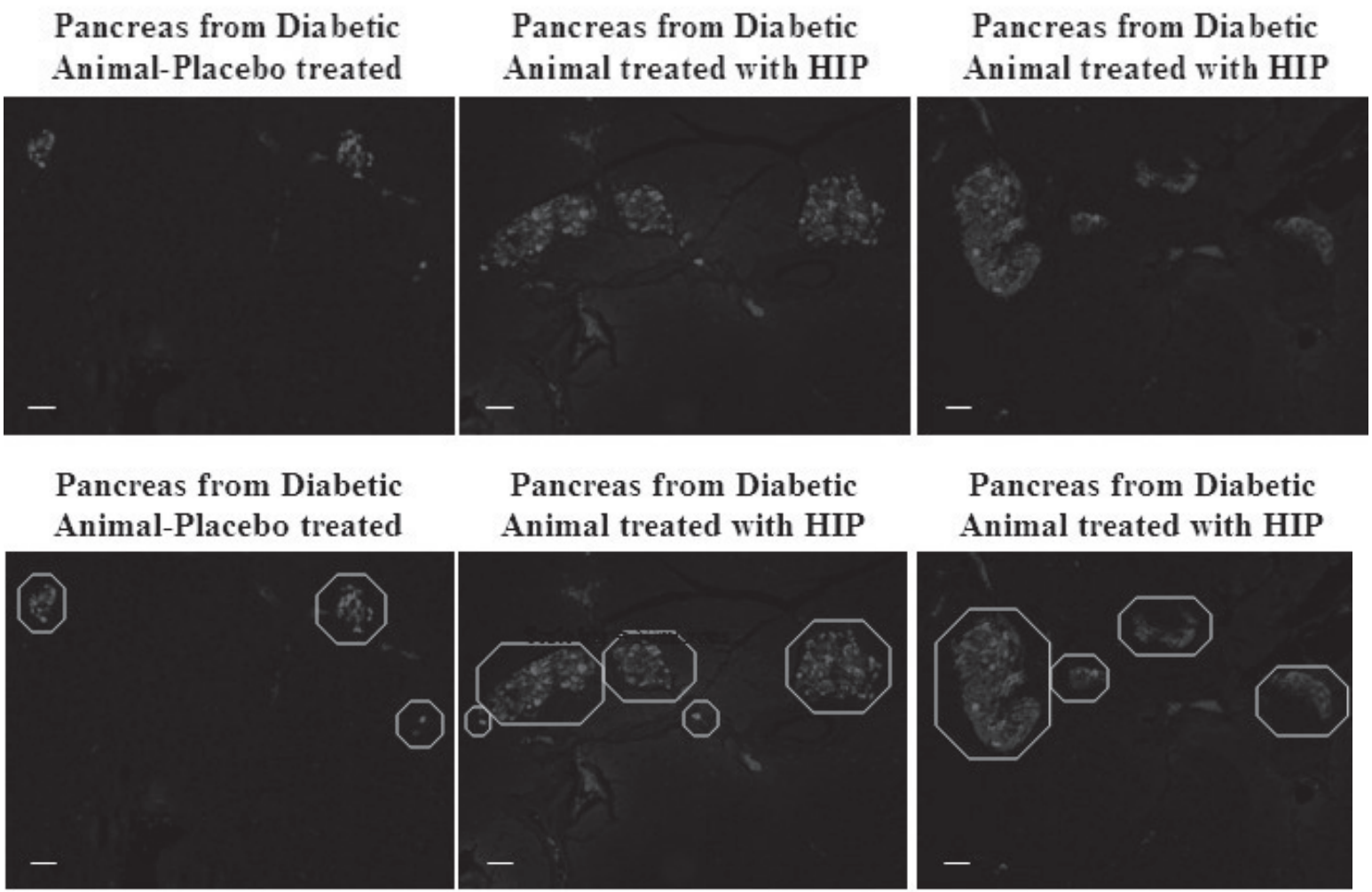
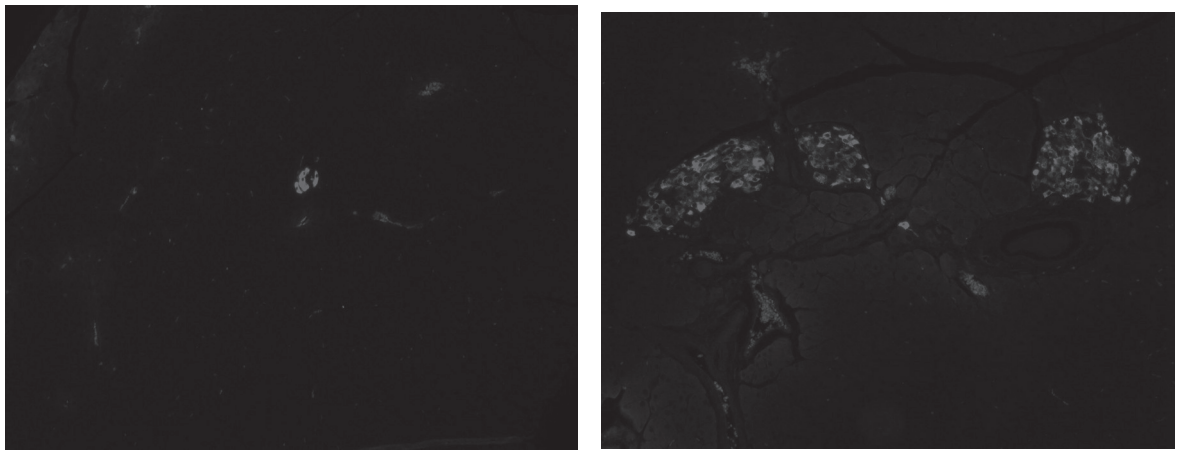

Pancreas from Diabetic Animal-Placebo treated
Pancreas from Diabetic Animal treated with HIP
Pancreas from Diabetic Animal treated with HIP
Pancreas from Diabetic Animal-Placebo treated
Pancreas from Diabetic Animal treated with HIP
Pancreas from Diabetic Animal treated with HIP

Fig. 4B



Control

HIP-
treated

Fig. 5

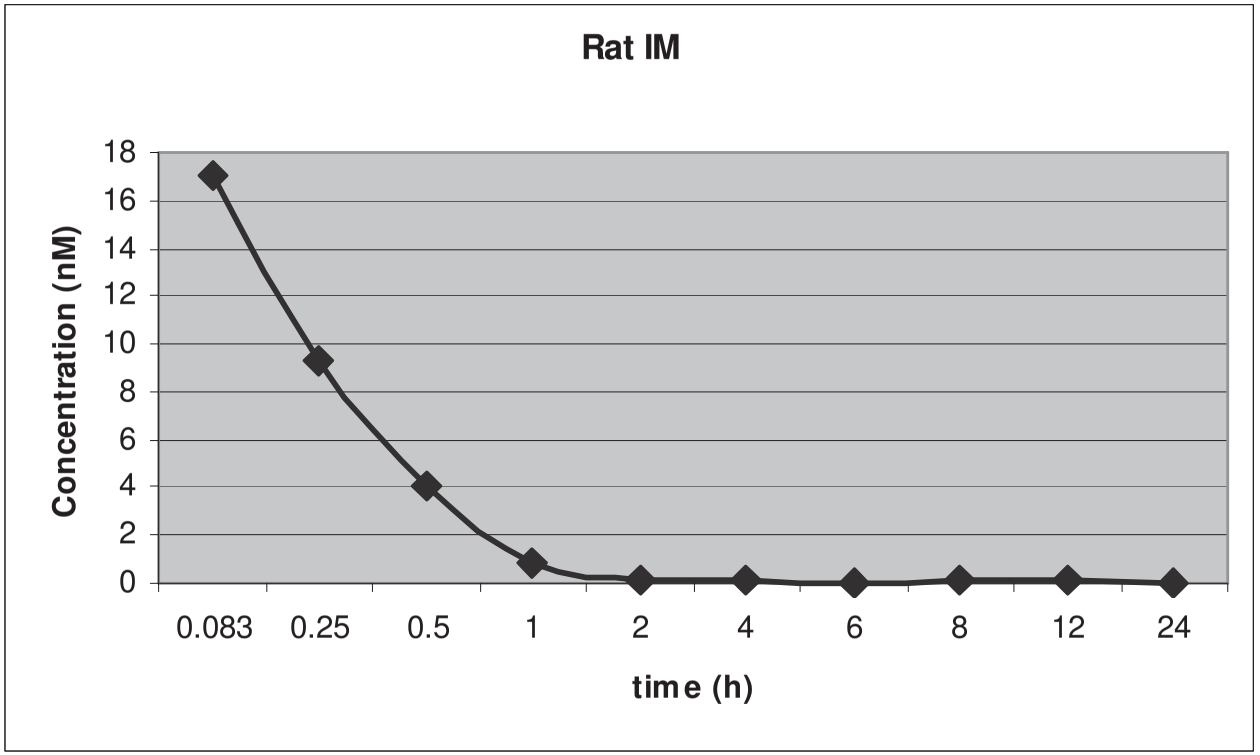

Rat IM
Concentration (nM)
18
16
14
12
10
8
6
4
2
0
0.083
0.25
0.5
1
2
4
6
8
12
24
time (h)

Fig. 6

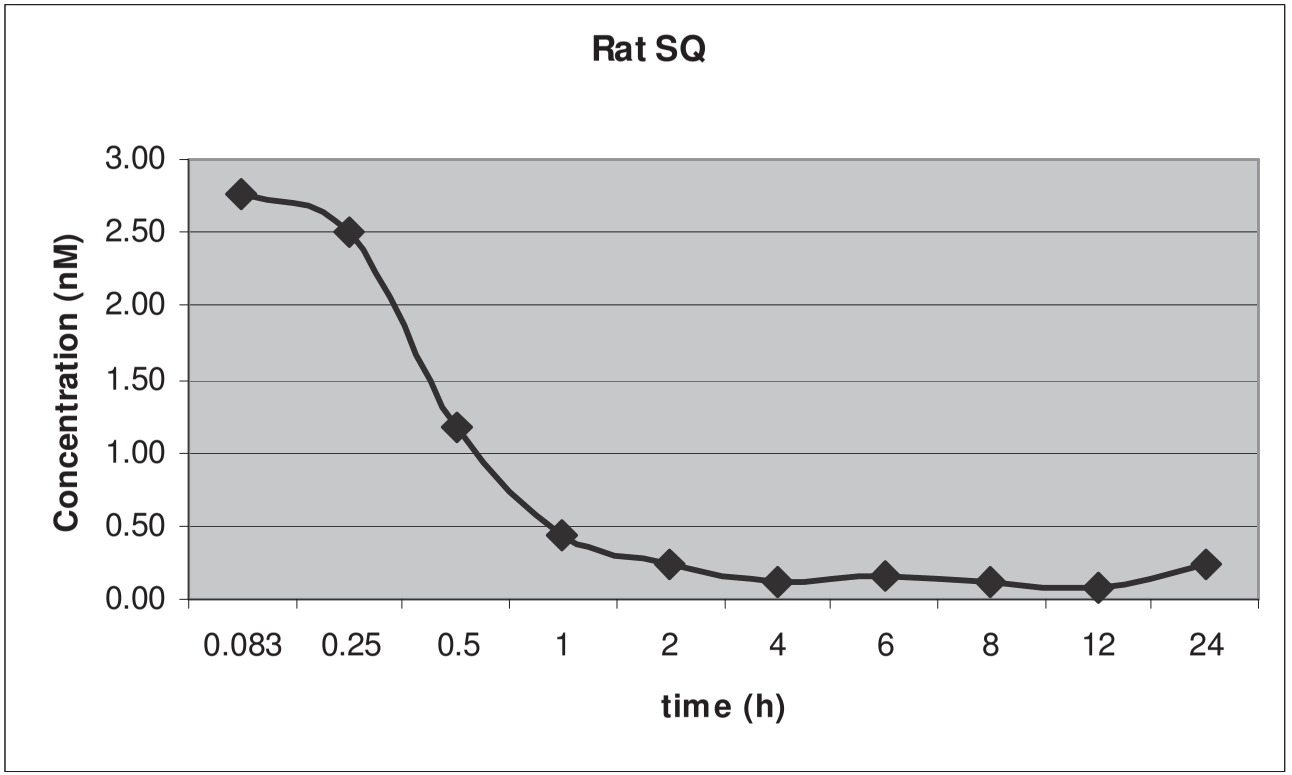

Rat SQ
Concentration (nM)
3.00
2.50
2.00
1.50
1.00
0.50
0.00
0.083
0.25
0.5
1
2
4
6
8
12
24
time (h)

Fig. 7

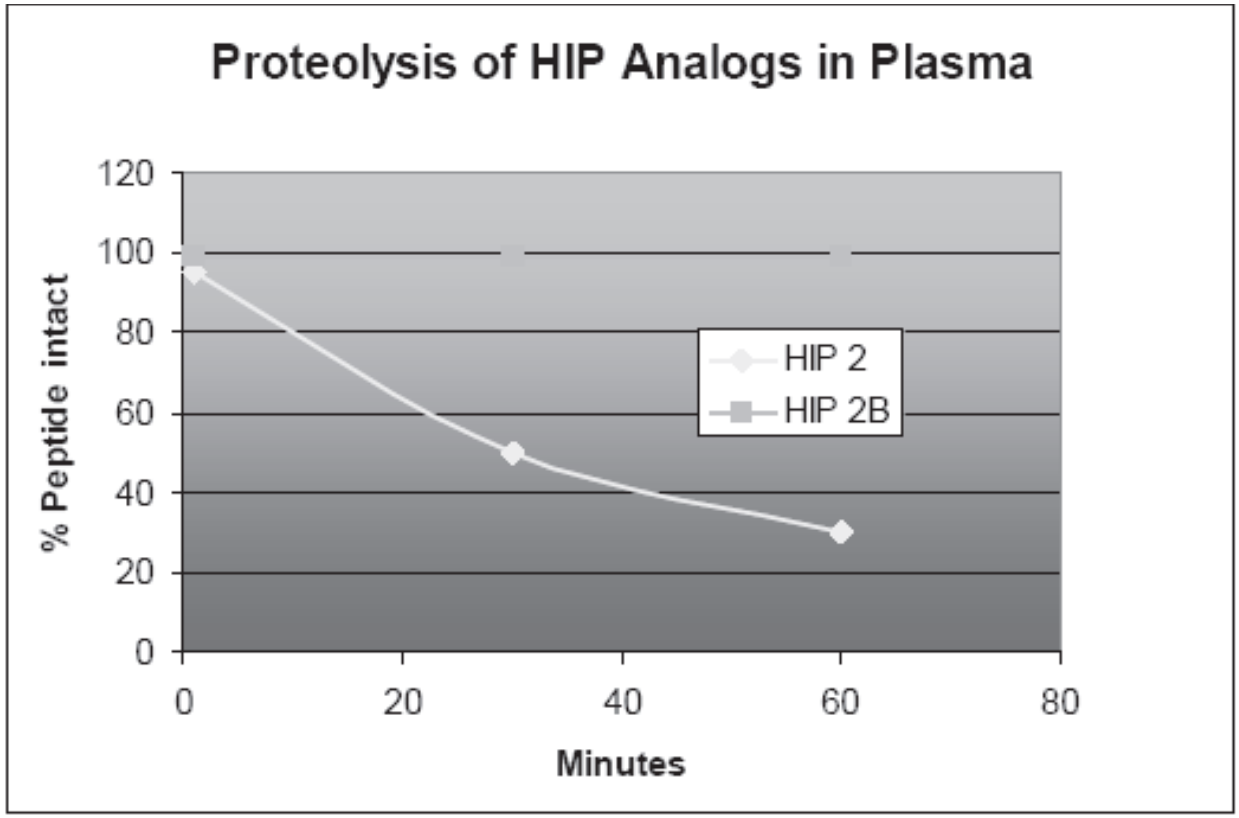

Proteolysis of HIP Analogs in Plasma
% Peptide intact
120
100
80
60
40
20
0
0
20
40
60
80
Minutes
HIP 2
HIP 2B

Fig. 8

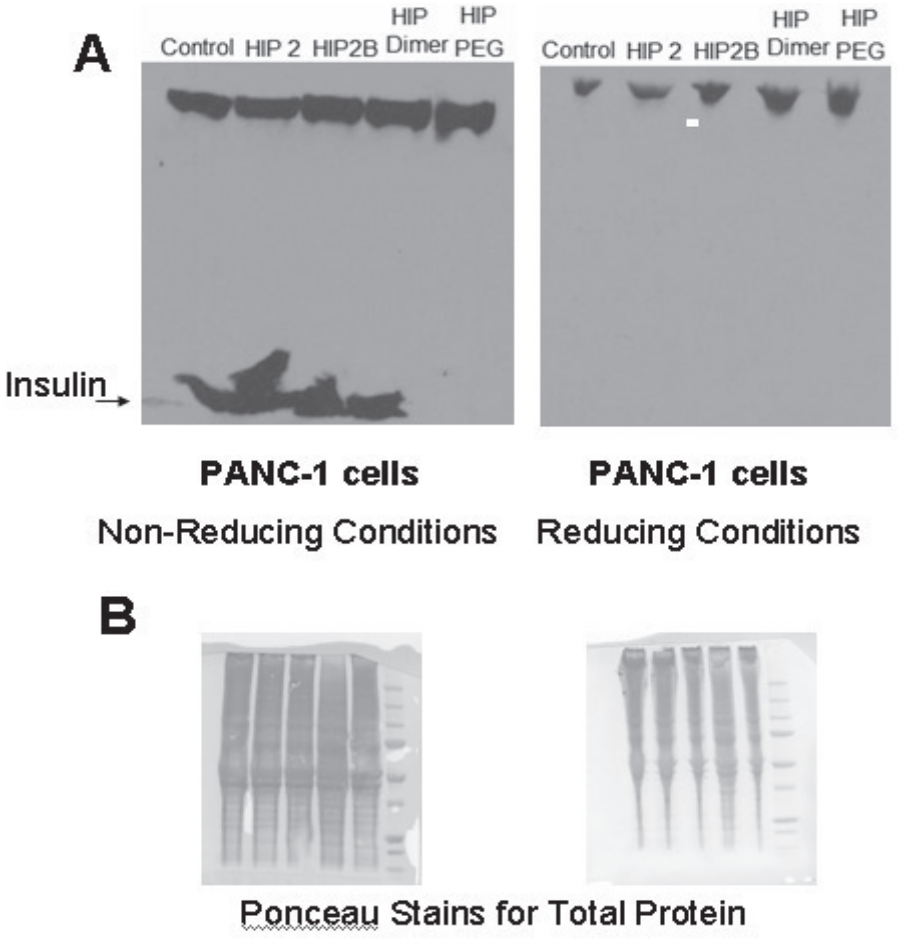

A
Control
HIP 2
HIP2B
HIP Dimer
HIP PEG
Insulin
PANC-1 cells
Non-Reducing Conditions
PANC-1 cells
Reducing Conditions
B
Ponceau Stains for Total Protein

Fig. 9

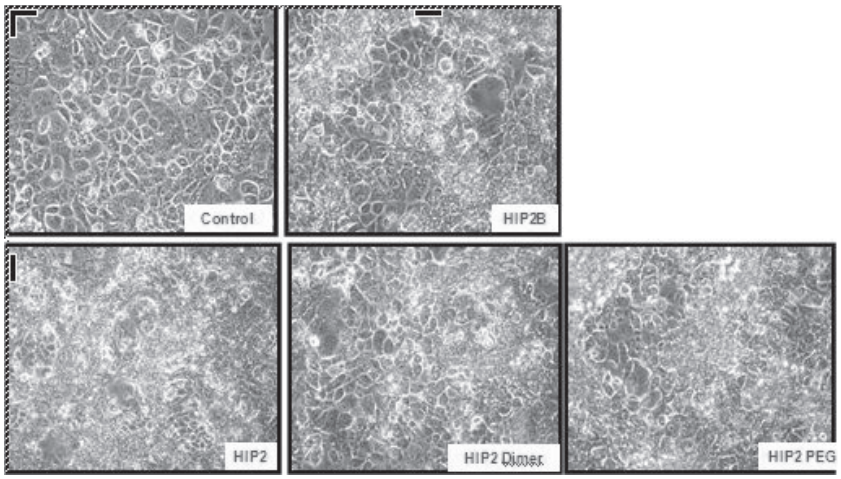


Fig. 10A

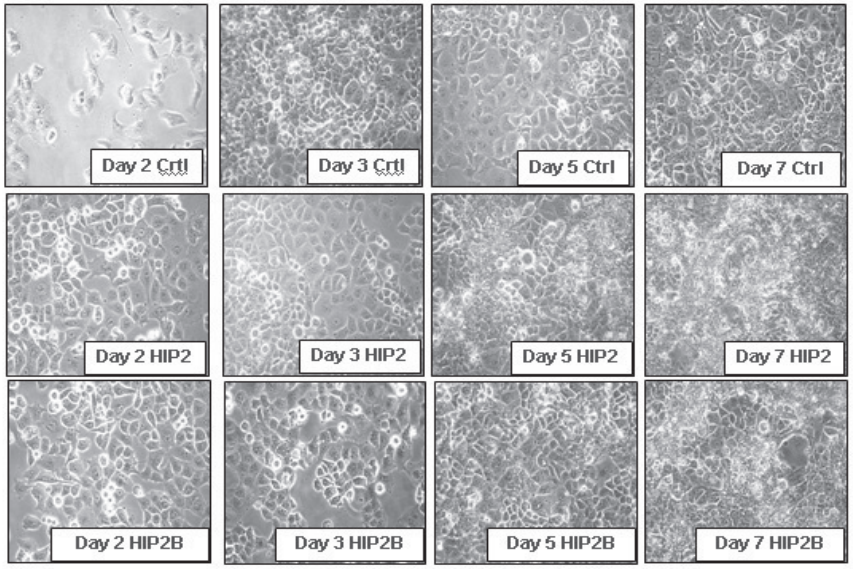


Fig. 10B

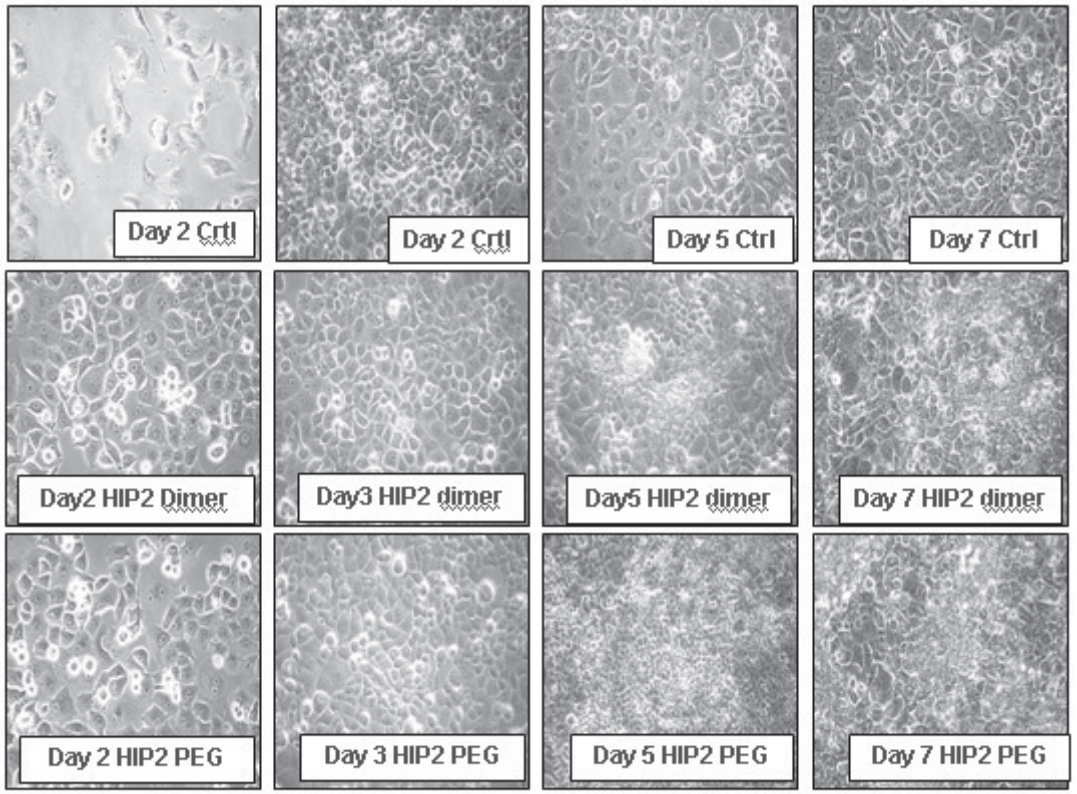

Day 2 Ctrl
Day 2 Ctrl
Day 5 Ctrl
Day 7 Ctrl
Day2 HIP2 Dimer
Day3 HIP2 dimer
Day5 HIP2 dimer
Day 7 HIP2 dimer
Day 2 HIP2 PEG
Day 3 HIP2 PEG
Day 5 HIP2 PEG
Day 7 HIP2 PEG

Fig. 10C

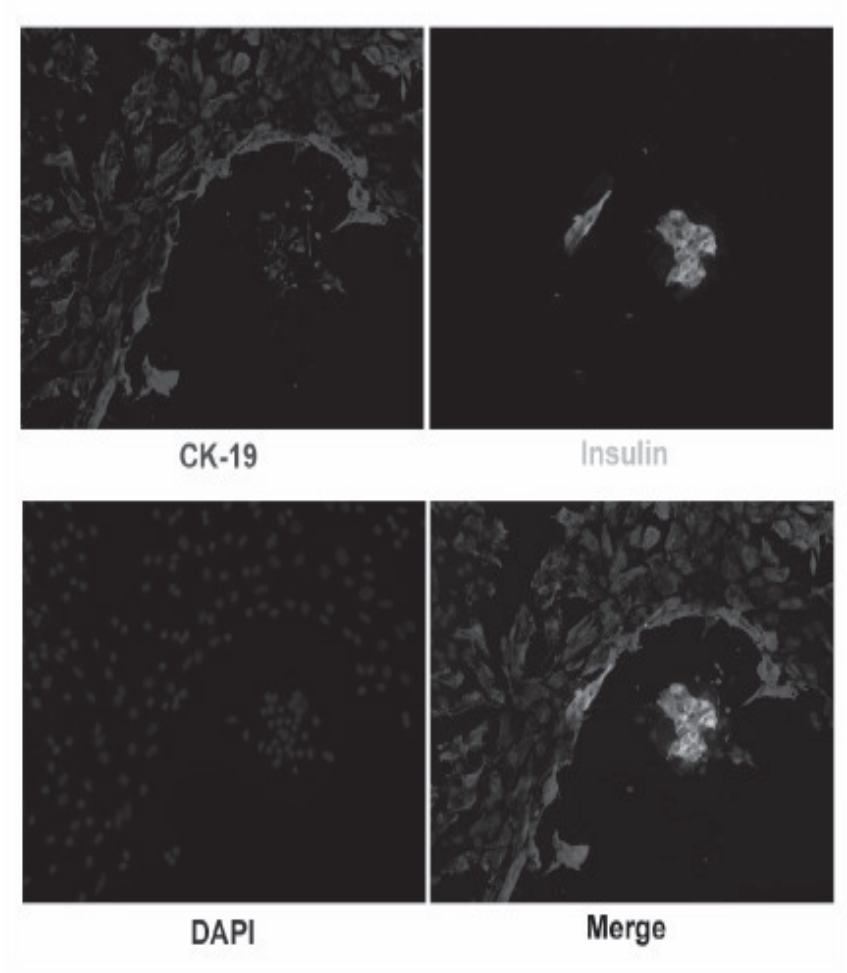


Fig. 11

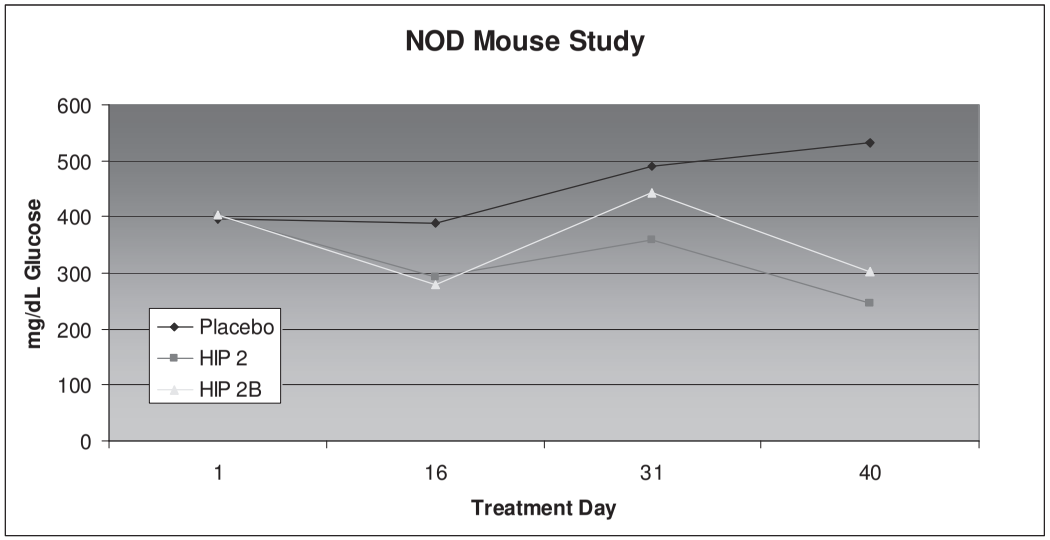

NOD Mouse Study
600
500
400
300
200
100
0
mg/dL Glucose
Placebo
HIP 2
HIP 2B
1
16
31
40
Treatment Day

Fig. 12

Translocation of HIP Receptor upon Stimulation of HIP and Optimized HIP

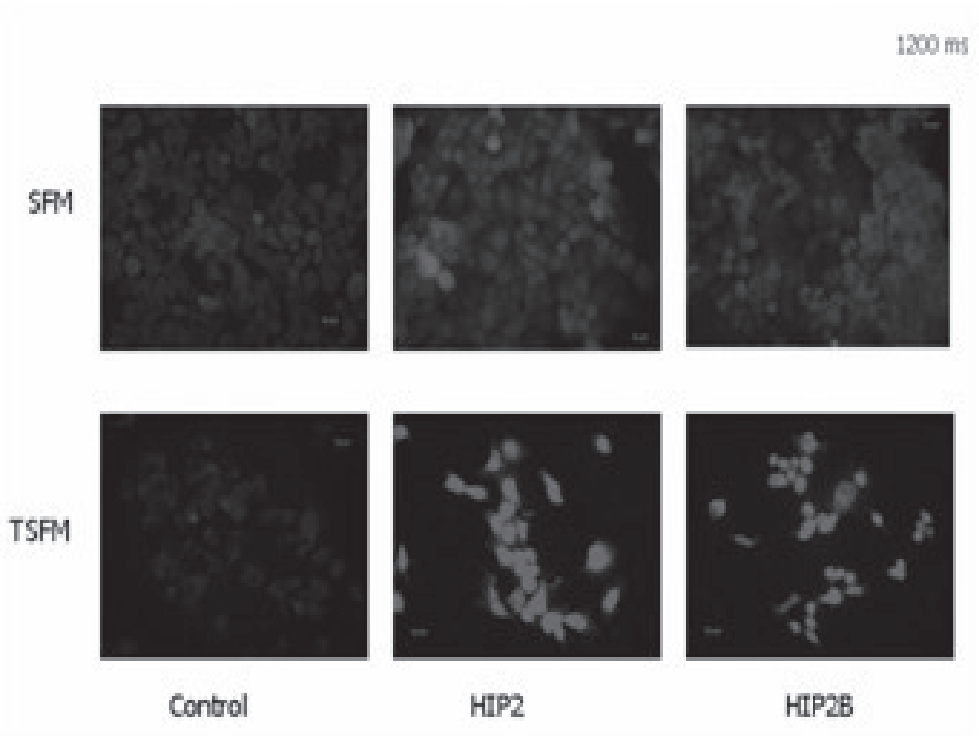


Fig. 13

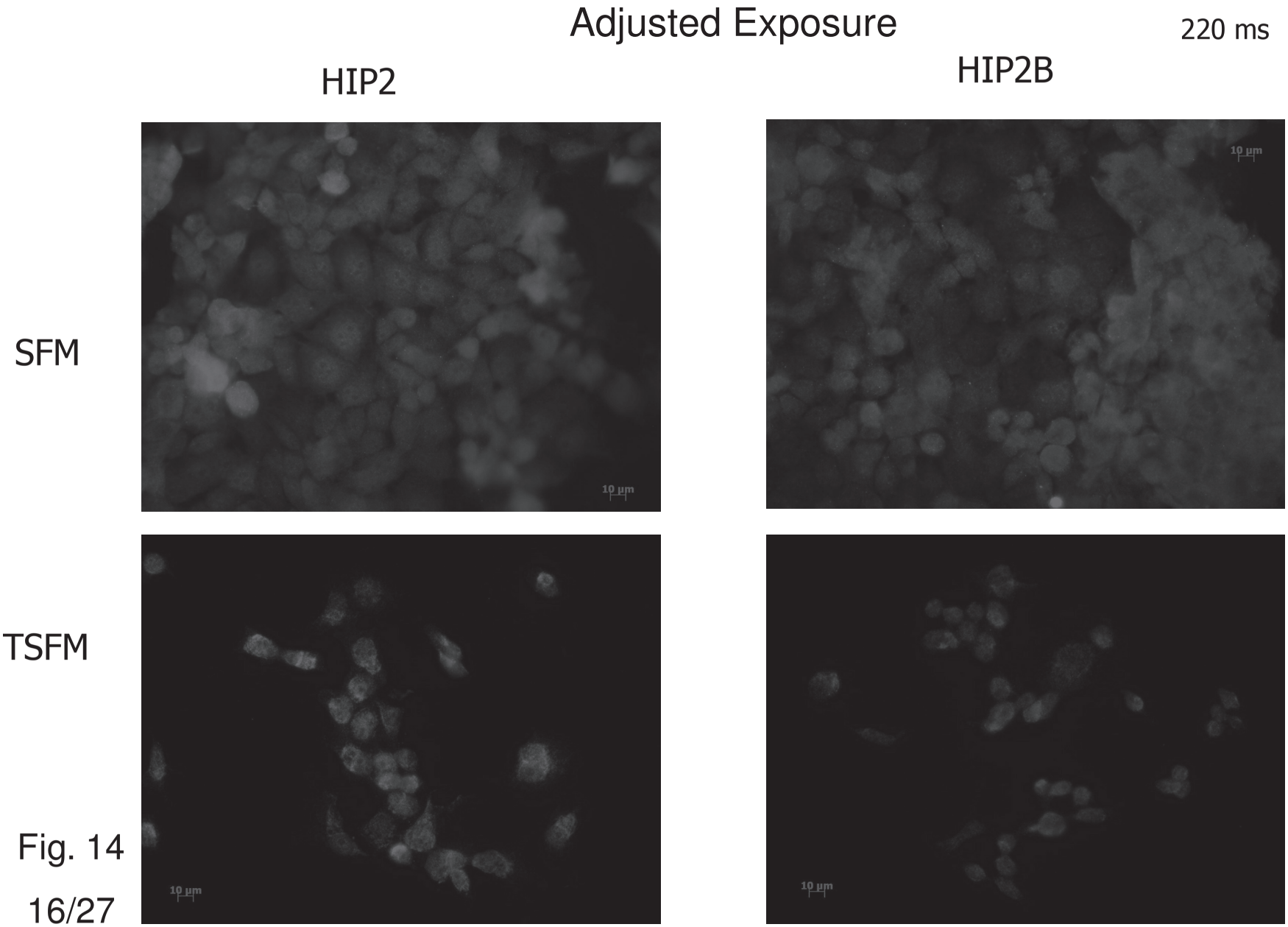

Adjusted Exposure
220 ms
HIP2
HIP2B
SFM
TSFM
10 µm
10 µm
10 µm
10 µm

Fig. 14

Translocation of HIP receptor from cytoplasmic membrane to nucleus upon stimulation with Optimized HIP2 Peptides

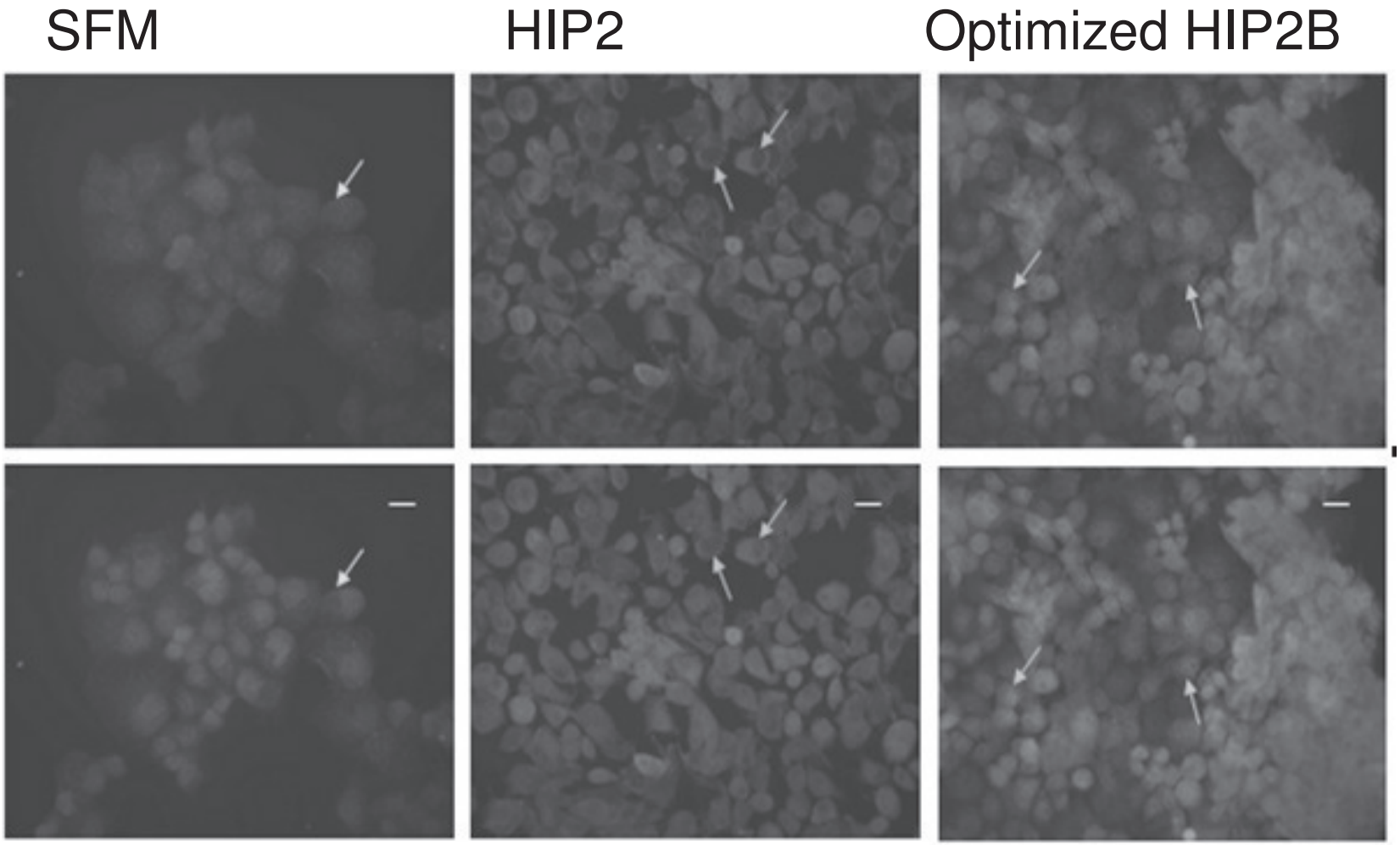


Fig. 15

Impact of Optimized HIP2B on translocation time from cytoplasm to nucleus

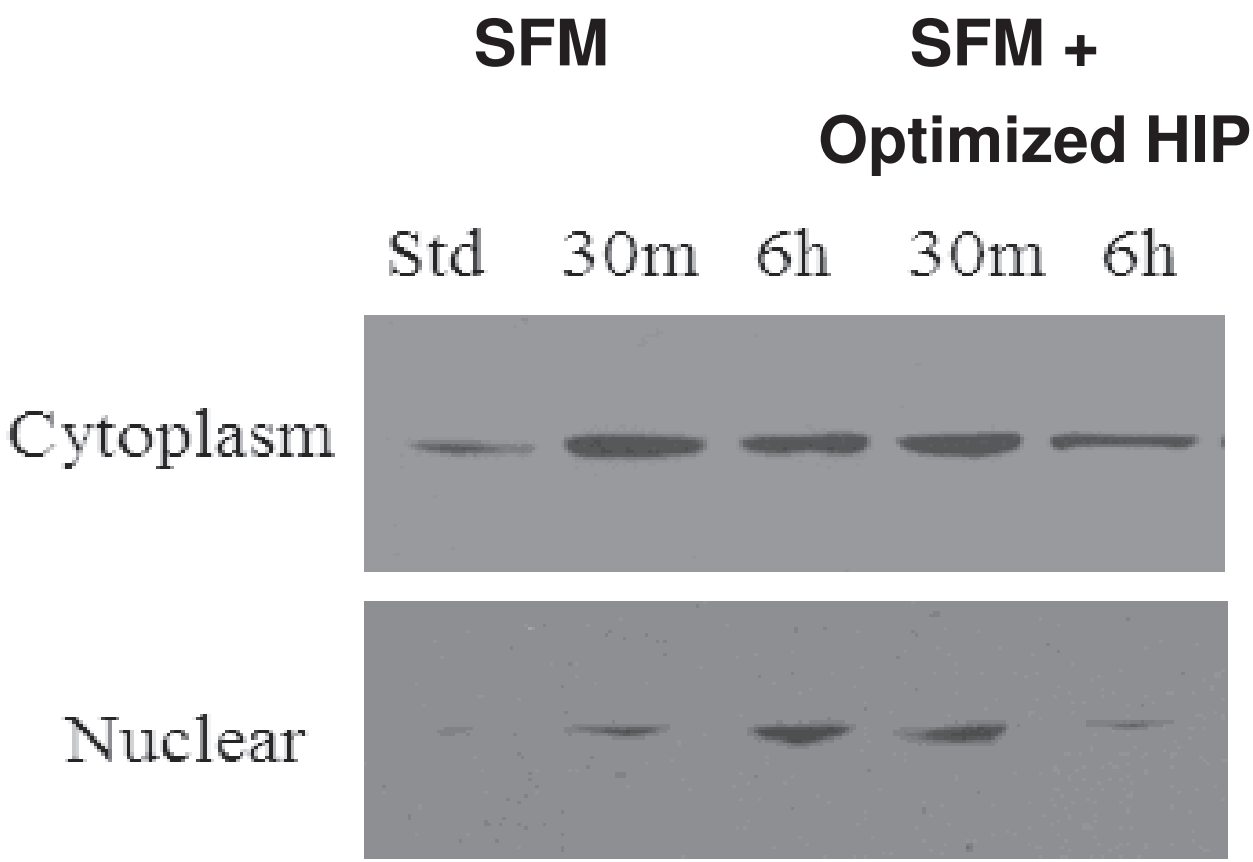
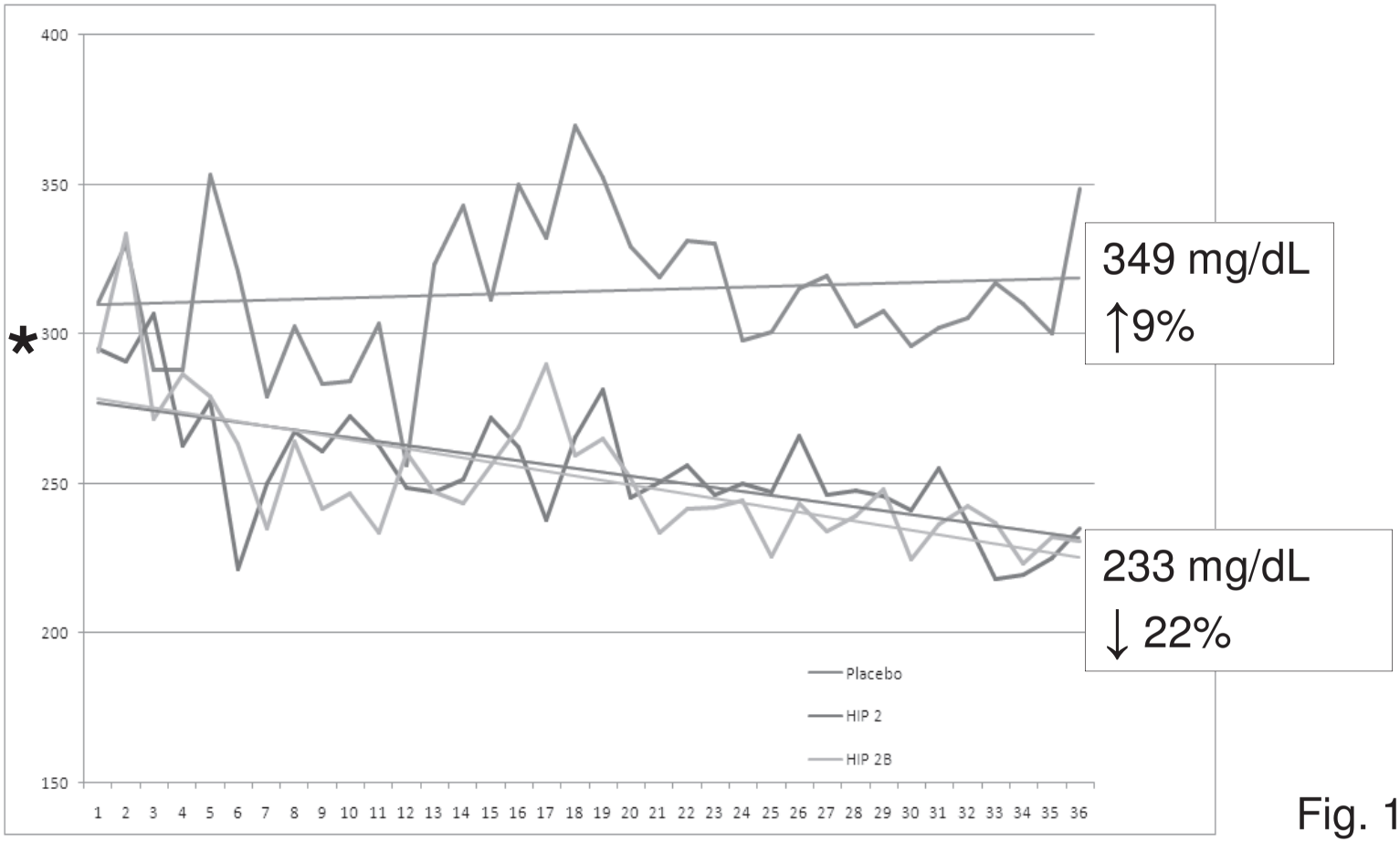


Fig.16

STZ-Diabetic Mouse Model
HIP 2 and HIP 2B vs. Placebo
Average Daily Glucose Levels



Treatment Days

Fig. 17

* Mean baseline glucose 300 +/-2% mg/dL with no significant differences between groups (p=0.301)

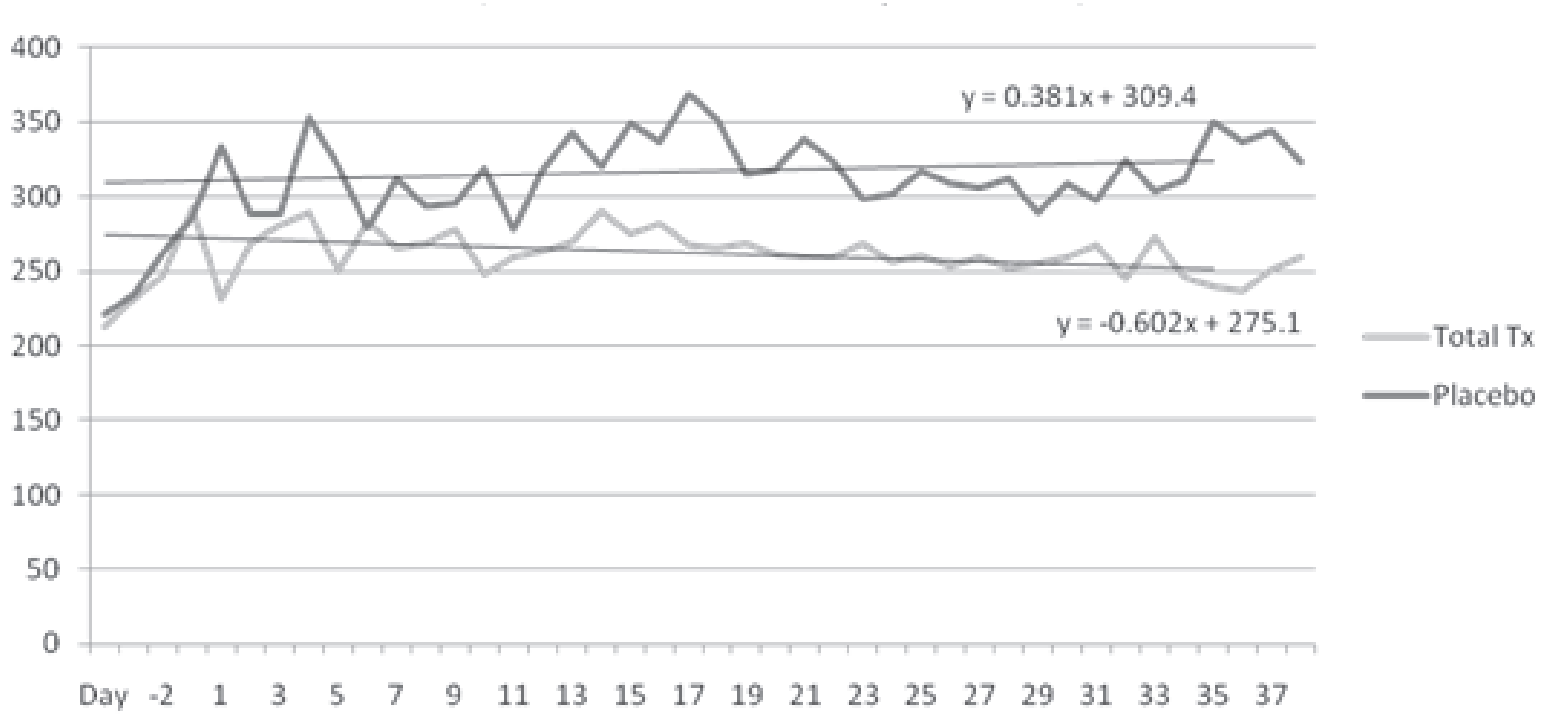

400
350
300
250
200
150
100
50
0
Day -2 1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 33 35 37
y = 0.381x + 309.4
y = -0.602x + 275.1
Total Tx
Placebo

Fig. 18

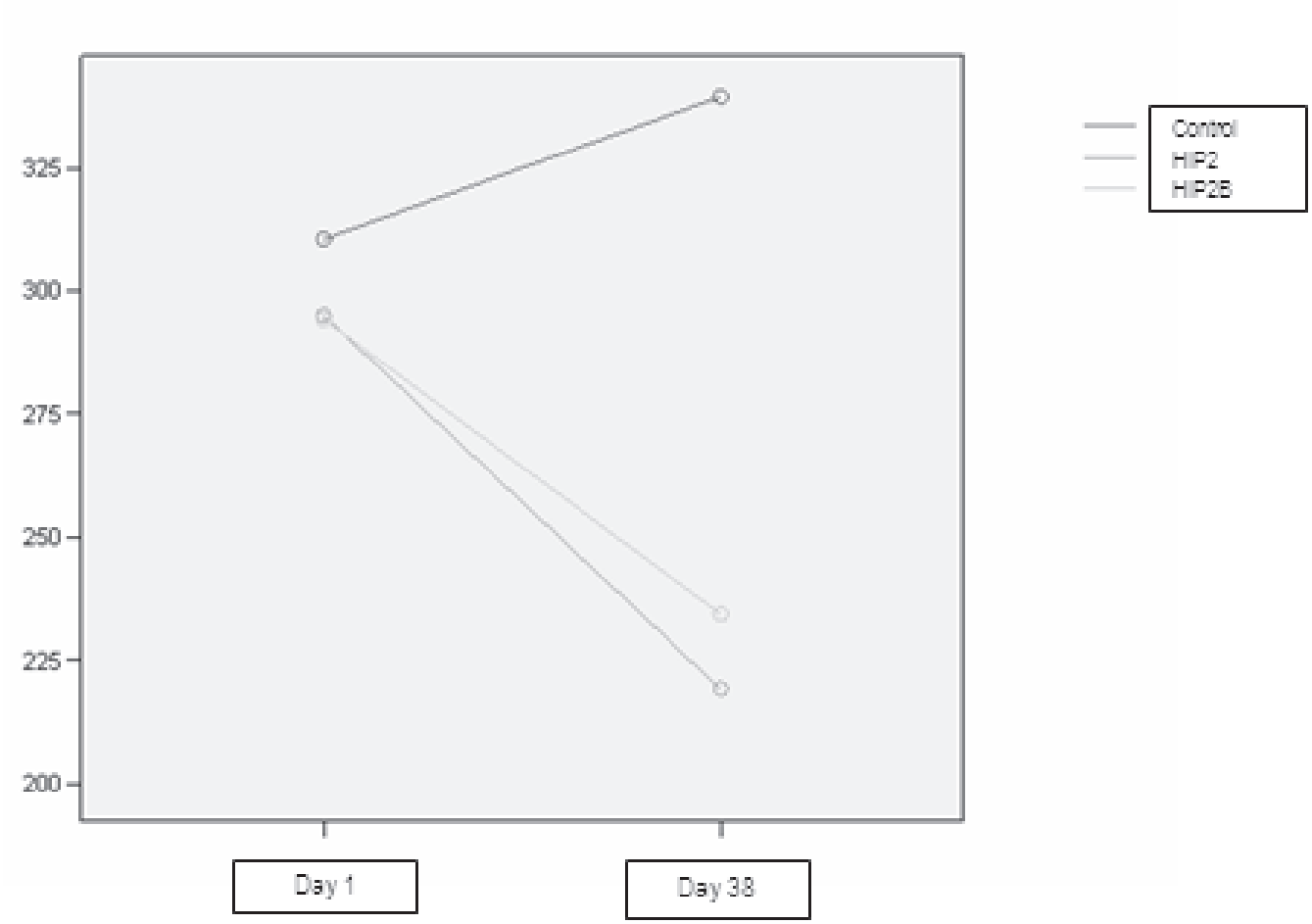


Fig. 19

Fasting glucose (mg/dL) levels after treatment with Optimized HIP2B

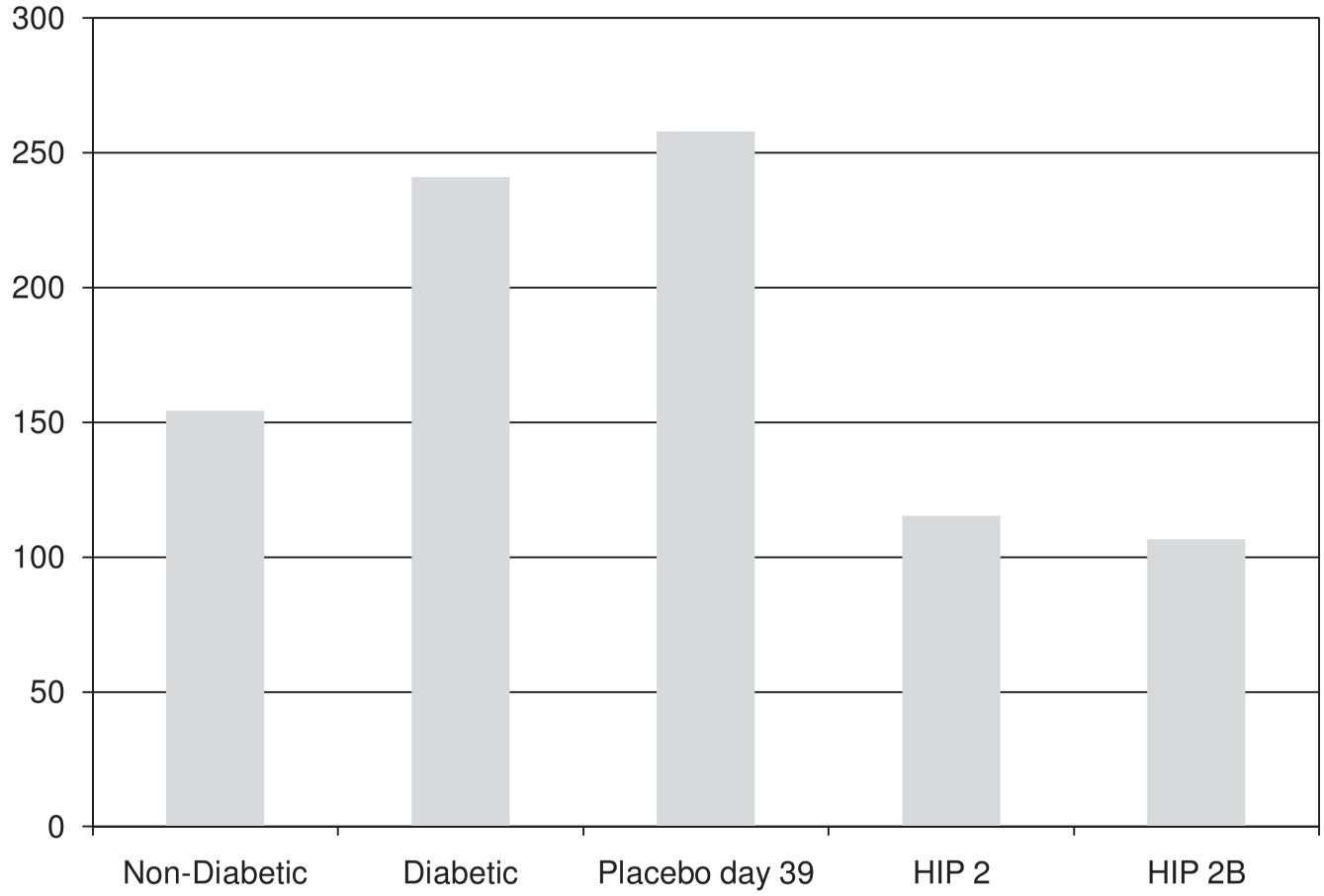


Fig. 20

Glucose Tolerance Test Results following administration of Optimized HIP2B

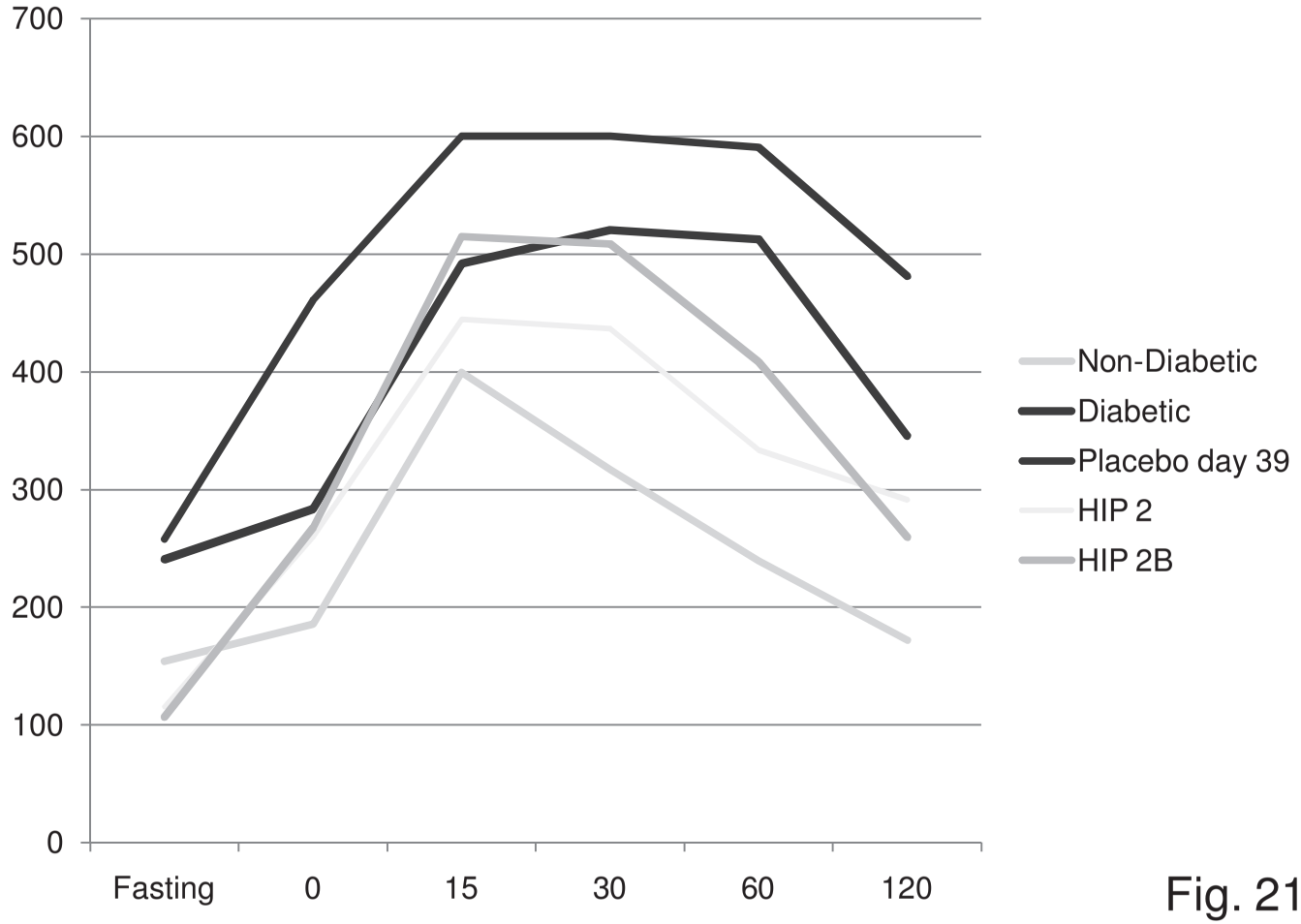


Fig. 21

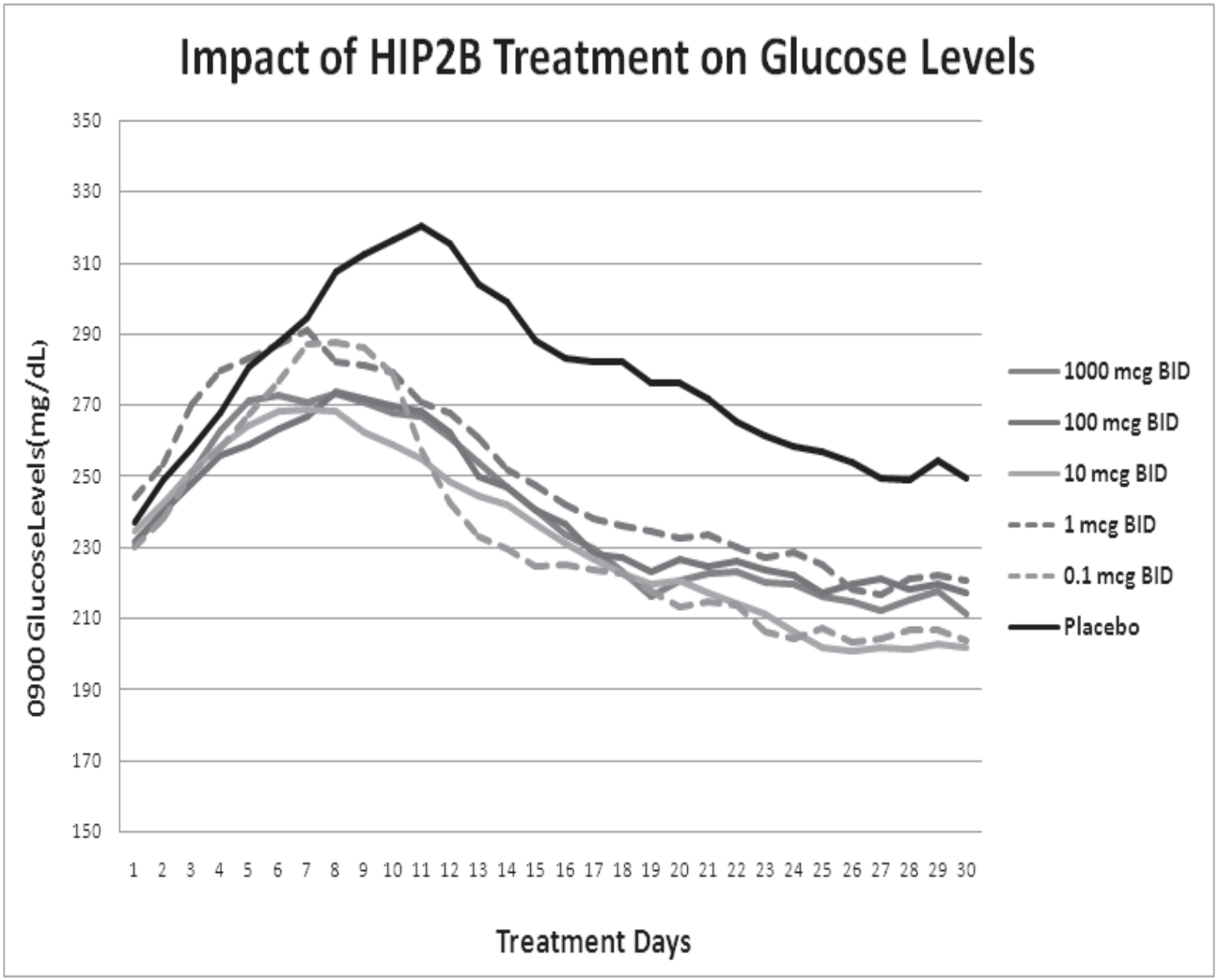

Impact of HIP2B Treatment on Glucose Levels
0900 GlucoseLevels(mg/dL)
350
330
310
290
270
250
230
210
190
170
150
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30
Treatment Days
1000 mcg BID
100 mcg BID
10 mcg BID
1 mcg BID
0.1 mcg BID
Placebo

Fig. 22

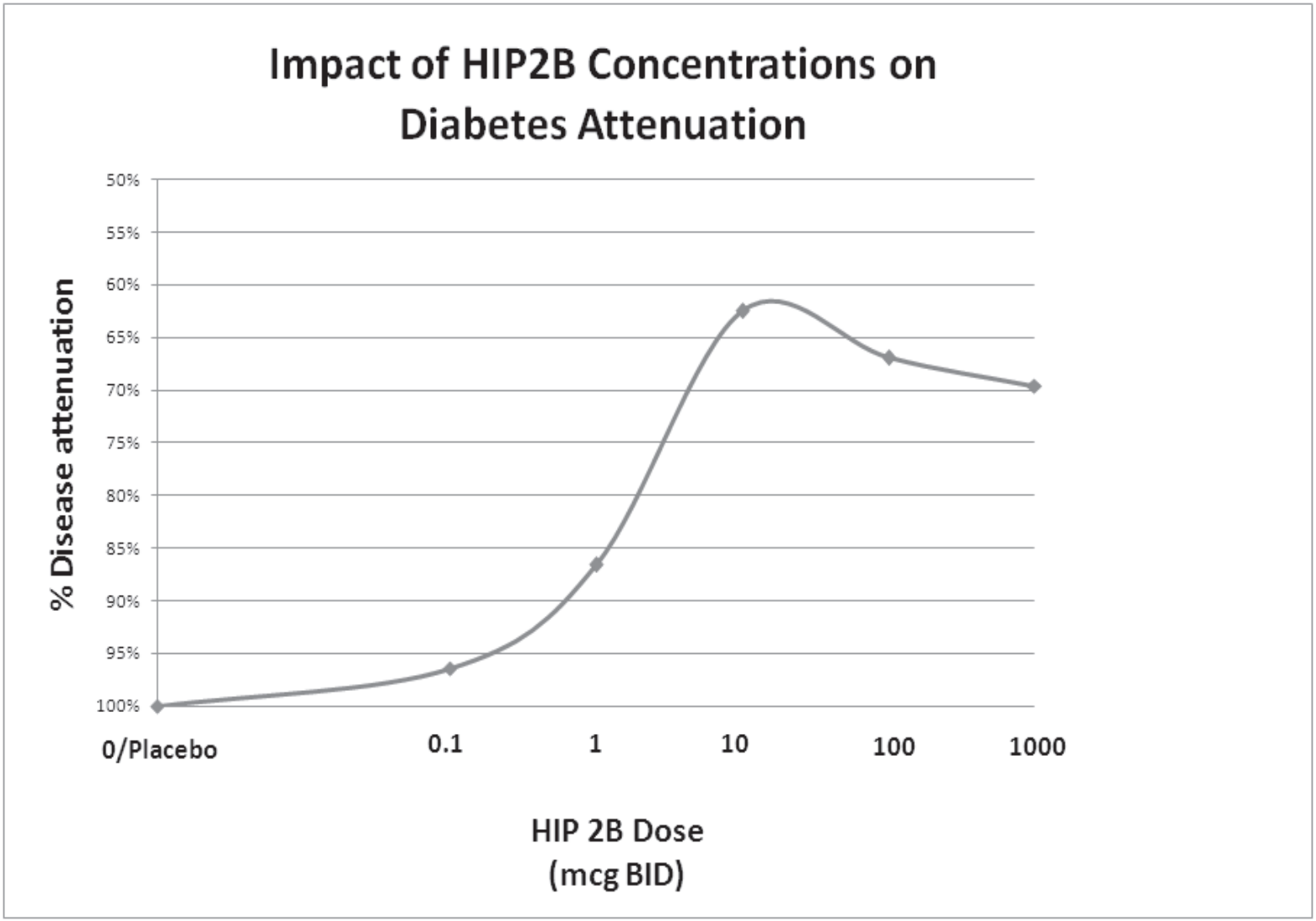

Impact of HIP2B Concentrations on Diabetes Attenuation
% Disease attenuation
50%
55%
60%
65%
70%
75%
80%
85%
90%
95%
100%
0/Placebo
0.1
1
10
100
1000
HIP 2B Dose
(mcg BID)

Fig. 23
25/27

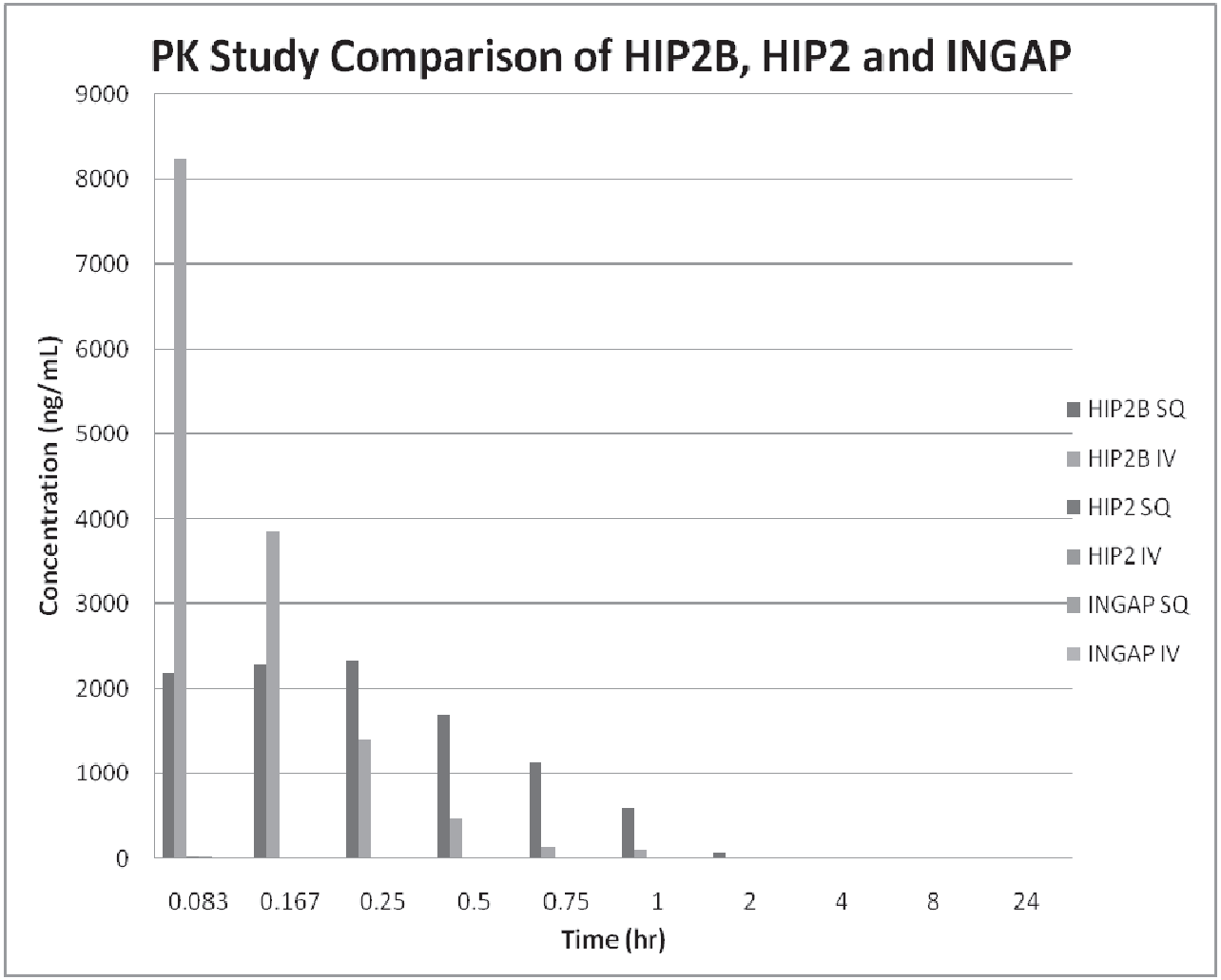

PK Study Comparison of HIP2B, HIP2 and INGAP
Concentration (ng/mL)
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
0.083
0.167
0.25
0.5
0.75
1
2
4
8
24
Time (hr)
HIP2B SQ
HIP2B IV
HIP2 SQ
HIP2 IV
INGAP SQ
INGAP IV

Fig. 24

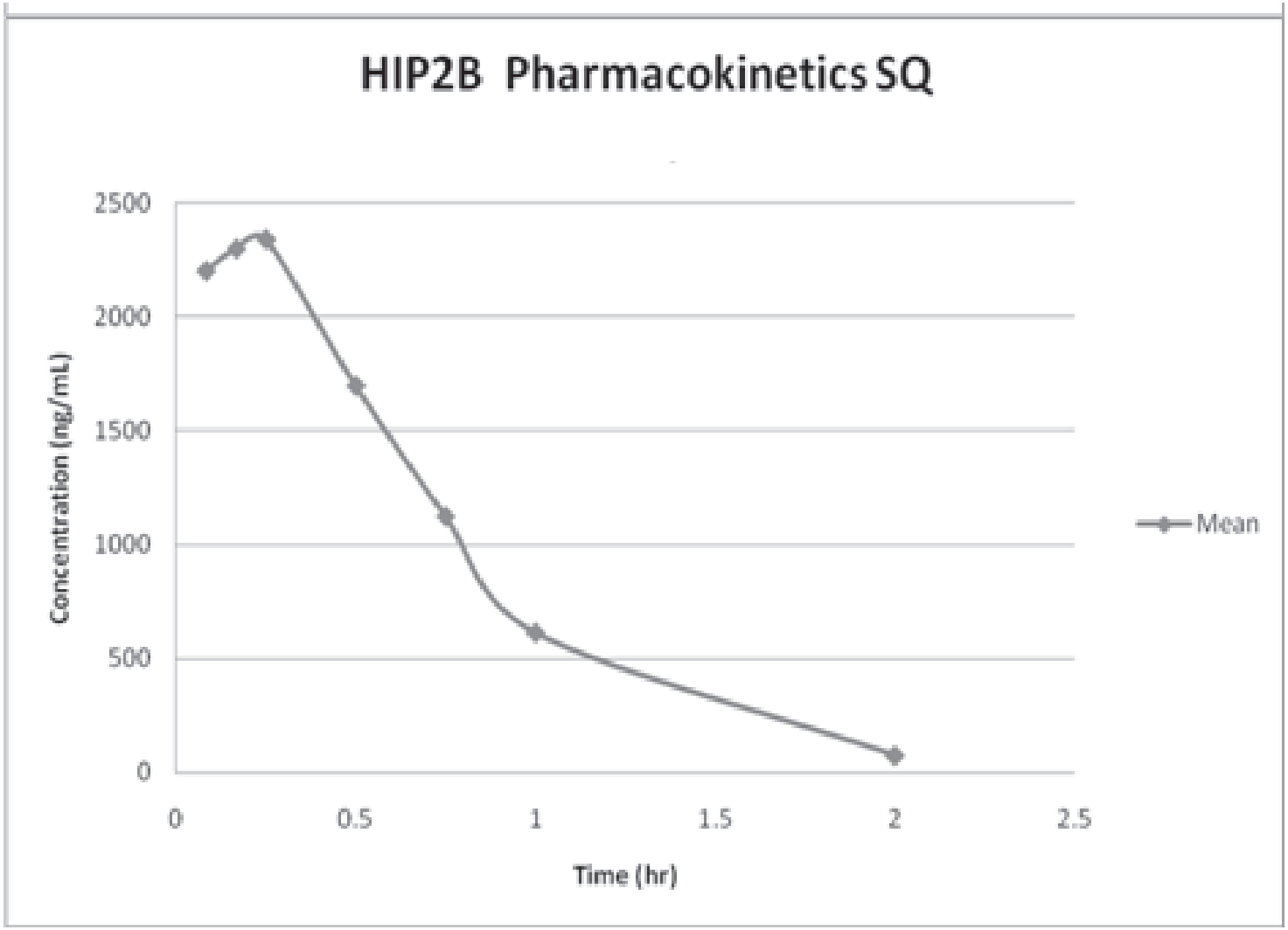

HIP2B Pharmacokinetics SQ
Concentration (ng/mL)
2500
2000
1500
1000
500
0
0
0.5
1
1.5
2
2.5
Time (hr)
Mean

Fig. 25