Figure 1

Fab	K_D (nM) 1-37 (WT)	K_D (nM) 19-37[a]	*K_D (nM) 25-37[a]*	K_D (mutant/parent) F27A	V28A	P29A	T30A	N31A	V32A	G33A	S34A	K35A	F37A
7E9	1.0	1.1±0.8	*0.14±0.05*	**1.0**	**1.0**	**26**	**7**	**9**	**41**	**1256**	**69**	**4**	**3598**
8B6	1.1	1.5±1.2	*0.45±0.08*	**1.0**	**1.0**	**9**	**2.2**	**3**	**5**	**496**	**26**	**3**	**2527**
10A8	2.1	2.4±1.4	*1.0±0.2*	**1.0**	**1.0**	**9**	**4**	**4**	**11**	**36**	**82**	**13**	**2152**
7D11	4.4	10±7	*3.4±0.4*	**1.1**	**1.0**	**7**	**4**	**5**	**5**	**86**	**18**	**1.4**	**420**
6H2	9.3	7.8±0.2	*8.5±0.5*	**0.9**	**1.0**	**1.0**	**0.8**	**4**	**11**	**14**	**0.5**	**1.0**	
4901	60.5	52±12	*296±115*	**0.8**	**0.8**	**0.2**	**0.2**	**0.3**	**0.9**	**1.3**	**0.8**	**0.3**	
14E10	79.7	91±3	*117.4±0.7*	**0.8**	**0.8**	**11**	**3**	**18**	**2**	**1**	**3**	**0.4[b]**	
9B8	84.7	76±20	*96±28*	**0.8**	**0.8**	**0.6**	**0.6**	**0.7**	**0.6**	**1.3**	**4**	**0.4[b]**	
13C2	94.4	86±13	*137±5*	**0.7**	**0.7**	**0.5**	**0.4**	**0.6**	**0.2**	**0.9**	**1.1**	**0.4[b]**	
14A9	148.4	219±114	*246±20*	**0.8**	**0.7**	**0.7**	**0.5**	**0.8**	**0.7**	**1.6**	**1.3**	**6**	
6D5	209.9	207±26	*378±22*	**0.8**	**0.7**	**0.5**	**0.4**	**0.6**	**0.5**	**3**	**1.1**	**5**	
1C5	296.4	223±51	*430±173*	**0.8**	**0.8**	**0.6**	**0.4**	**0.6**	**0.6**	**1.1**	**1.1**	**5**	

Figure 2A

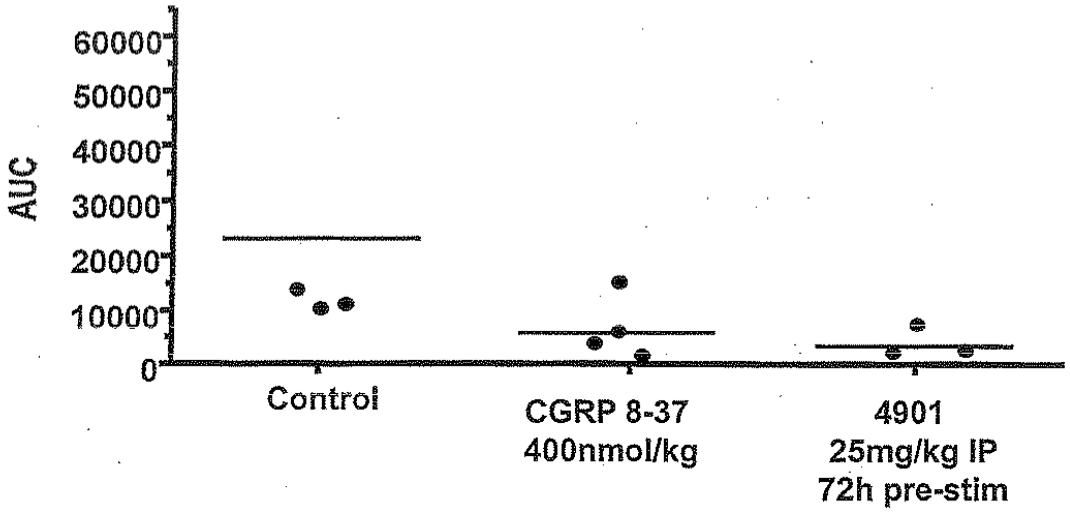

AUC
60000
50000
40000
30000
20000
10000
0
Control
CGRP 8-37
400nmol/kg
4901
25mg/kg IP
72h pre-stim

Figure 2B

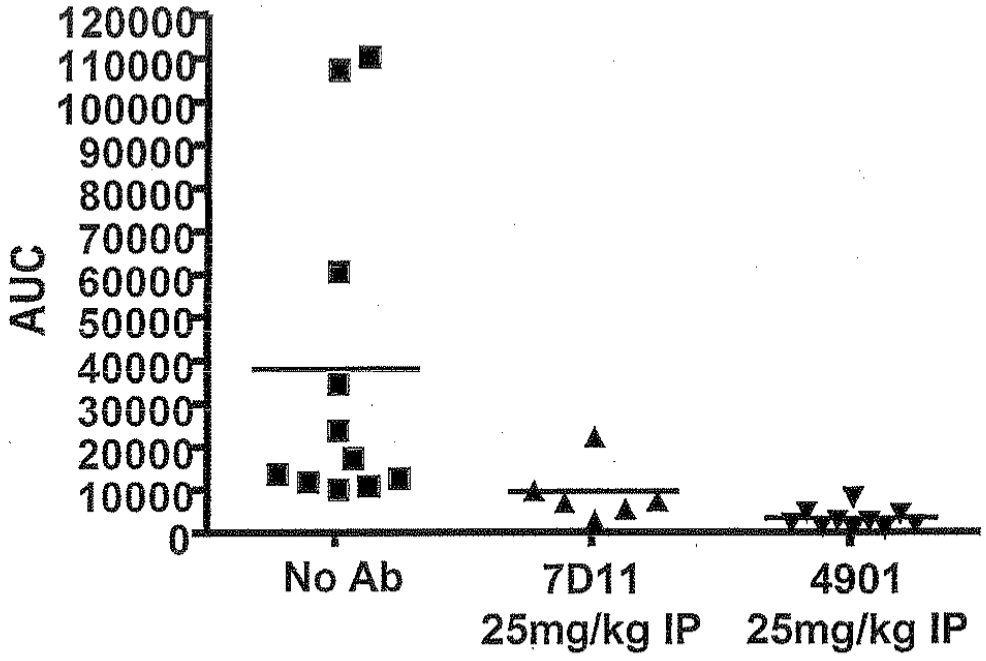

AUC
120000
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
No Ab
7D11
25mg/kg IP
4901
25mg/kg IP

Figure 3

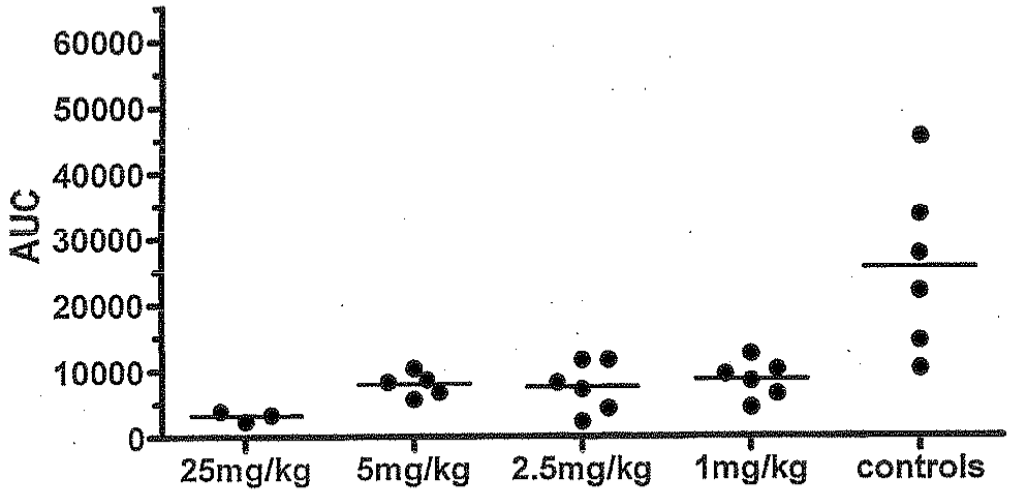

60000
50000
40000
30000
20000
10000
0
AUC
25mg/kg
5mg/kg
2.5mg/kg
1mg/kg
controls

Figure 4A

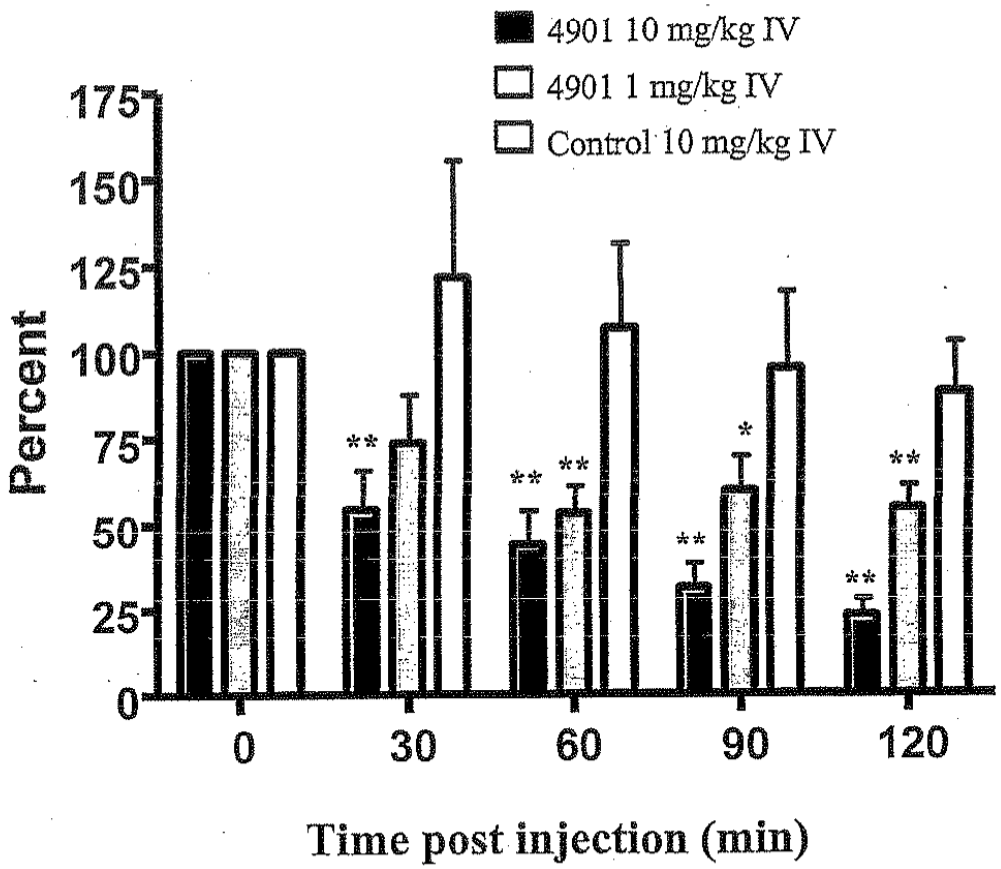

4901 10 mg/kg IV
4901 1 mg/kg IV
Control 10 mg/kg IV
Percent
175
150
125
100
75
50
25
0
0
30
60
90
120
Time post injection (min)

Figure 4B

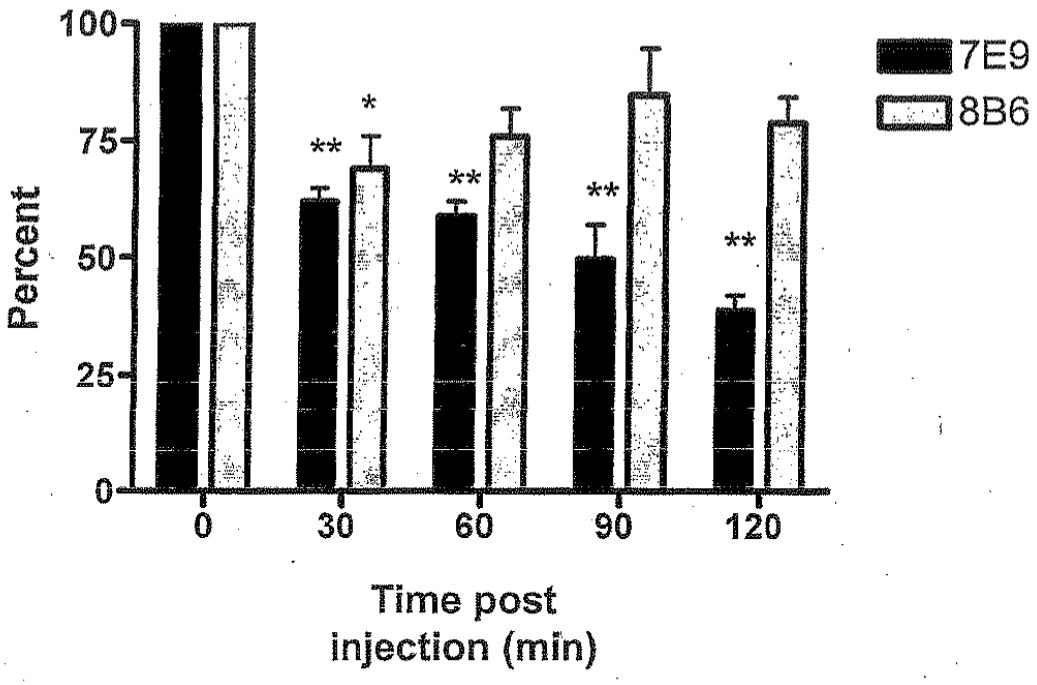

100
75
50
25
0
Percent
0
30
60
90
120
Time post injection (min)
7E9
8B6
**
*
**
**
**

Figure 5

Bold=Kabat CDR
Underline=Chothia CDR

G1 Heavy chain

H1
1 5 10 15 20 25 30
E V Q L V E S G G G L V Q P G G S L R L S C A A S G F T F S

H2
31 35 40 45 50 55 60
N Y W I S W V R Q A P G K G L E W V A **E I R S E S D A S A T**

61 65 70 75 80 85 90
H Y A E A V K G R F T I S R D N A K N S L Y L Q M N S L R A

H3
91 95 100 105 110 115 120
E D T A V Y Y C L A **Y F D Y G L A I Q N Y** W G Q G T L V T V

121 122
S S

G1 Light chain

L1
1 5 10 15 20 25 30
E I V L T Q S P A T L S L S P G E R A T L S C **K A S K R V T**

L2
31 35 40 45 50 55 60
T Y V S W Y Q Q K P G Q A P R L L I Y **G A S N R Y L** G I P A

61 65 70 75 80 85 90
R F S G S G S G T D F T L T I S S L E P E D F A V Y Y C **S Q**

L3
91 95 100 105 107
S Y N Y P Y T F G Q G T K L E I K

Figure 6

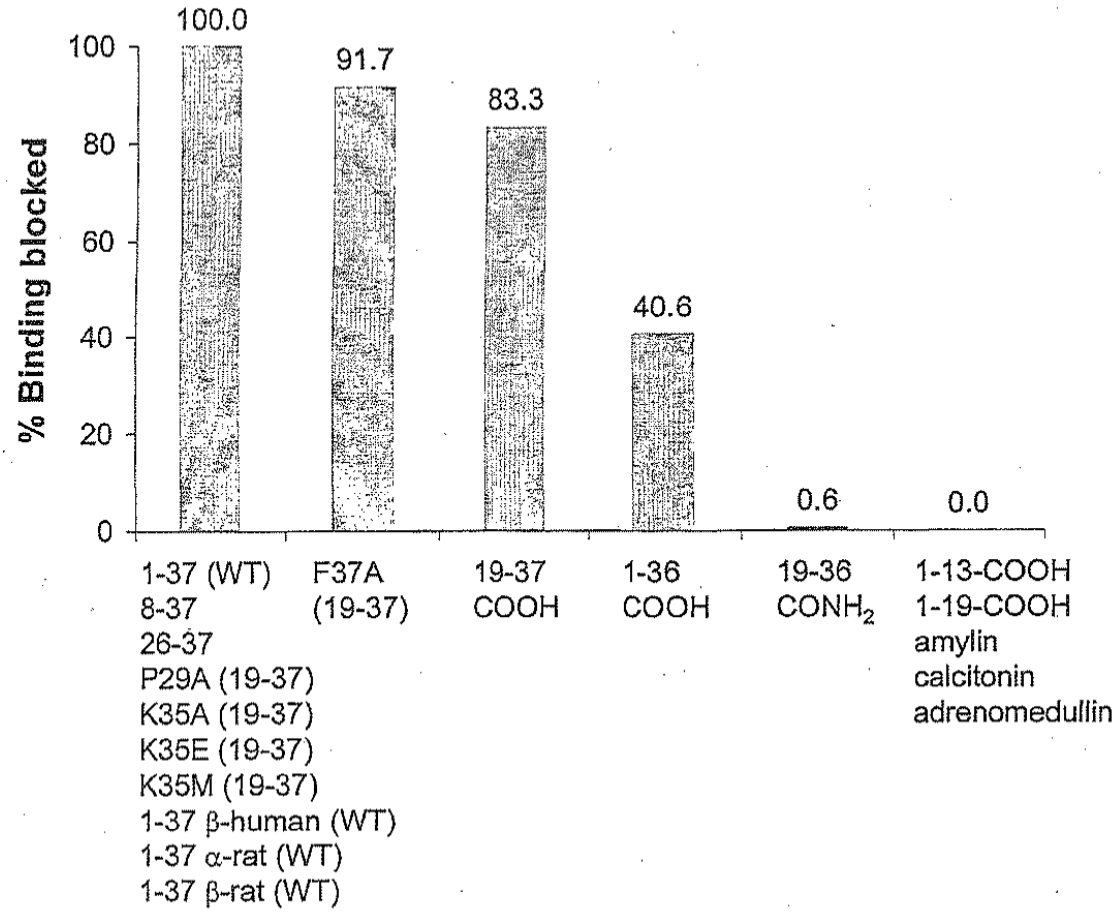

100.0
91.7
83.3
40.6
0.6
0.0
100
80
60
40
20
0
% Binding blocked
1-37 (WT)
8-37
26-37
P29A (19-37)
K35A (19-37)
K35E (19-37)
K35M (19-37)
1-37 β-human (WT)
1-37 α-rat (WT)
1-37 β-rat (WT)
F37A (19-37)
19-37 COOH
1-36 COOH
19-36 CONH2
1-13-COOH
1-19-COOH
amylin
calcitonin
adrenomedullin
Competing Peptides

Figure 7

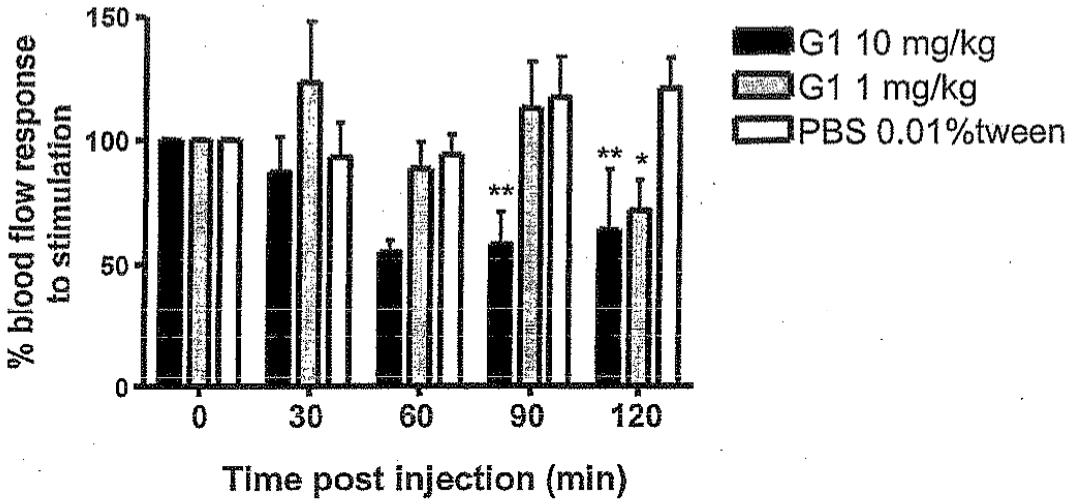

% blood flow response to stimulation
150
100
50
0
0
30
60
90
120
Time post injection (min)
**
**
*
G1 10 mg/kg
G1 1 mg/kg
PBS 0.01%tween

Figure 8A

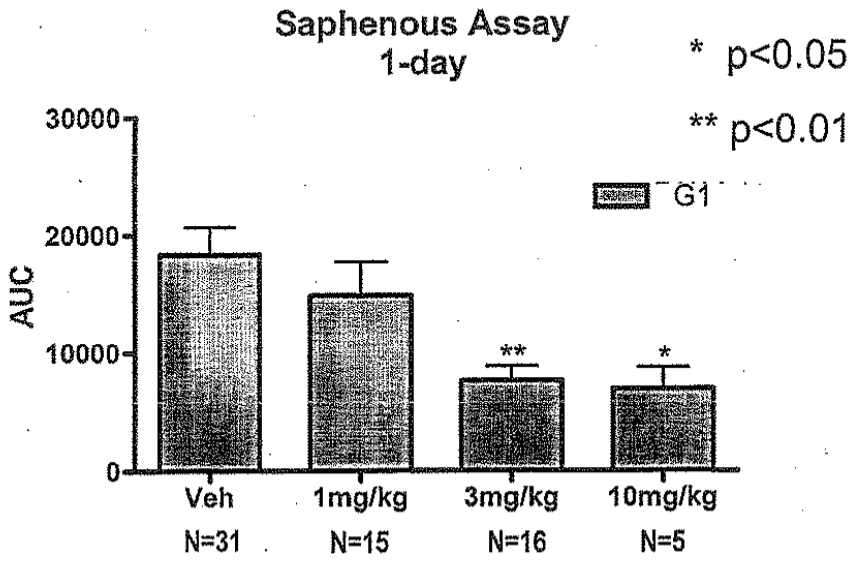

Saphenous Assay
1-day
* p<0.05
** p<0.01
G1
AUC
30000
20000
10000
0
**
*
Veh
N=31
1mg/kg
N=15
3mg/kg
N=16
10mg/kg
N=5

Figure 8B

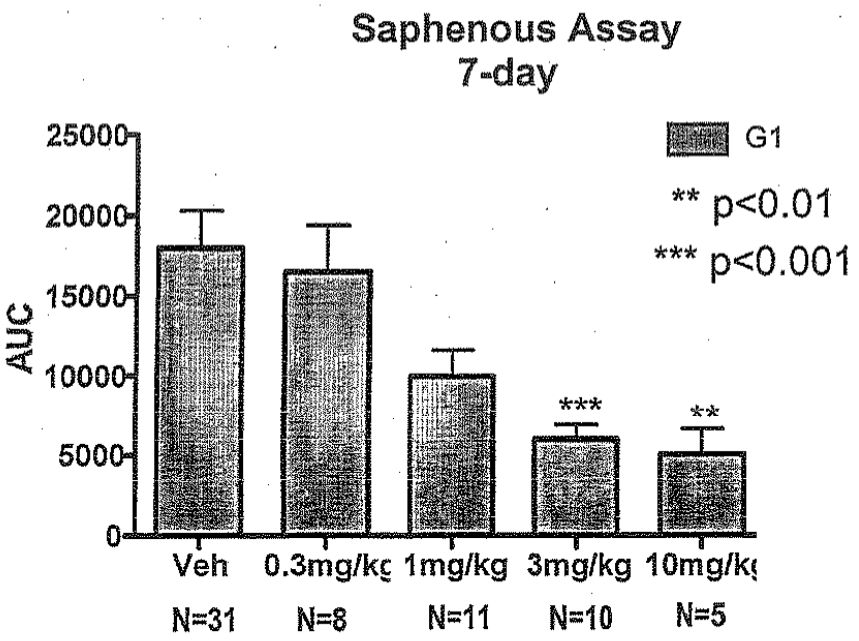

Saphenous Assay
7-day
G1
** p<0.01
*** p<0.001
AUC
25000
20000
15000
10000
5000
0
***
**
Veh
0.3mg/kg
1mg/kg
3mg/kg
10mg/kg
N=31
N=8
N=11
N=10
N=5

Figure 8C

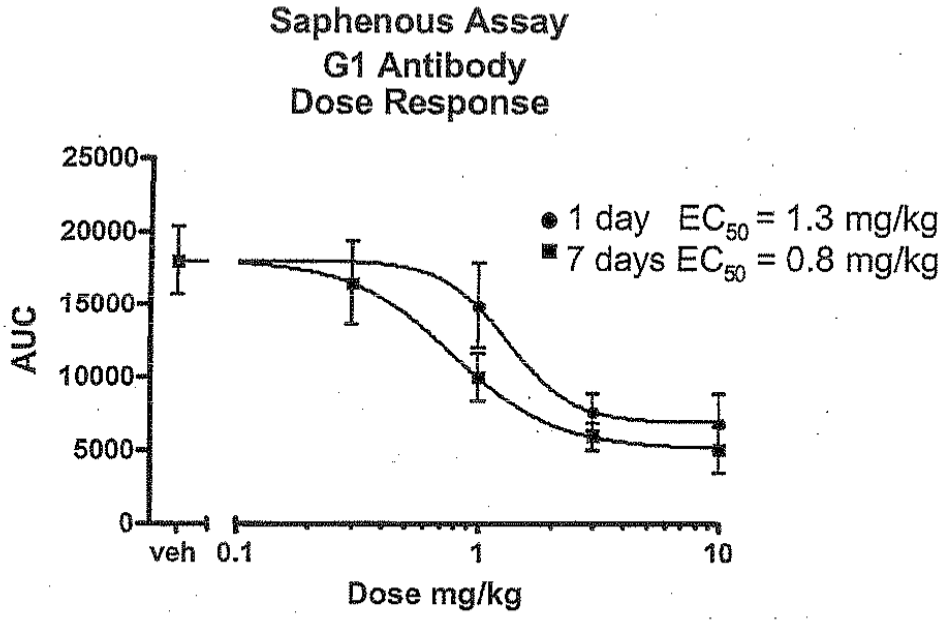

Saphenous Assay
G1 Antibody
Dose Response
25000
20000
15000
10000
5000
0
AUC
veh
0.1
1
10
Dose mg/kg
1 day EC50 = 1.3 mg/kg
7 days EC50 = 0.8 mg/kg

Figure 9

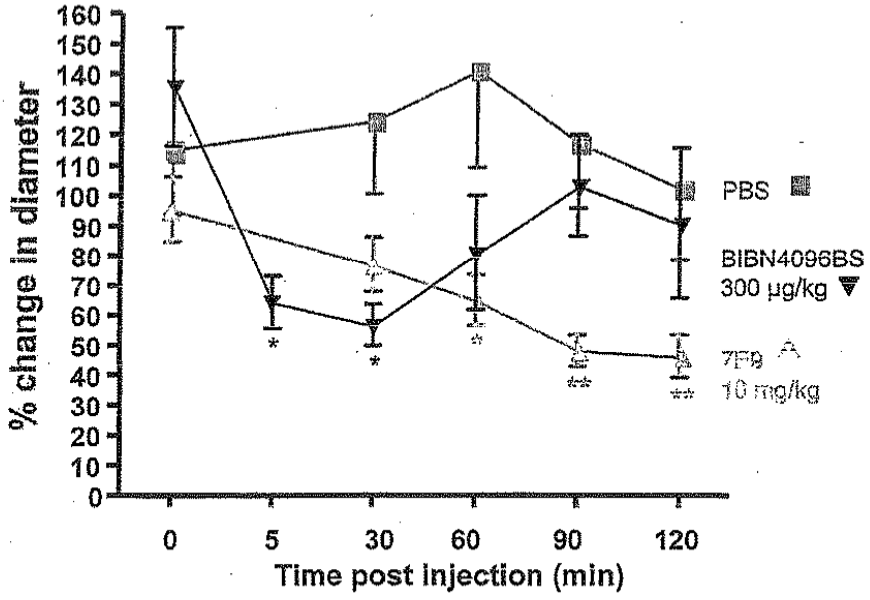

% change in diameter
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
0
5
30
60
90
120
Time post injection (min)
PBS
BIBN4096BS
300 µg/kg
7F9
10 mg/kg
*
*
*
**
**

Figure 10

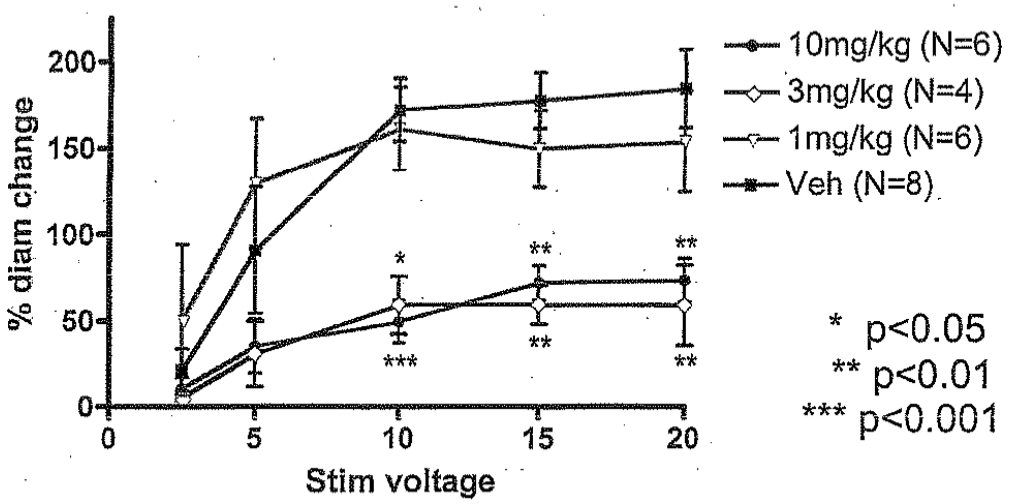

% diam change
200
150
100
50
0
0
5
10
15
20
Stim voltage
10mg/kg (N=6)
3mg/kg (N=4)
1mg/kg (N=6)
Veh (N=8)
*
**
***
* p<0.05
** p<0.01
*** p<0.001

Figure 11A

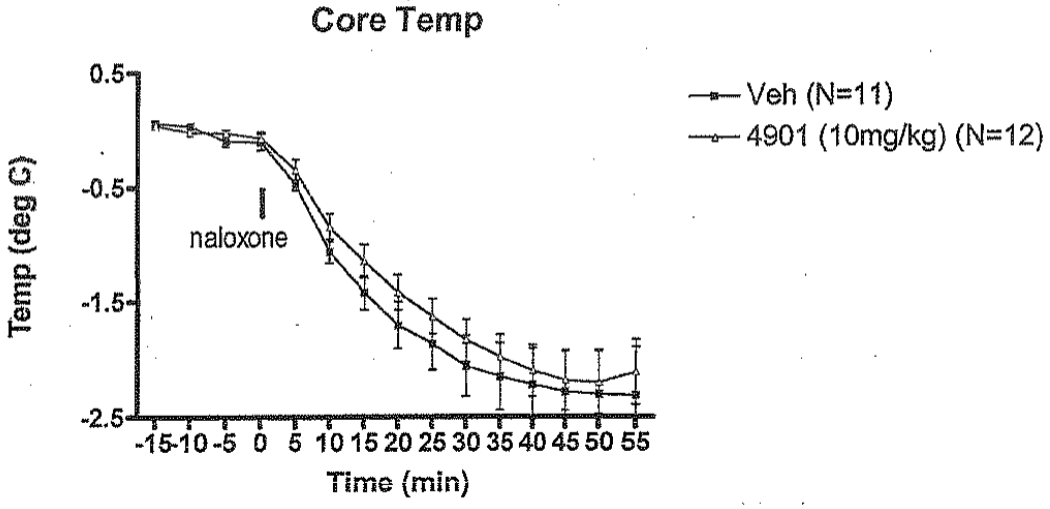
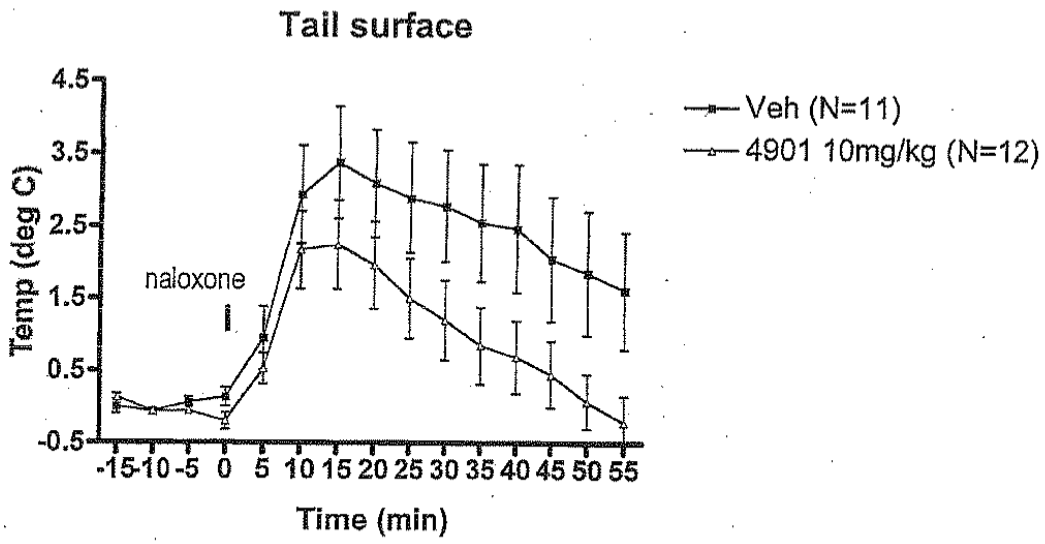

Core Temp
Temp (deg C)
0.5
-0.5
-1.5
-2.5
naloxone
-15 -10 -5 0 5 10 15 20 25 30 35 40 45 50 55
Time (min)
Veh (N=11)
4901 (10mg/kg) (N=12)

Figure 11B


Tail surface
Temp (deg C)
4.5
3.5
2.5
1.5
0.5
-0.5
naloxone
-15 -10 -5 0 5 10 15 20 25 30 35 40 45 50 55
Time (min)
Veh (N=11)
4901 10mg/kg (N=12)