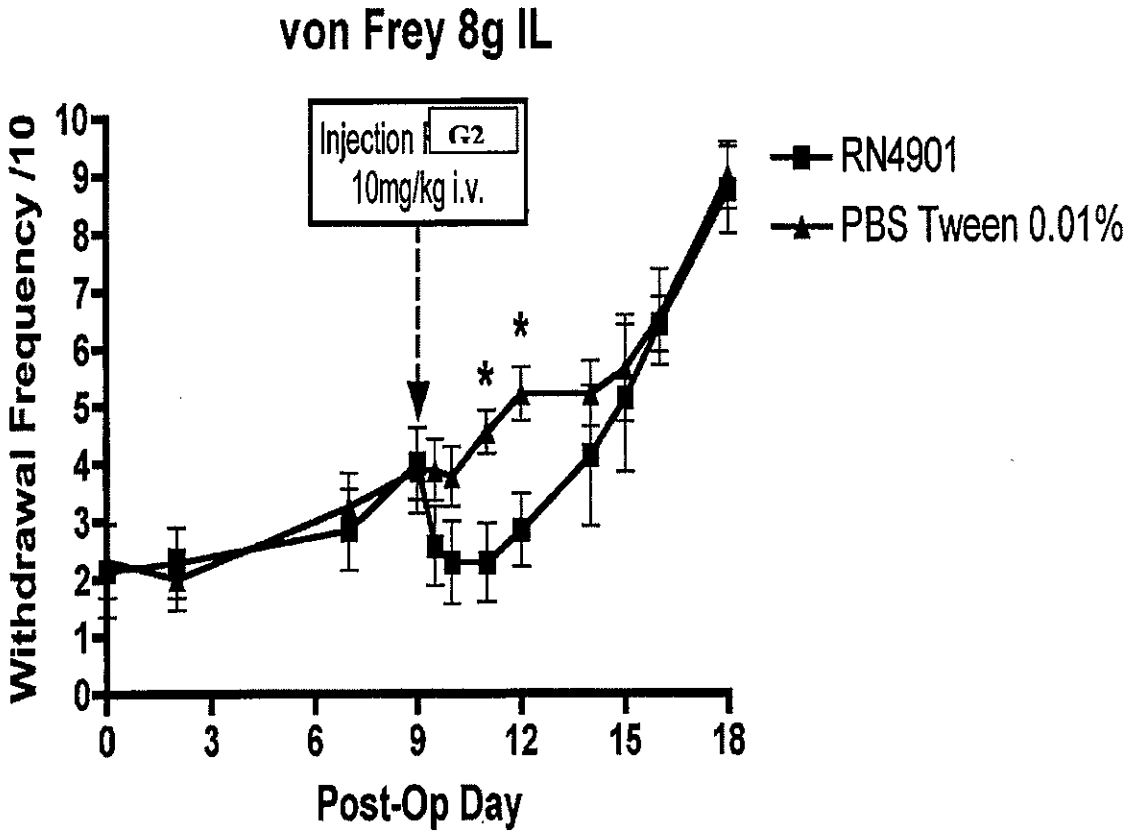

von Frey 8g IL
Injection G2
10mg/kg i.v.
RN4901
PBS Tween 0.01%
Withdrawal Frequency /10
Post-Op Day
0
1
2
3
4
5
6
7
8
9
10
0
3
6
9
12
15
18
*
*

Figure 1

5

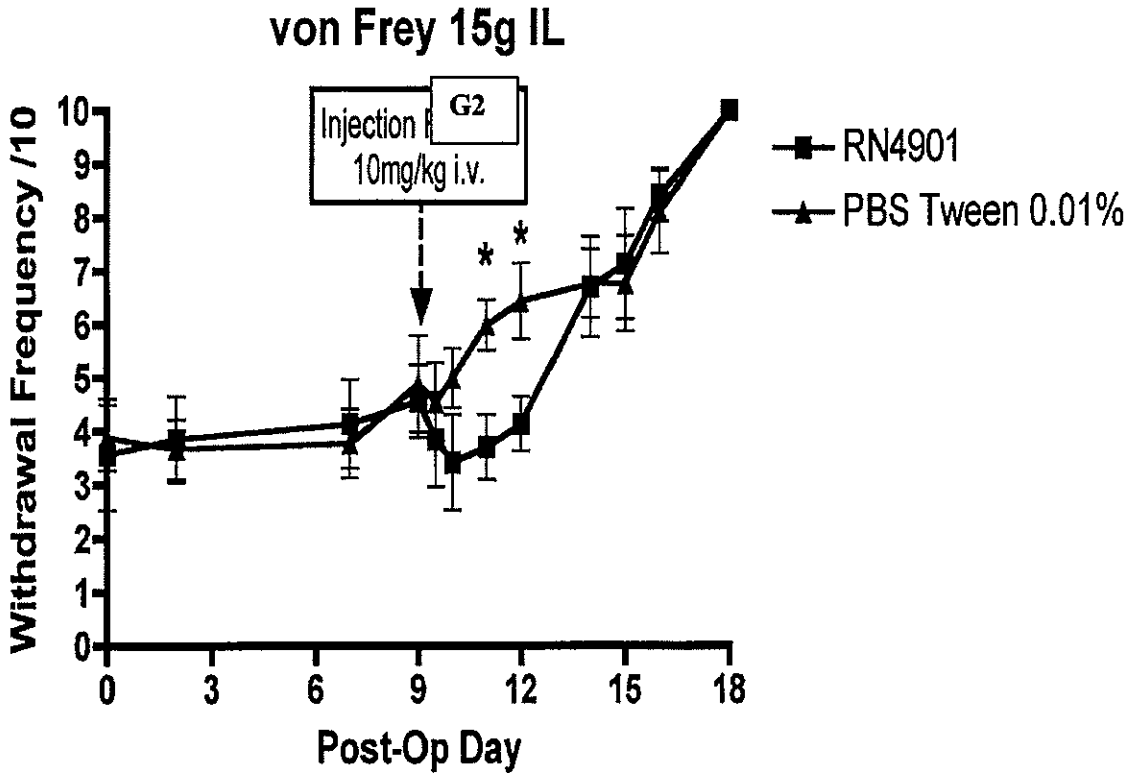

von Frey 15g IL
Injection
10mg/kg i.v.
G2
RN4901
PBS Tween 0.01%
Withdrawal Frequency /10
Post-Op Day
0
1
2
3
4
5
6
7
8
9
10
0
3
6
9
12
15
18
*
*

Figure 2

5

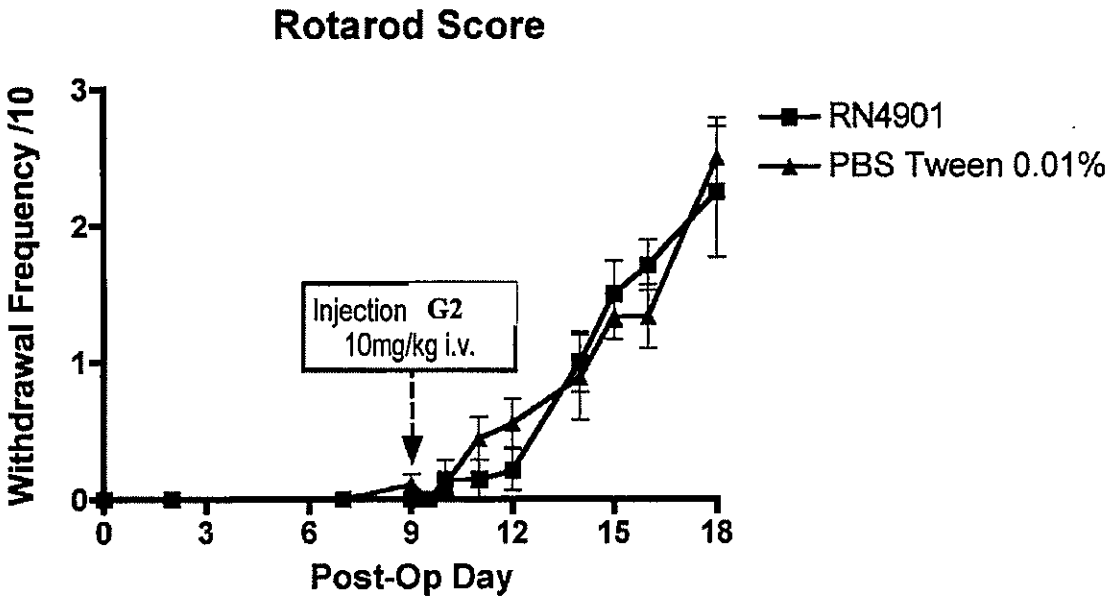

Rotarod Score
Withdrawal Frequency /10
3
2
1
0
0
3
6
9
12
15
18
Post-Op Day
Injection G2
10mg/kg i.v.
RN4901
PBS Tween 0.01%

Figure 3

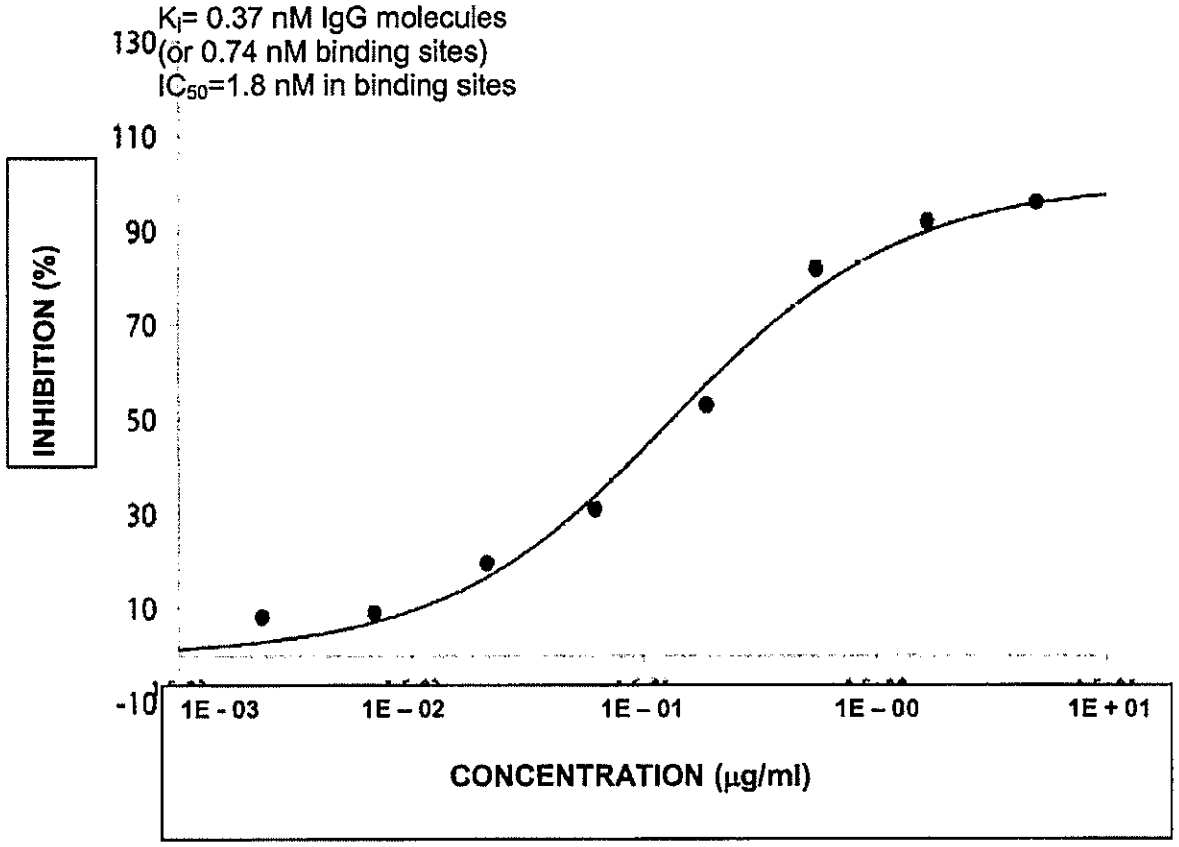

K_I= 0.37 nM IgG molecules
(or 0.74 nM binding sites)
IC_{50}=1.8 nM in binding sites
130
110
90
70
50
30
10
-10
INHIBITION (%)
1E - 03
1E – 02
1E – 01
1E – 00
1E + 01
CONCENTRATION (µg/ml)

Figure 4:

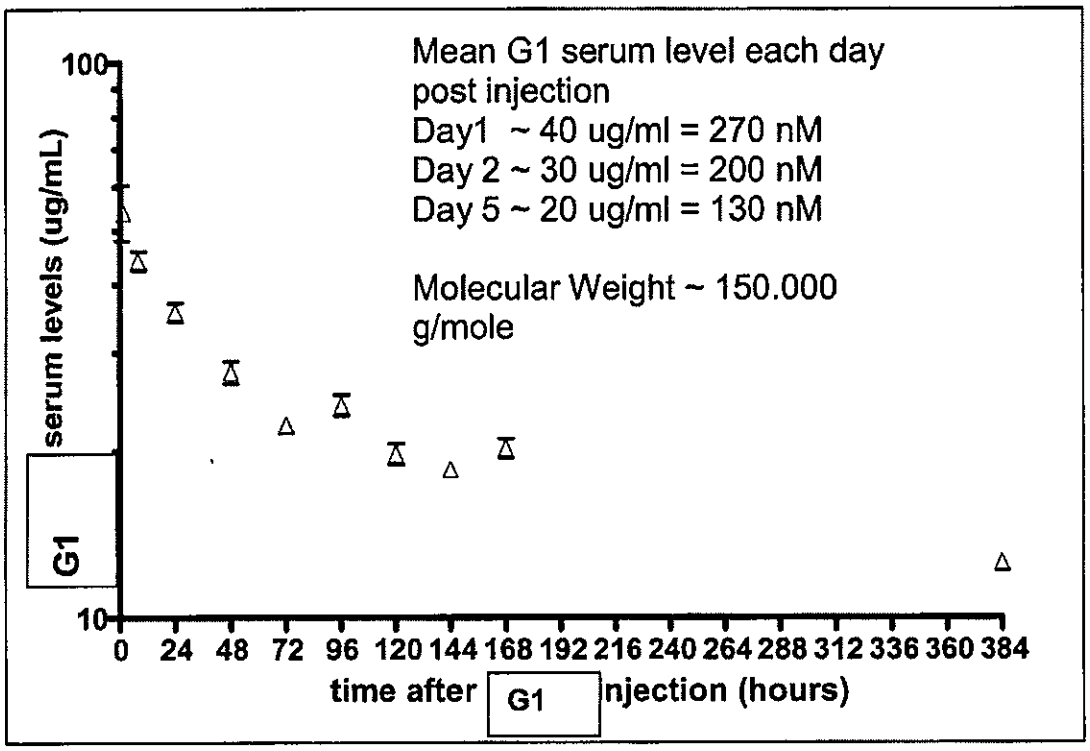

Mean G1 serum level each day post injection
Day1 ~ 40 ug/ml = 270 nM
Day 2 ~ 30 ug/ml = 200 nM
Day 5 ~ 20 ug/ml = 130 nM
Molecular Weight ~ 150.000 g/mole
serum levels (ug/mL)
100
10
G1
0 24 48 72 96 120 144 168 192 216 240 264 288 312 336 360 384
time after G1 injection (hours)

Figure 5a

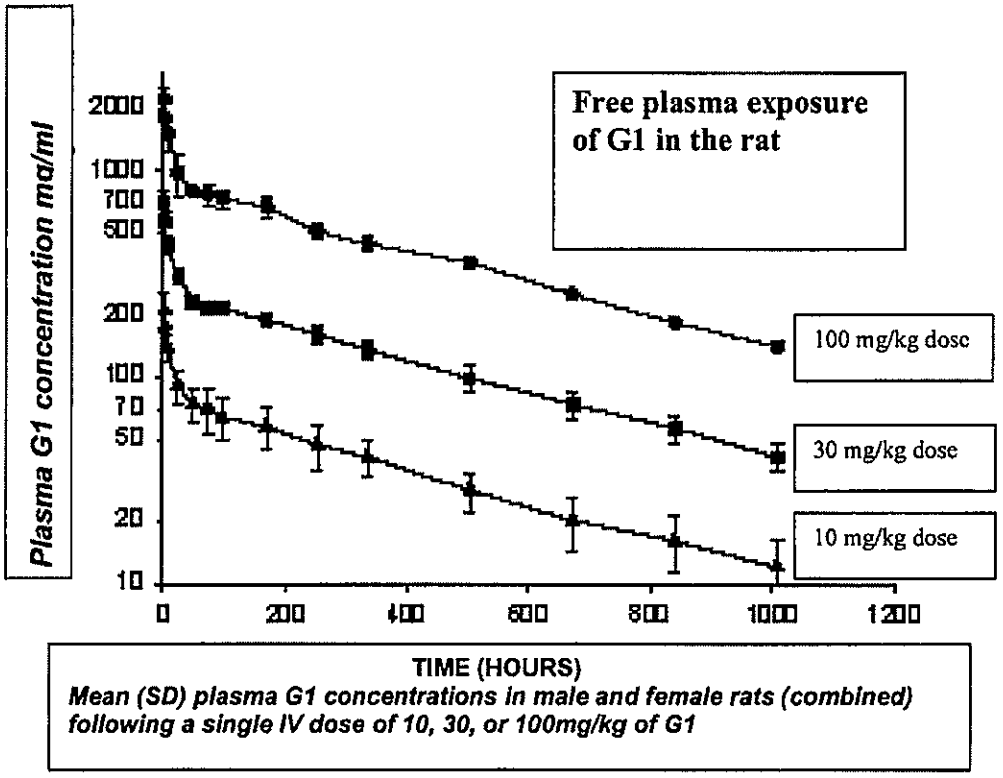

Plasma G1 concentration mg/ml
2000
1000
700
500
200
100
70
50
20
10
0
200
400
600
800
1000
1200
Free plasma exposure of G1 in the rat
100 mg/kg dose
30 mg/kg dose
10 mg/kg dose
TIME (HOURS)
Mean (SD) plasma G1 concentrations in male and female rats (combined) following a single IV dose of 10, 30, or 100mg/kg of G1

Figure 5b

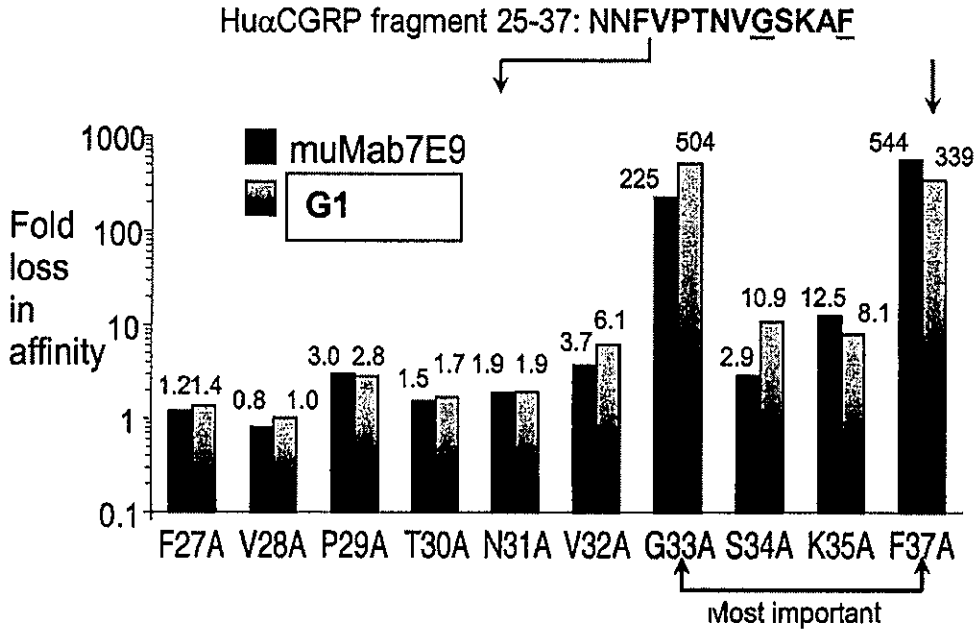

HuαCGRP fragment 25-37: NNFVPTNVGSKAF
muMab7E9
G1
Fold loss in affinity
1000
100
10
1
0.1
1.2 1.4
0.8
1.0
3.0 2.8
1.5
1.7 1.9 1.9
3.7
6.1
225
504
2.9
10.9
12.5
8.1
544
339
F27A V28A P29A T30A N31A V32A G33A S34A K35A F37A
Most important

Figure 6

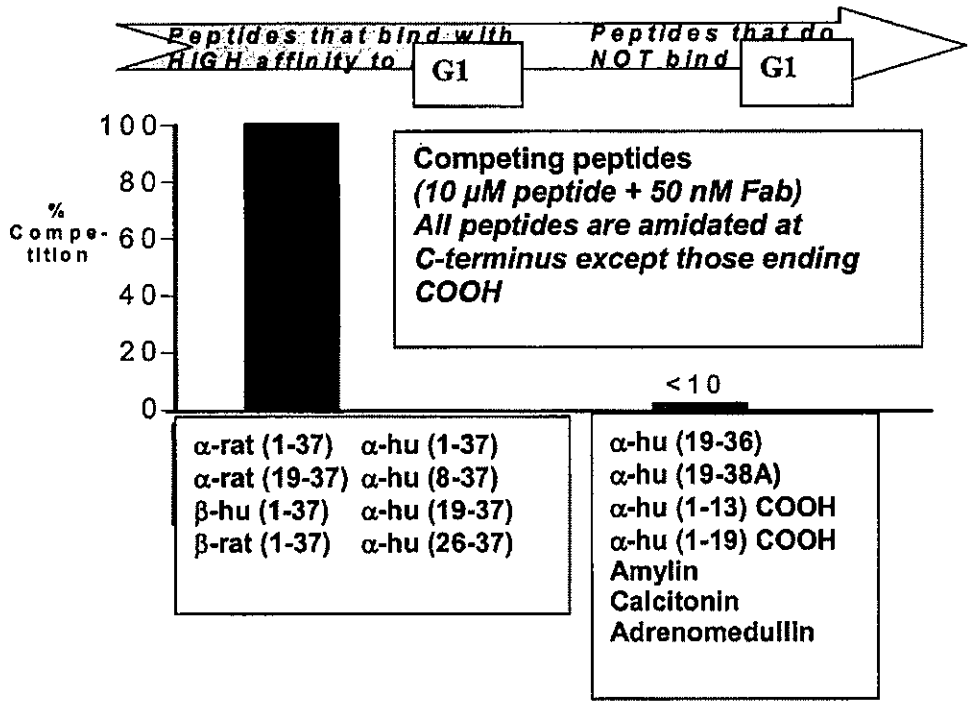

Peptides that bind with HIGH affinity to G1
Peptides that do NOT bind G1
% Competition
100
80
60
40
20
0
Competing peptides
(10 µM peptide + 50 nM Fab)
All peptides are amidated at C-terminus except those ending COOH
α-rat (1-37)
α-rat (19-37)
β-hu (1-37)
β-rat (1-37)
α-hu (1-37)
α-hu (8-37)
α-hu (19-37)
α-hu (26-37)
<10
α-hu (19-36)
α-hu (19-38A)
α-hu (1-13) COOH
α-hu (1-19) COOH
Amylin
Calcitonin
Adrenomedullin

Figure 7

*NH2-ACDTATCVTHRLAGLLSRSGGVVKNNFVPTNV**GSKAF**-CONH2*
Human α-CGRP (identical to *cynomolgus* α-CGRP)

*NH2-ACNTATCVTHRLAGLLSRSGGMVKSNFVPTNV**GSKAF**-CONH2*
Human β-CGRP (identical to *cynomolgus* β-CGRP)

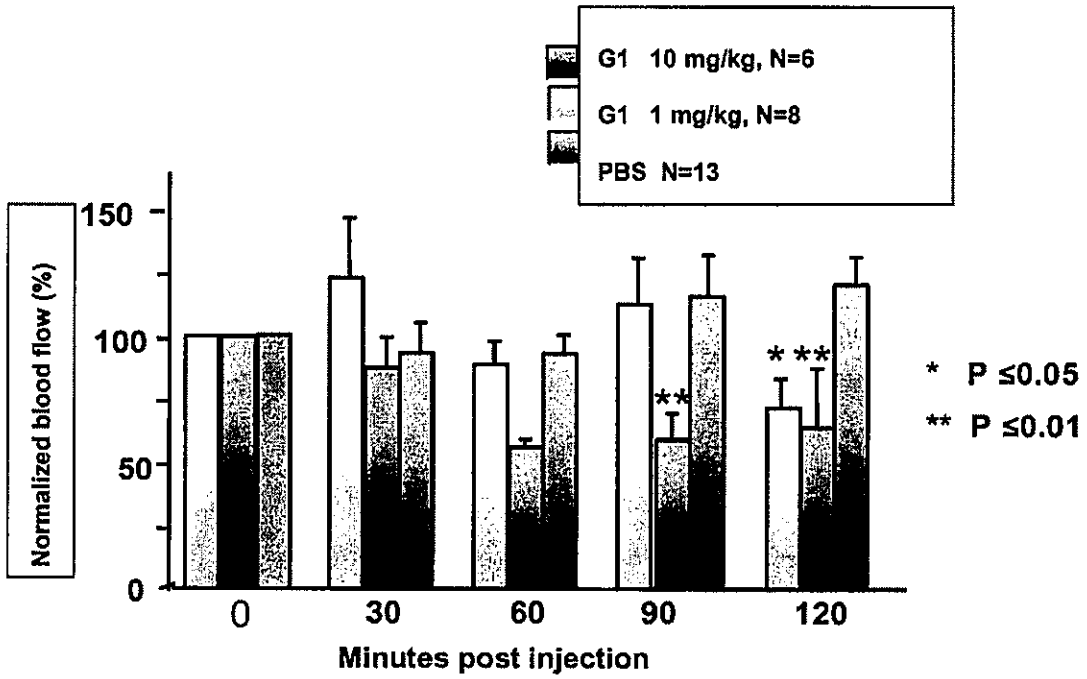
*NH2-SCNTATCVTHRLAGLLSRSGGVVKDNFVPTNV**GSEAF**-CONH2*
Rat α-CGRP (identical to mouse and dog α-CGRP)

*NH2-SCNTATCVTHRLAGLLSRSGGVVKDNFVPTNV**GSKAF**-CONH2*
Rat β-CGRP

*NH2-SCNTATCVTHRLADLLSRSGGVLKDNFVPTDV**GSEAF**-CONH2*
Mouse β-CGRP

*NH2-GCNTATCVTHRLAGLLSRSGGMVKSNFVPTNV**GSEAF**-CONH2*
Rabbit CGRP

Figure 8


G1 10 mg/kg, N=6
G1 1 mg/kg, N=8
PBS N=13
Normalized blood flow (%)
150
100
50
0
0
30
60
90
120
Minutes post injection
* P ≤0.05
** P ≤0.01

5

Figure 9