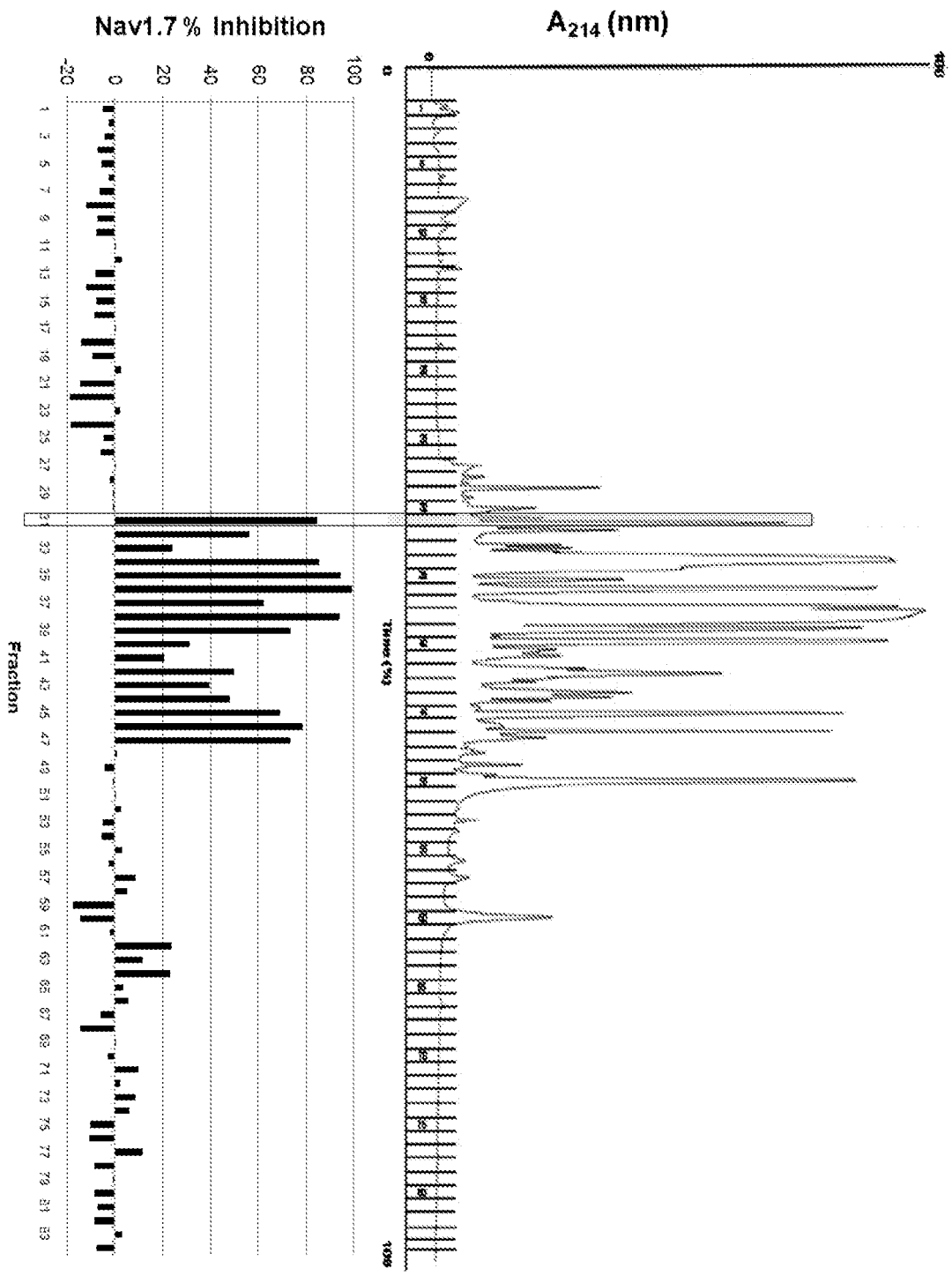


FIG.1

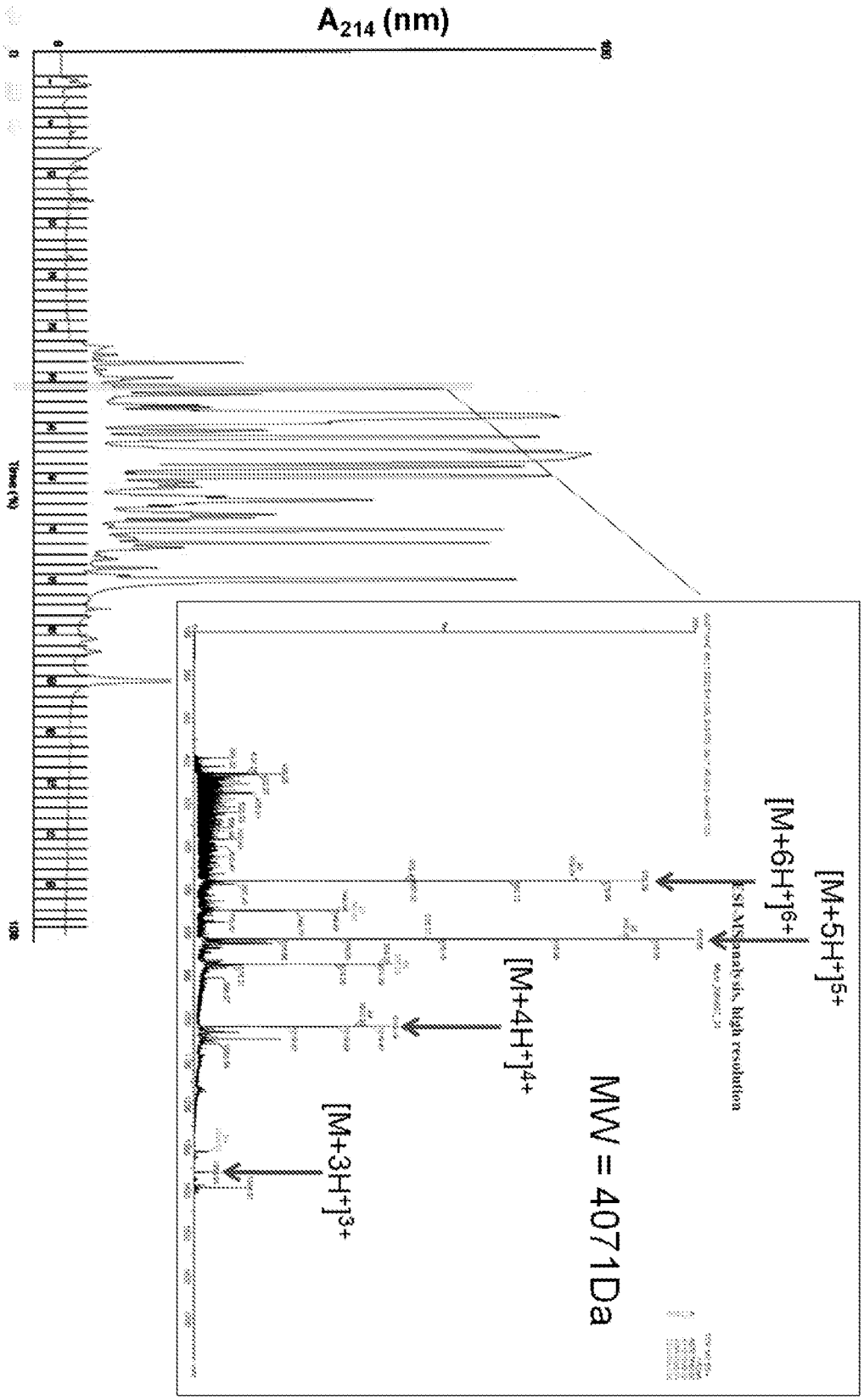


FIG. 2

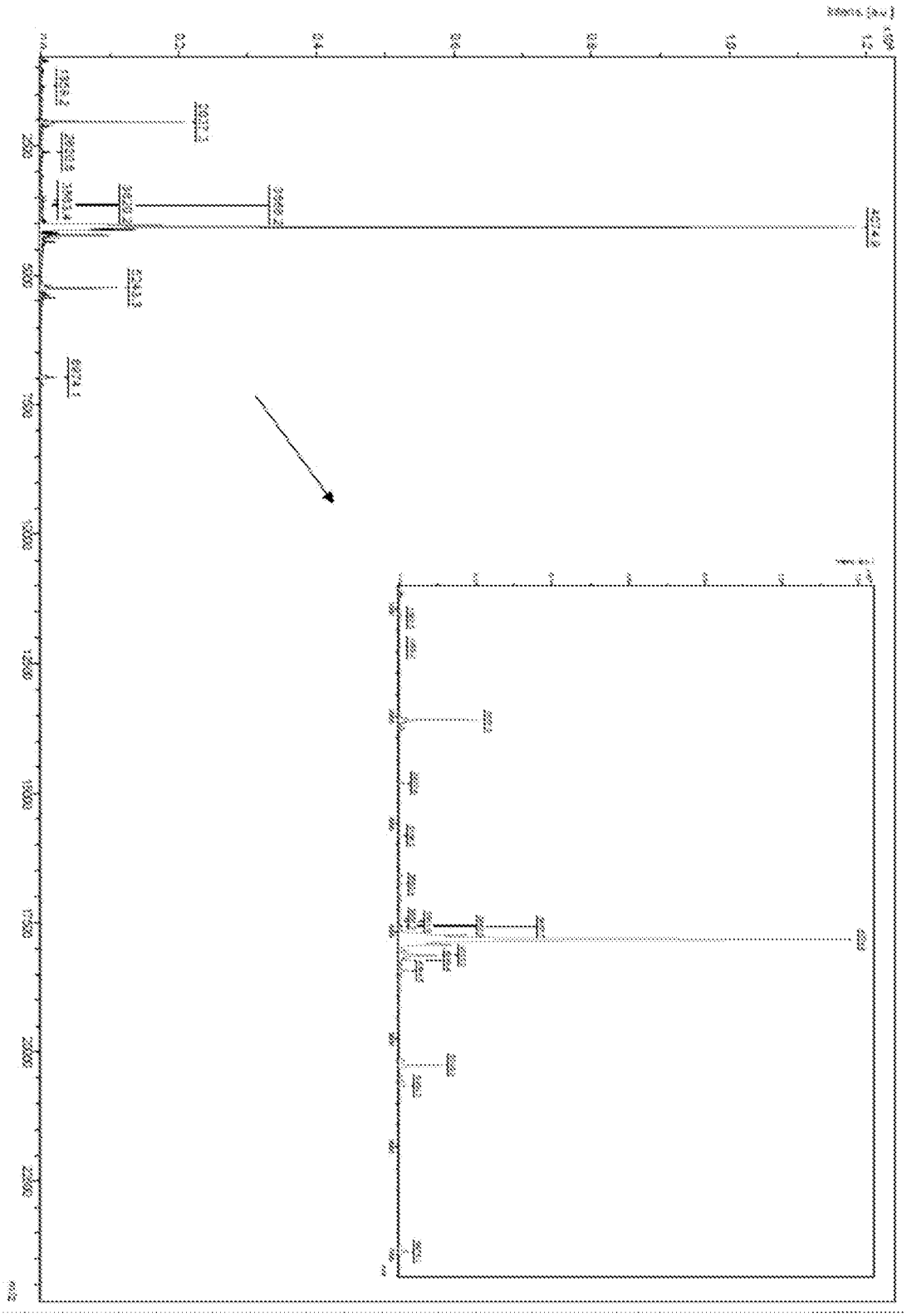


FIG. 3

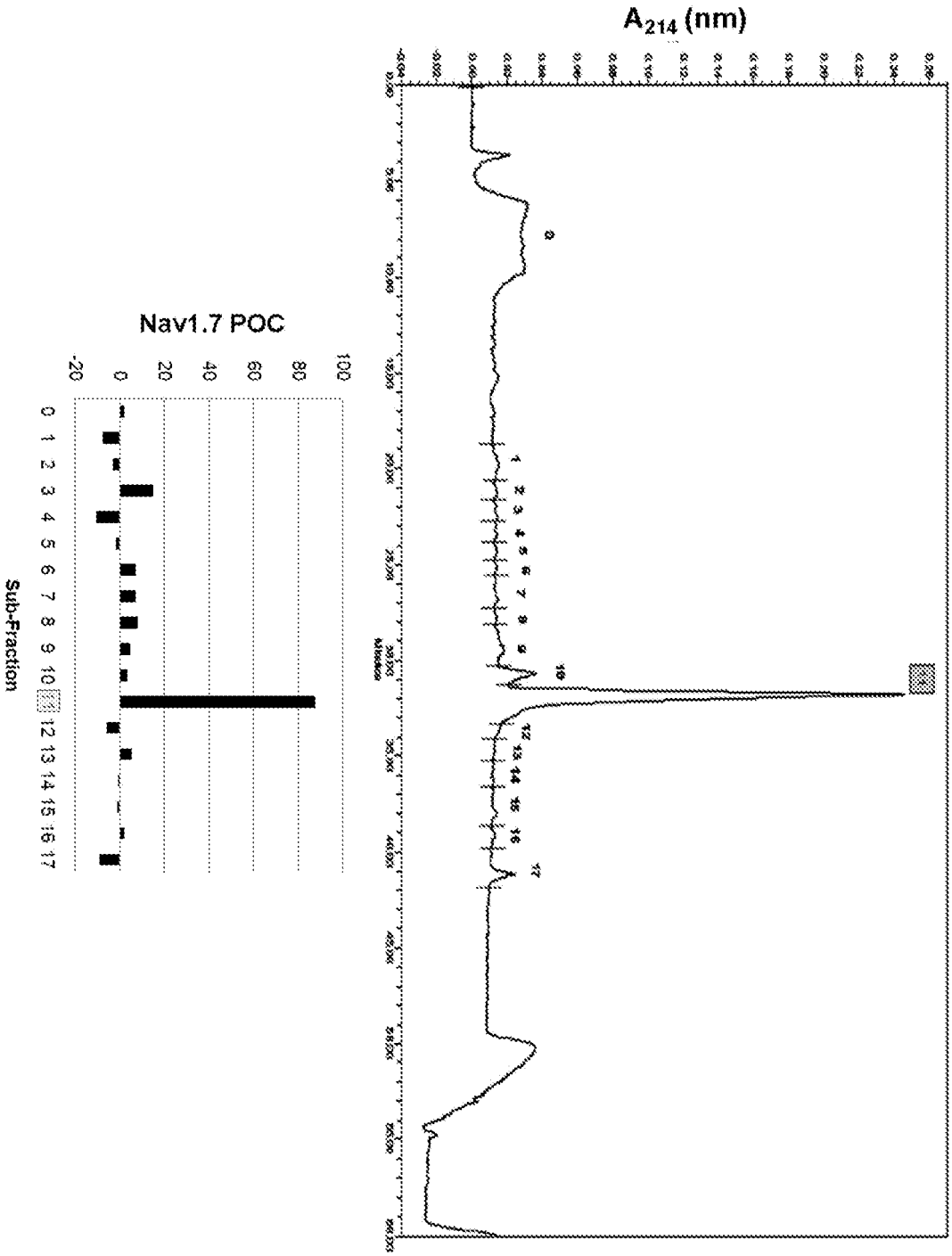

A214 (nm)
Nav1.7 POC
-20
0
20
40
60
80
100
0 1 2 3 4 5 6 7 8 9 10 12 13 14 15 16 17
Sub-Fraction

FIG.4

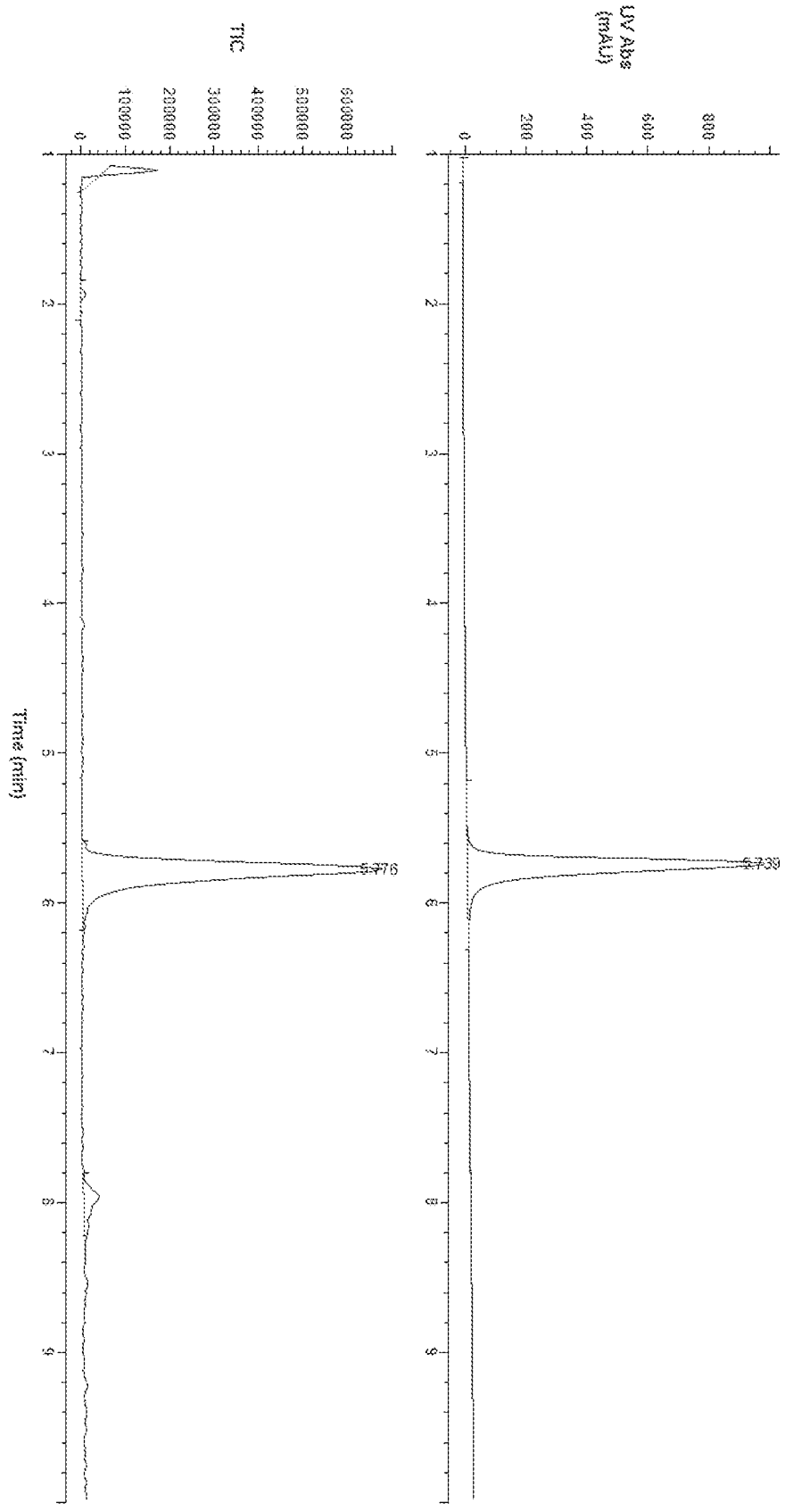


FIG. 5

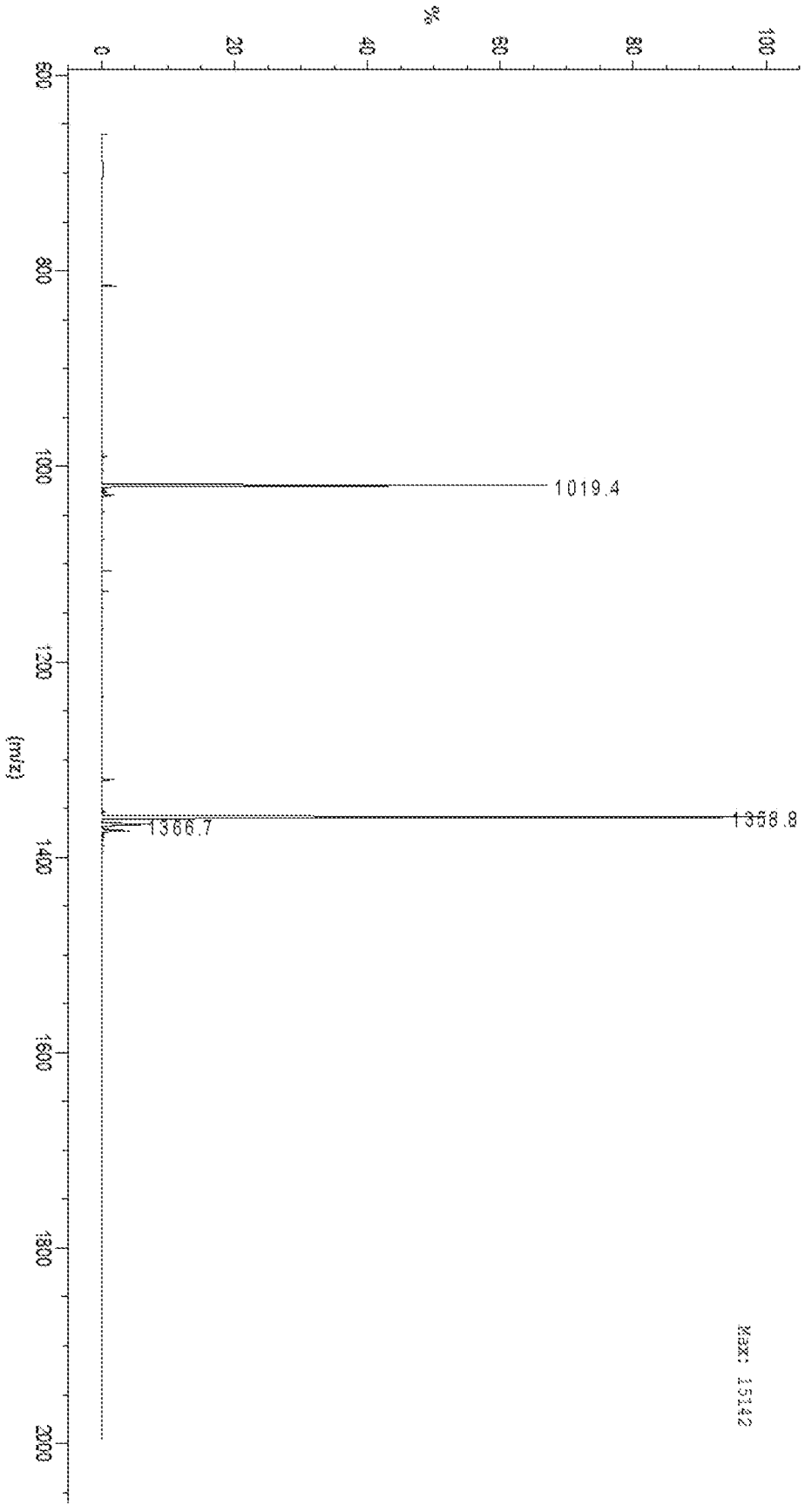

%
0
20
40
60
80
100
800
900
1000
1100
1200
1300
1400
1500
1600
1700
1800
1900
2000
m/z
1019.4
1366.7
1368.9
Max: 15142

FIG. 6

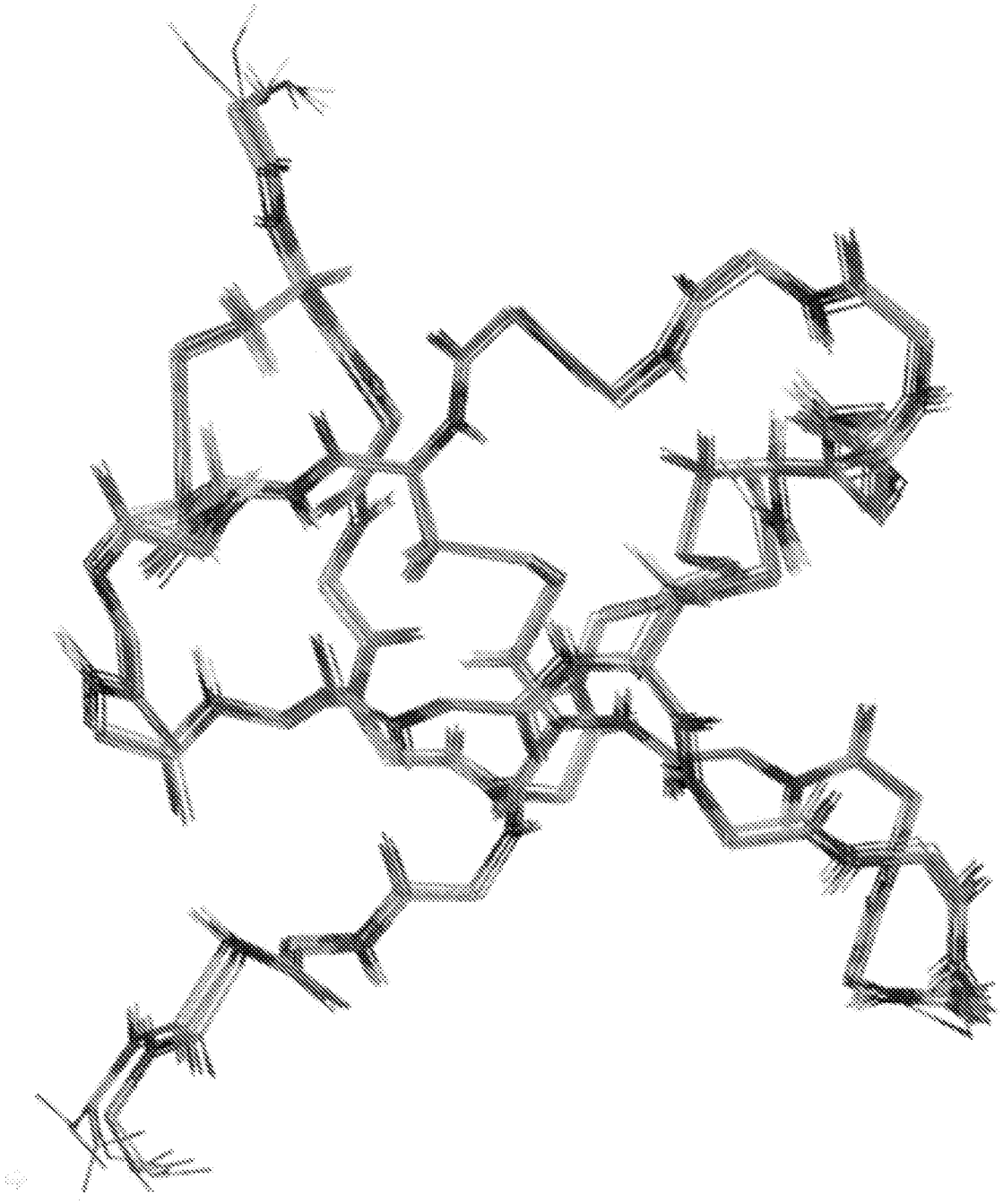


FIG. 7

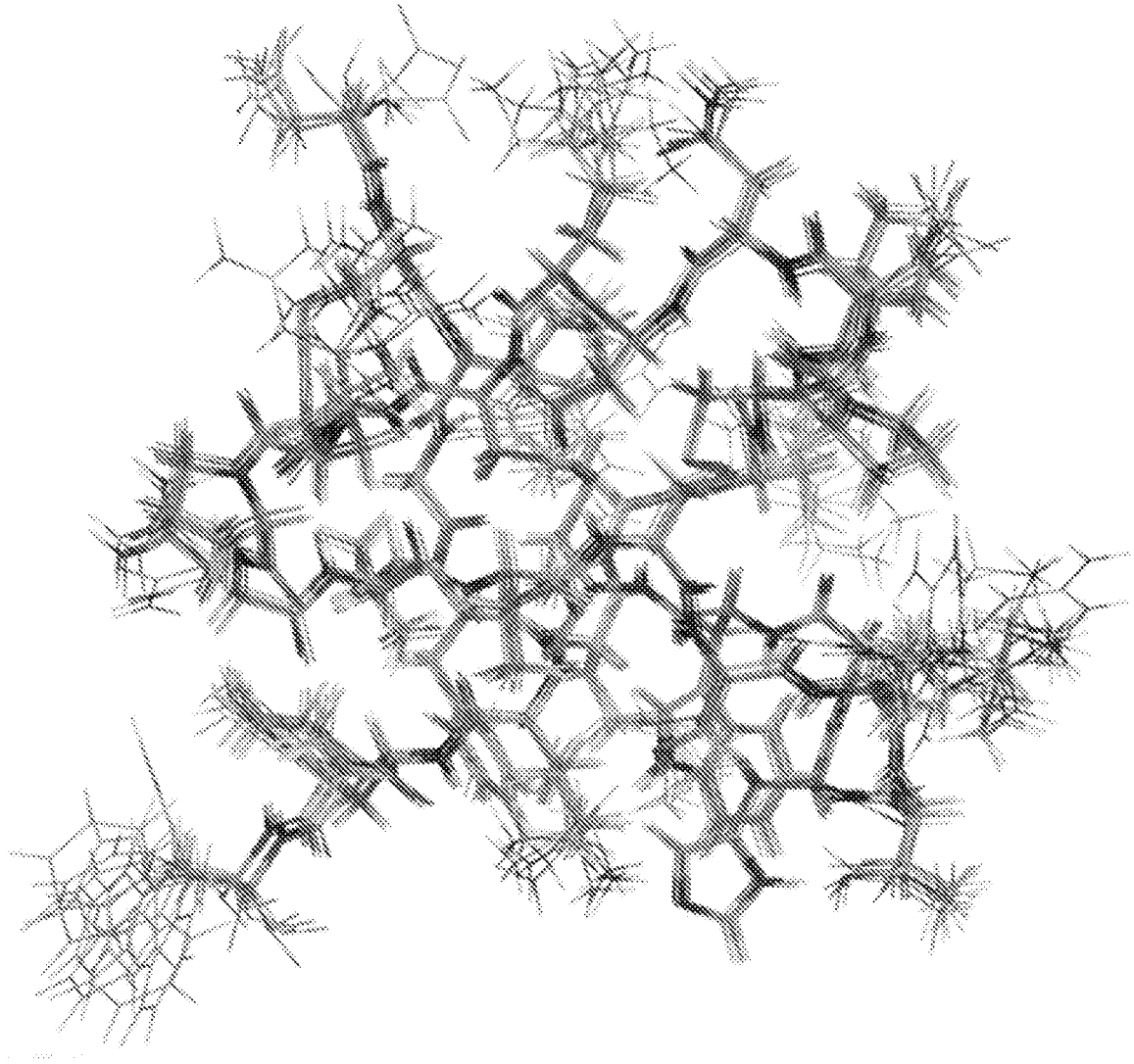


FIG. 8

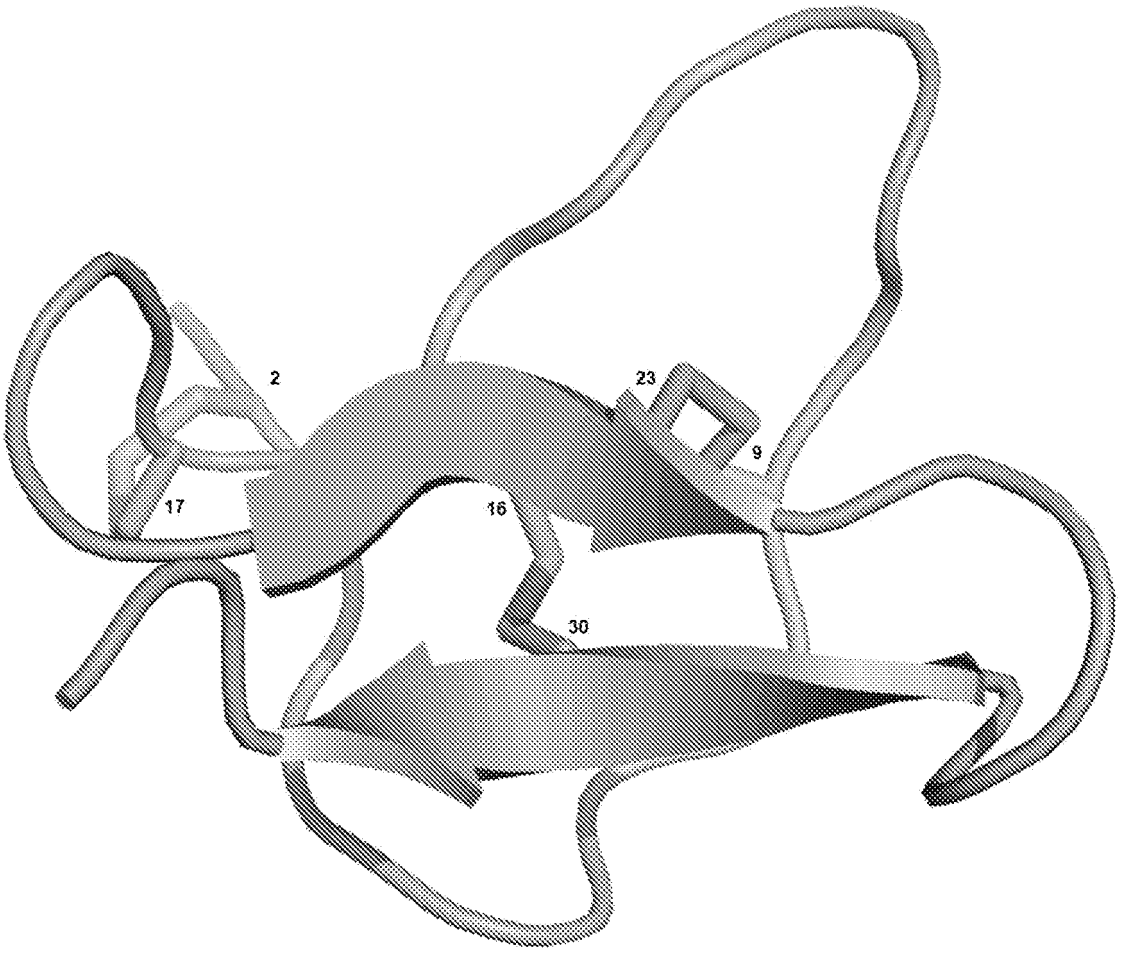
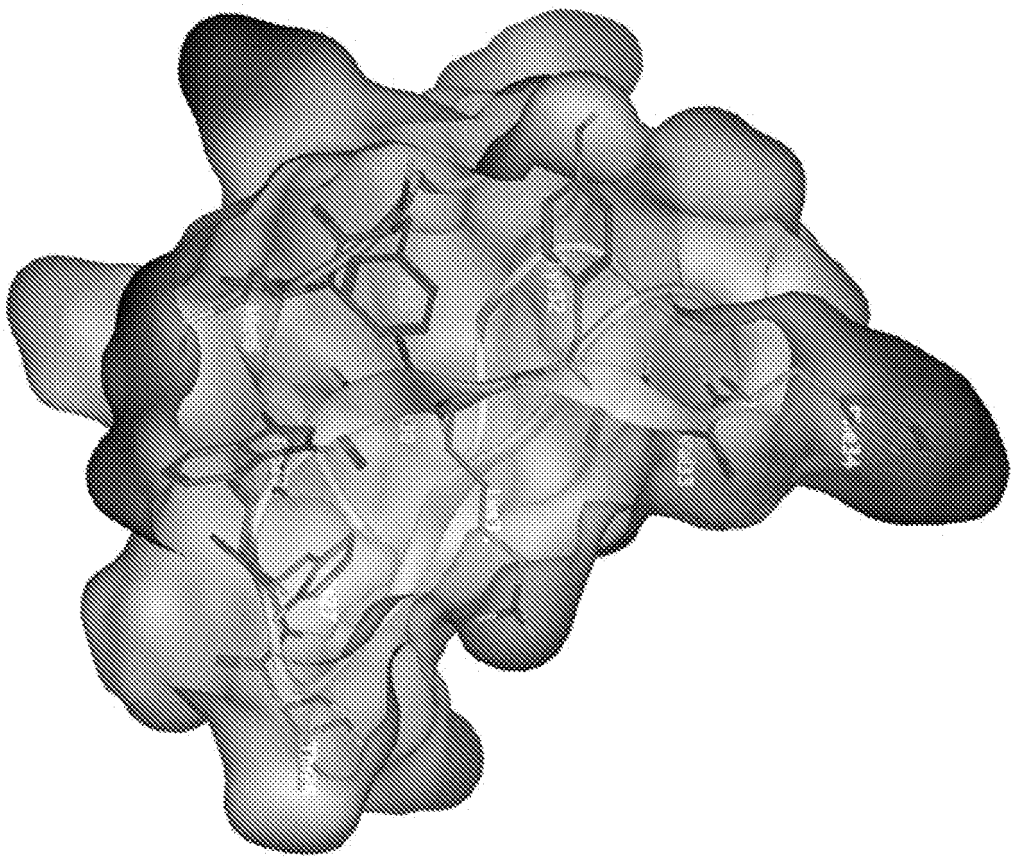


FIG. 9



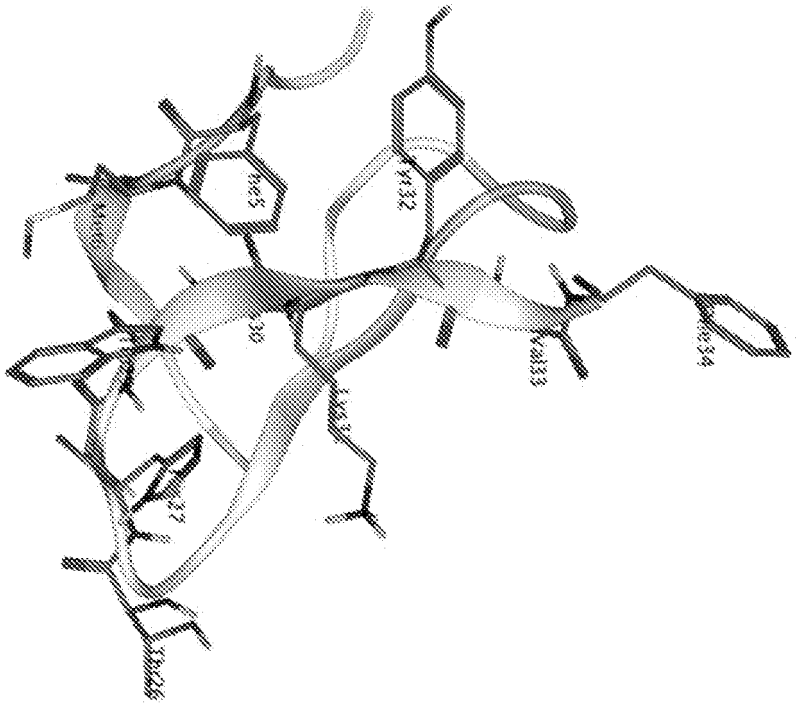


FIG. 10

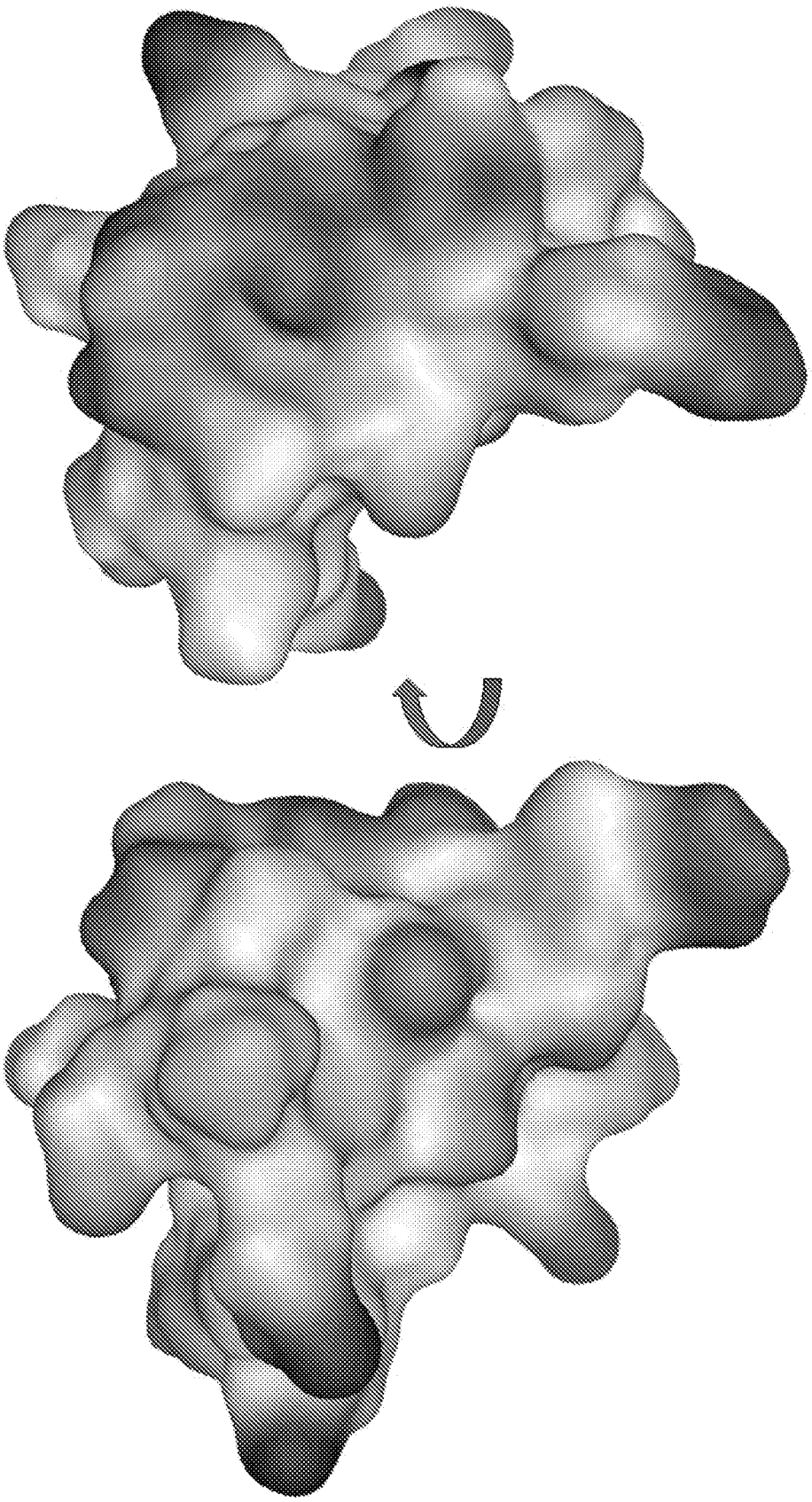


FIG. 11

FIG. 12A

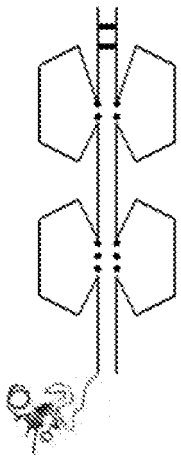


FIG. 12B

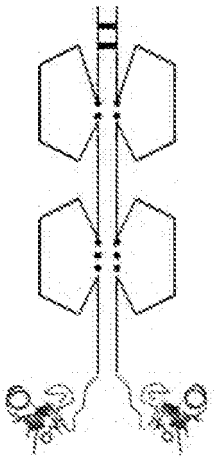


FIG. 12C

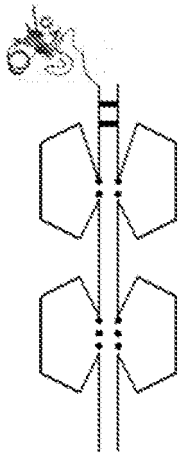


FIG. 12D

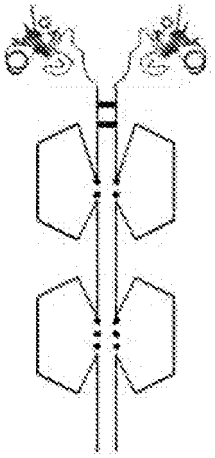


FIG. 12E

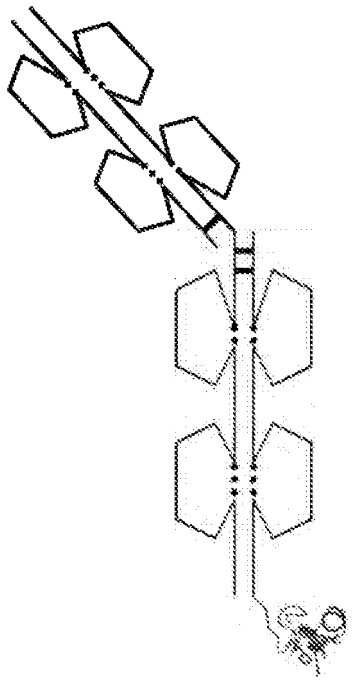


FIG. 12F

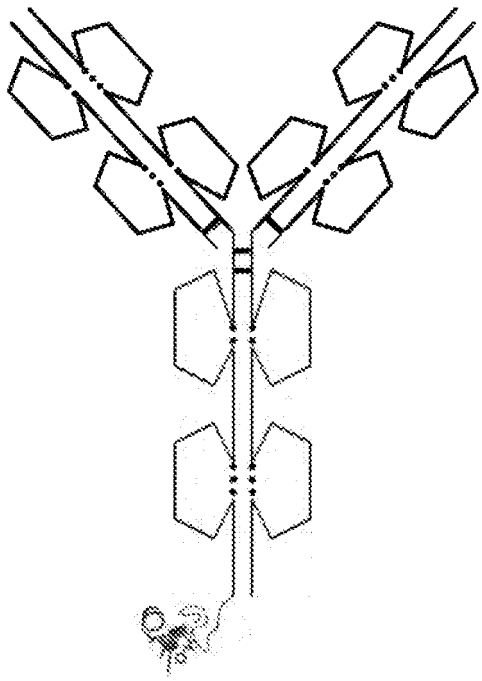


FIG. 12G

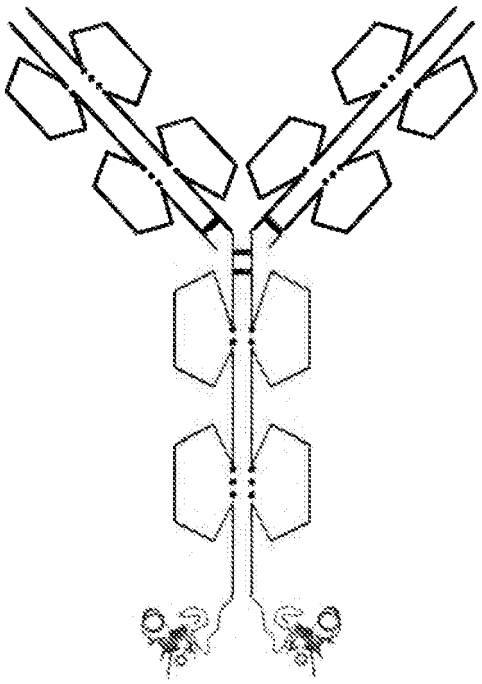


FIG. 12H

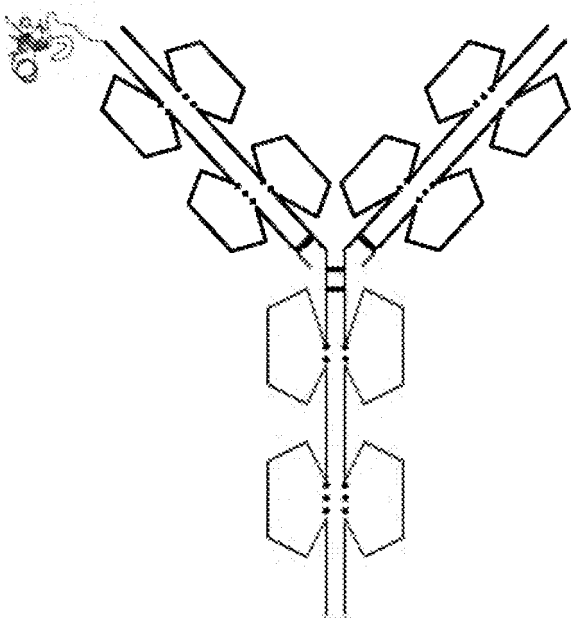


FIG. 12I

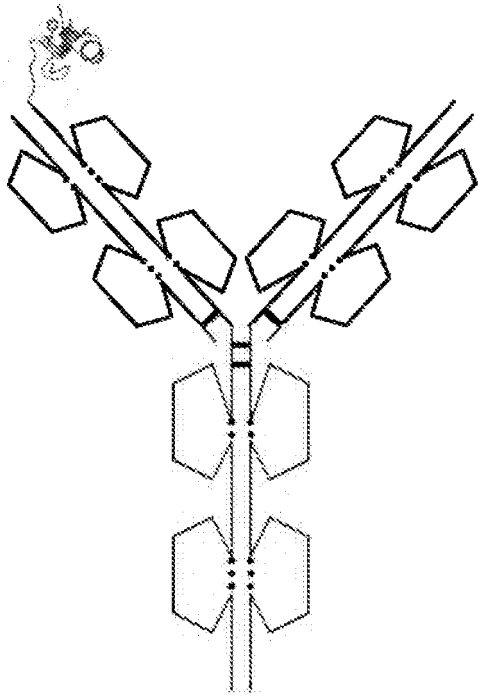


FIG. 12J

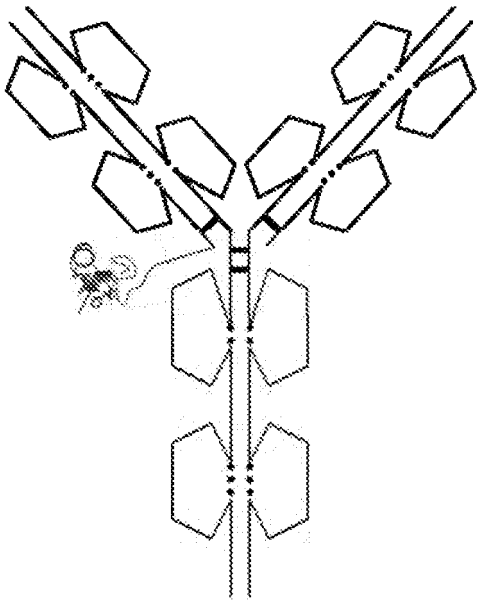


FIG. 12K

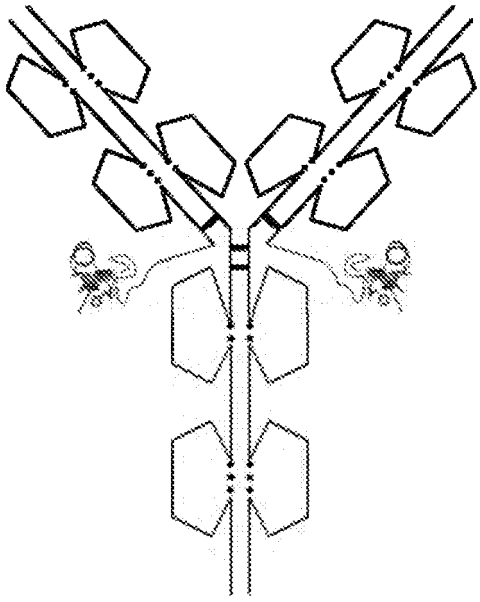


FIG. 12L

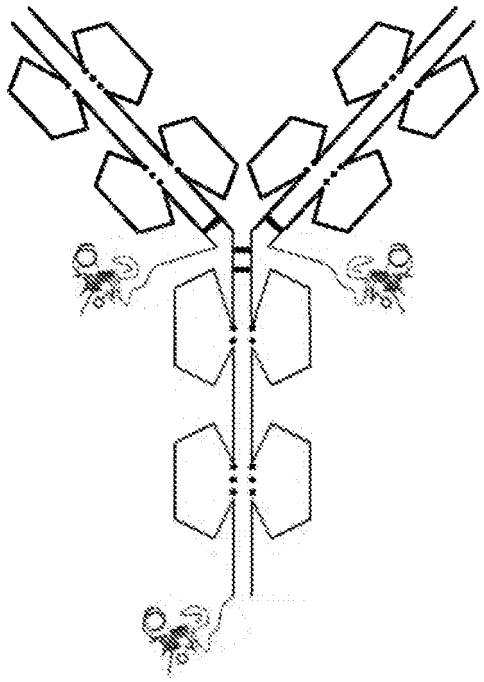


FIG. 12M

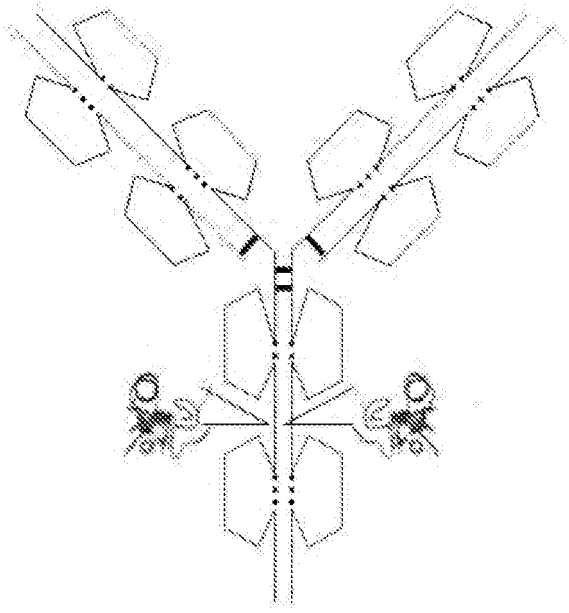
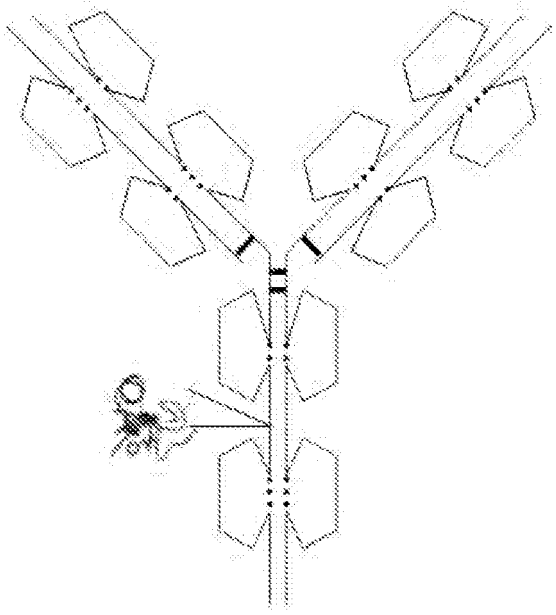


FIG. 12N



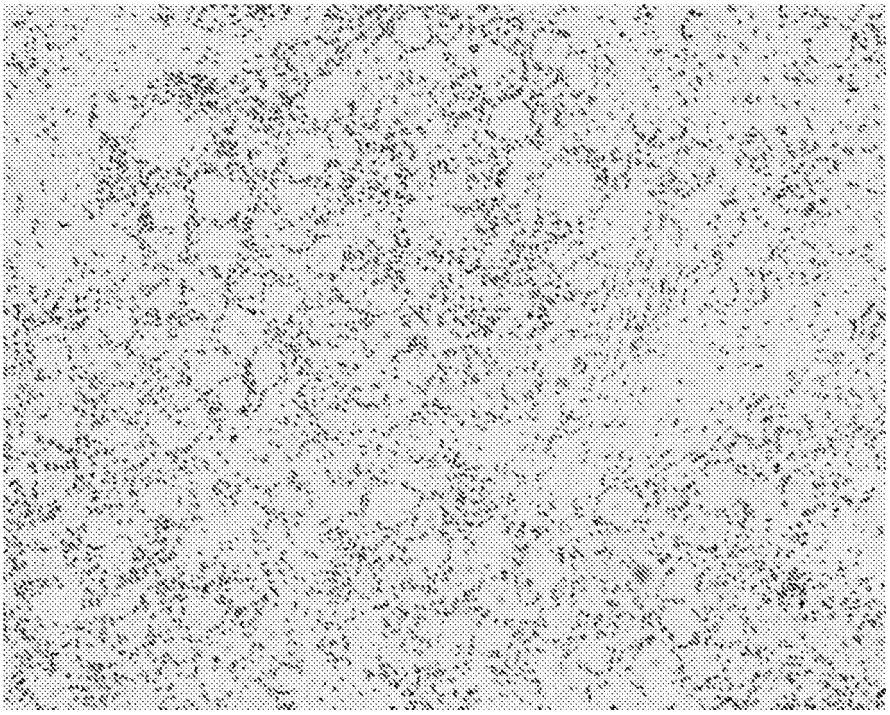


FIG. 13A

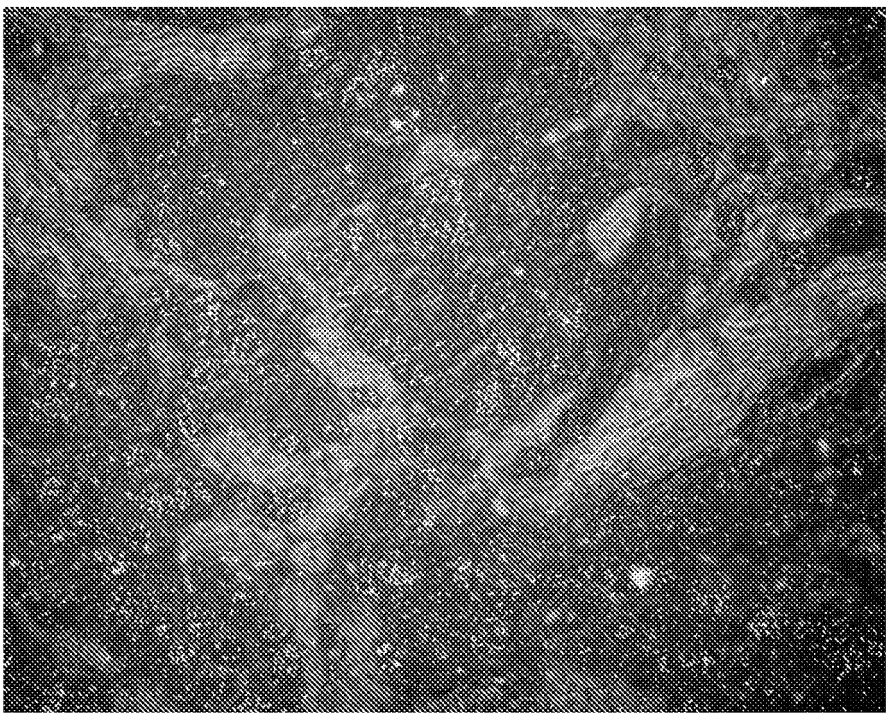


FIG. 13B

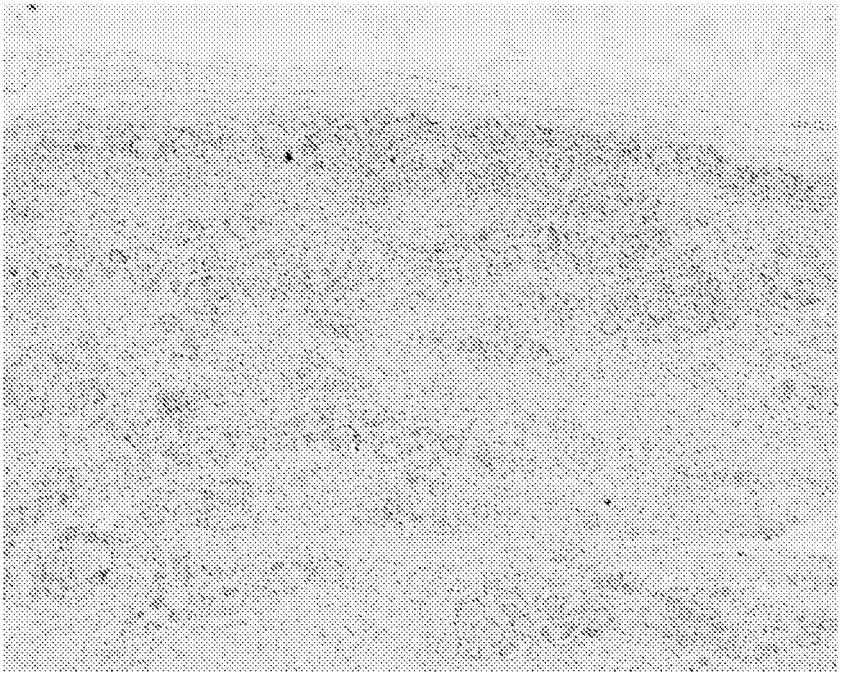


FIG. 13C

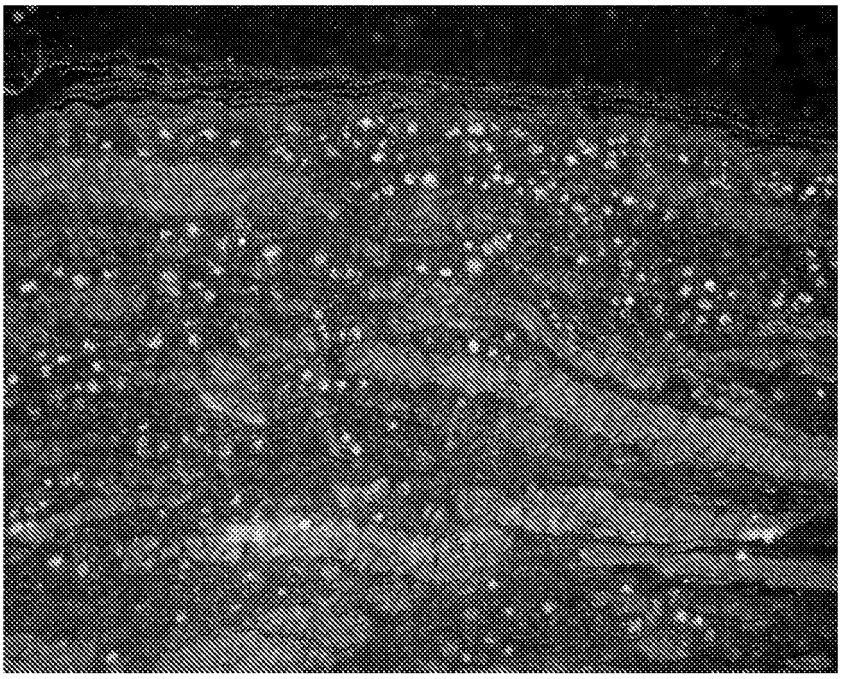


FIG. 13D

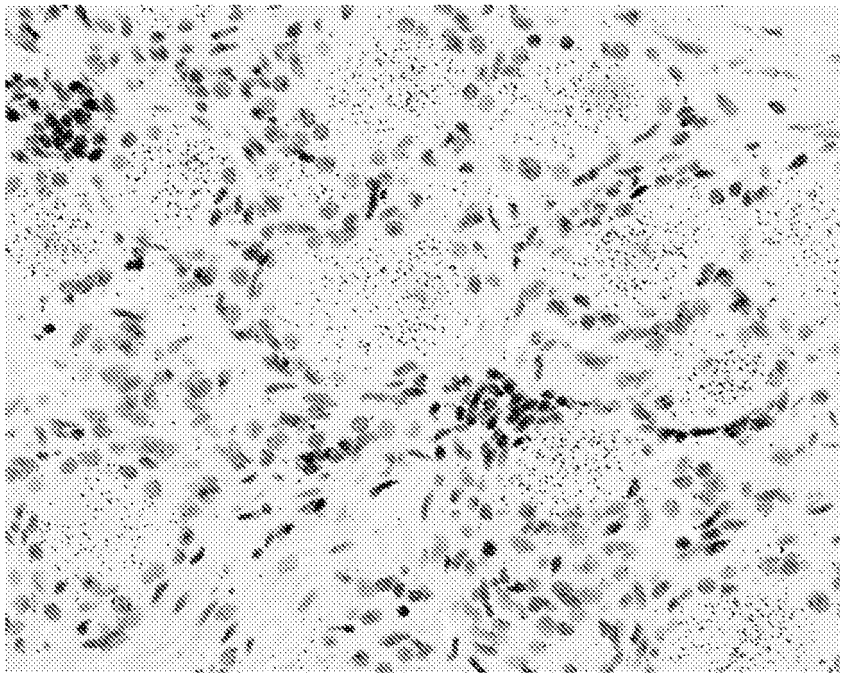


FIG. 13E

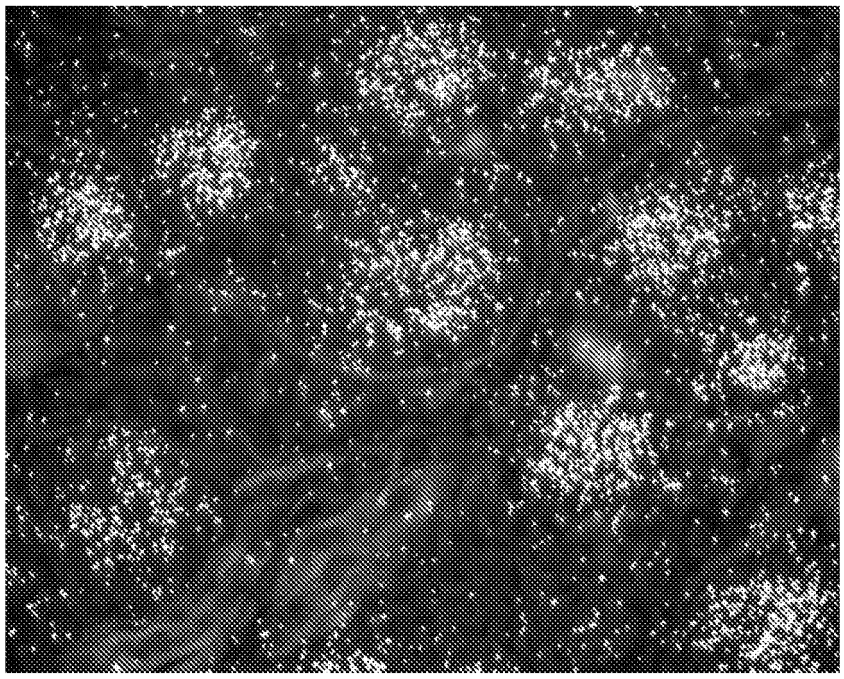


FIG. 13F

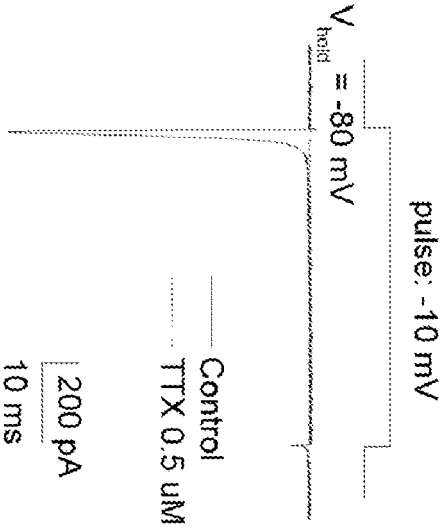


FIG. 14A

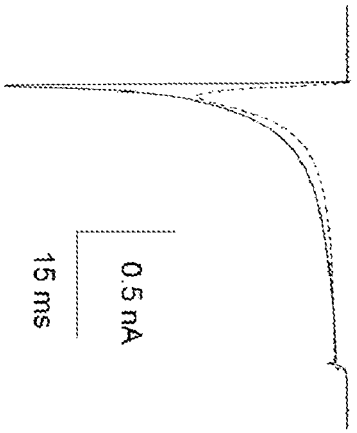


FIG. 14B

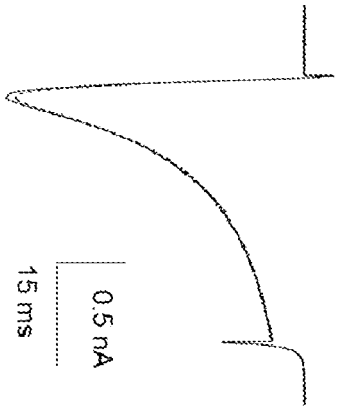


FIG. 14C

SNL

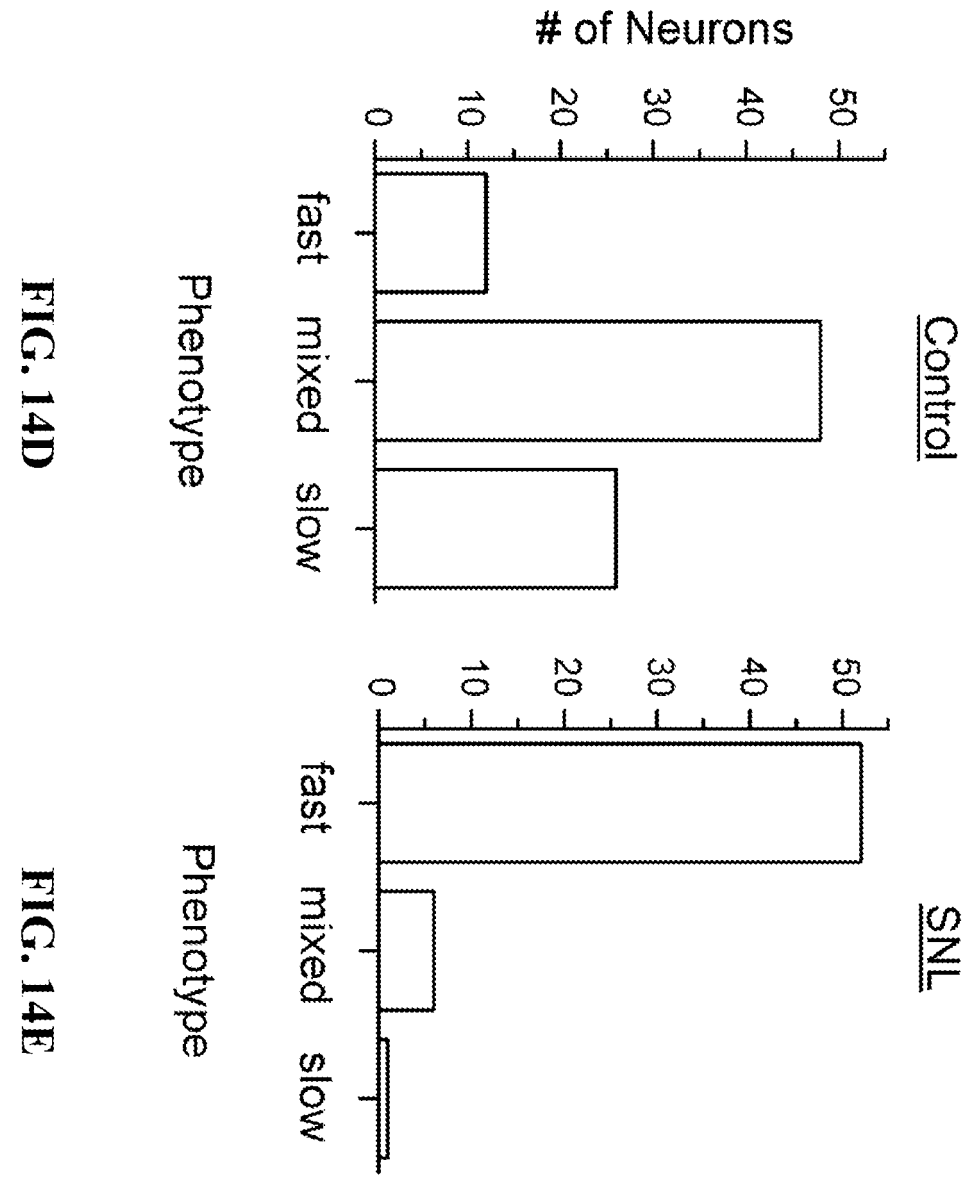


FIG. 14D

FIG. 14E

```
KIIIA              1 CCNCSSKWCR-DHSRCC                          16
GpTx-1{1-34}       1 DCLGFMRKCIPDNDKCCRPN-LVCSRTHKWCKYVF        34
Huwentoxin-IV      1 ECLEIFKACNPSNDQCCKSSKLVCSRKTRWCKYQI        35
Huwentoxin-I       1 ACKGVFDACTPGKNECCPNR--VCSDKHKWCKWKL        33
ProTx II           1 YCQKWMWTCD-SERKCCEGM--VCR---LWCKKKLW        30
                       *       *       **
```

FIG 15A

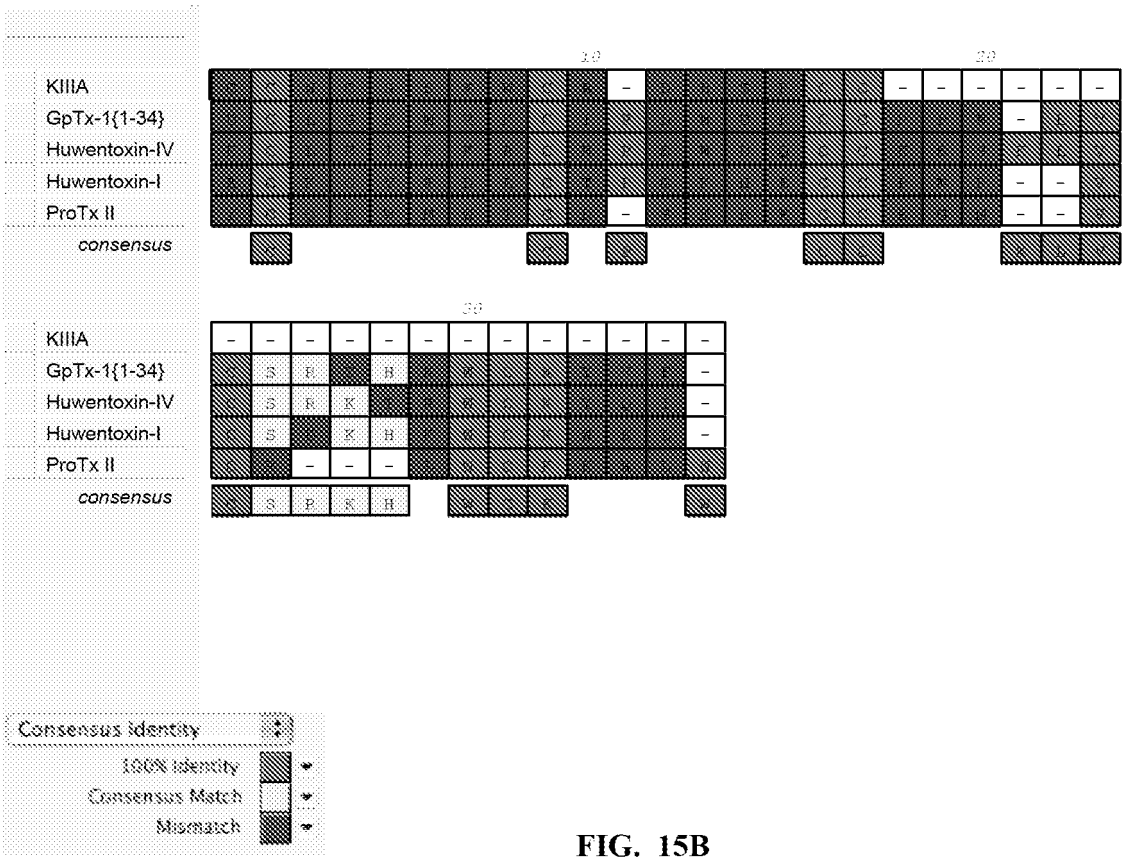


FIG. 15B

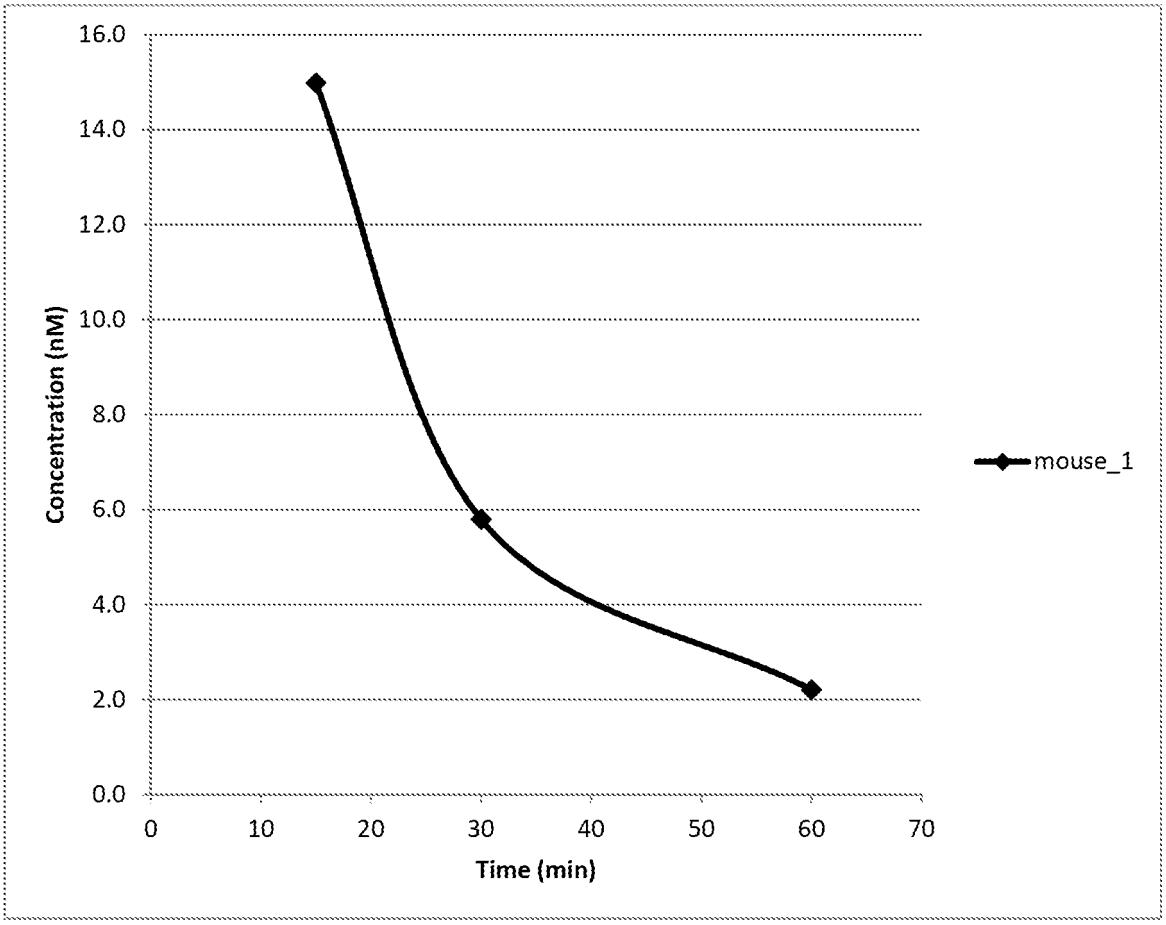

16.0
14.0
12.0
10.0
8.0
6.0
4.0
2.0
0.0
Concentration (nM)
0
10
20
30
40
50
60
70
Time (min)
mouse_1

FIG. 16

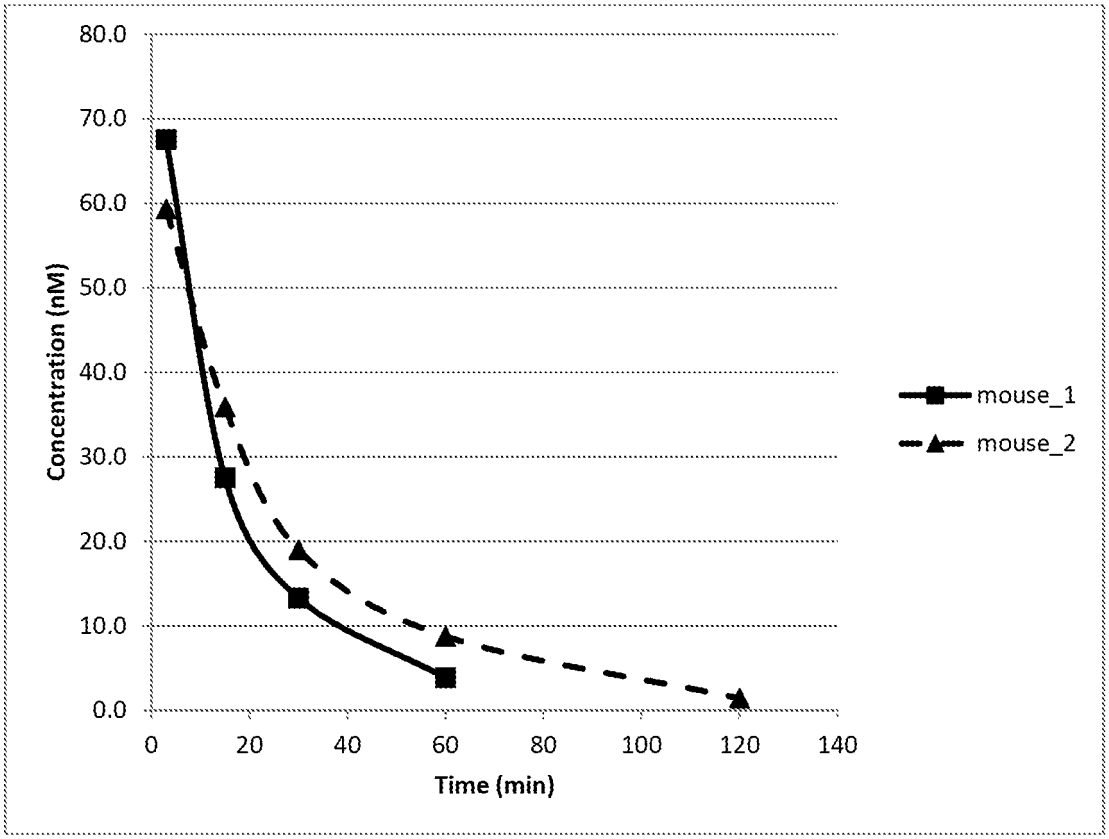

80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
Concentration (nM)
0
20
40
60
80
100
120
140
Time (min)
mouse_1
mouse_2

FIG.17A

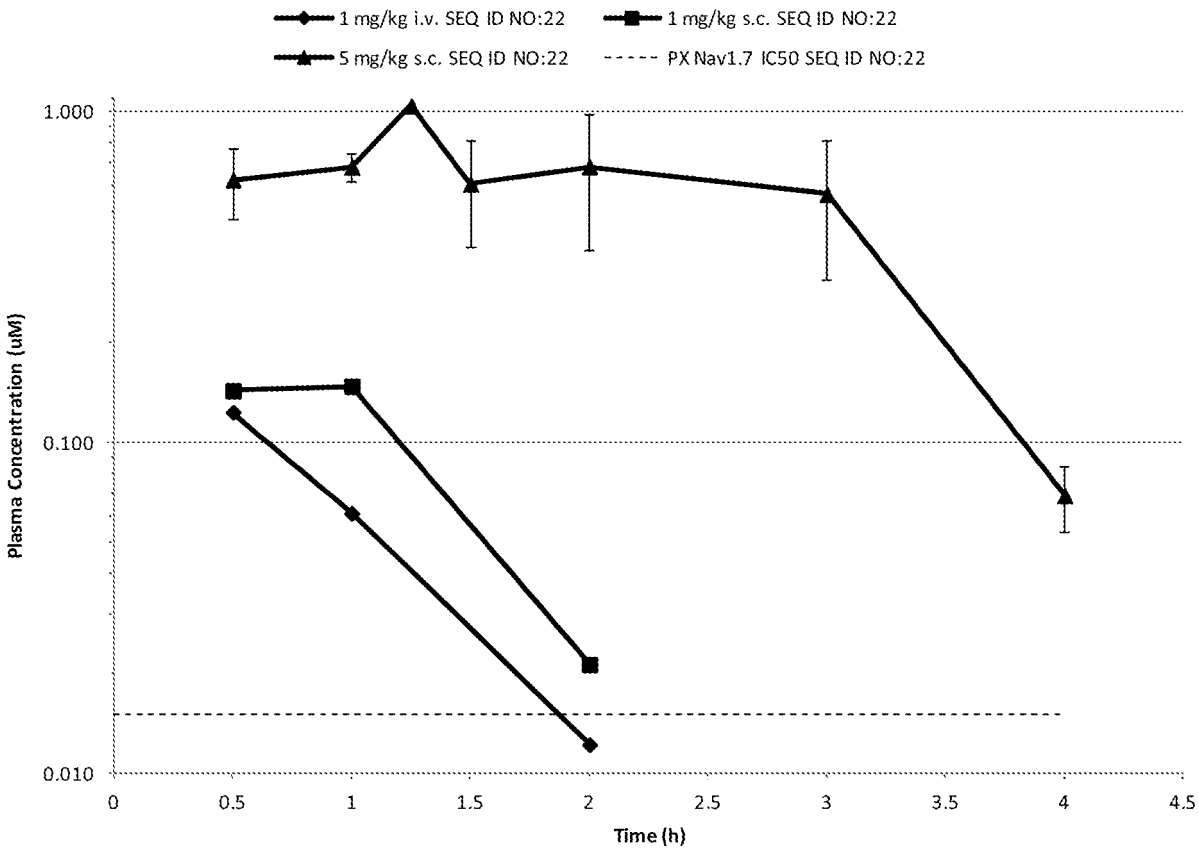

1 mg/kg i.v. SEQ ID NO:22
1 mg/kg s.c. SEQ ID NO:22
5 mg/kg s.c. SEQ ID NO:22
PX Nav1.7 IC50 SEQ ID NO:22
1.000
0.100
0.010
Plasma Concentration (uM)
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
Time (h)

FIG. 17B

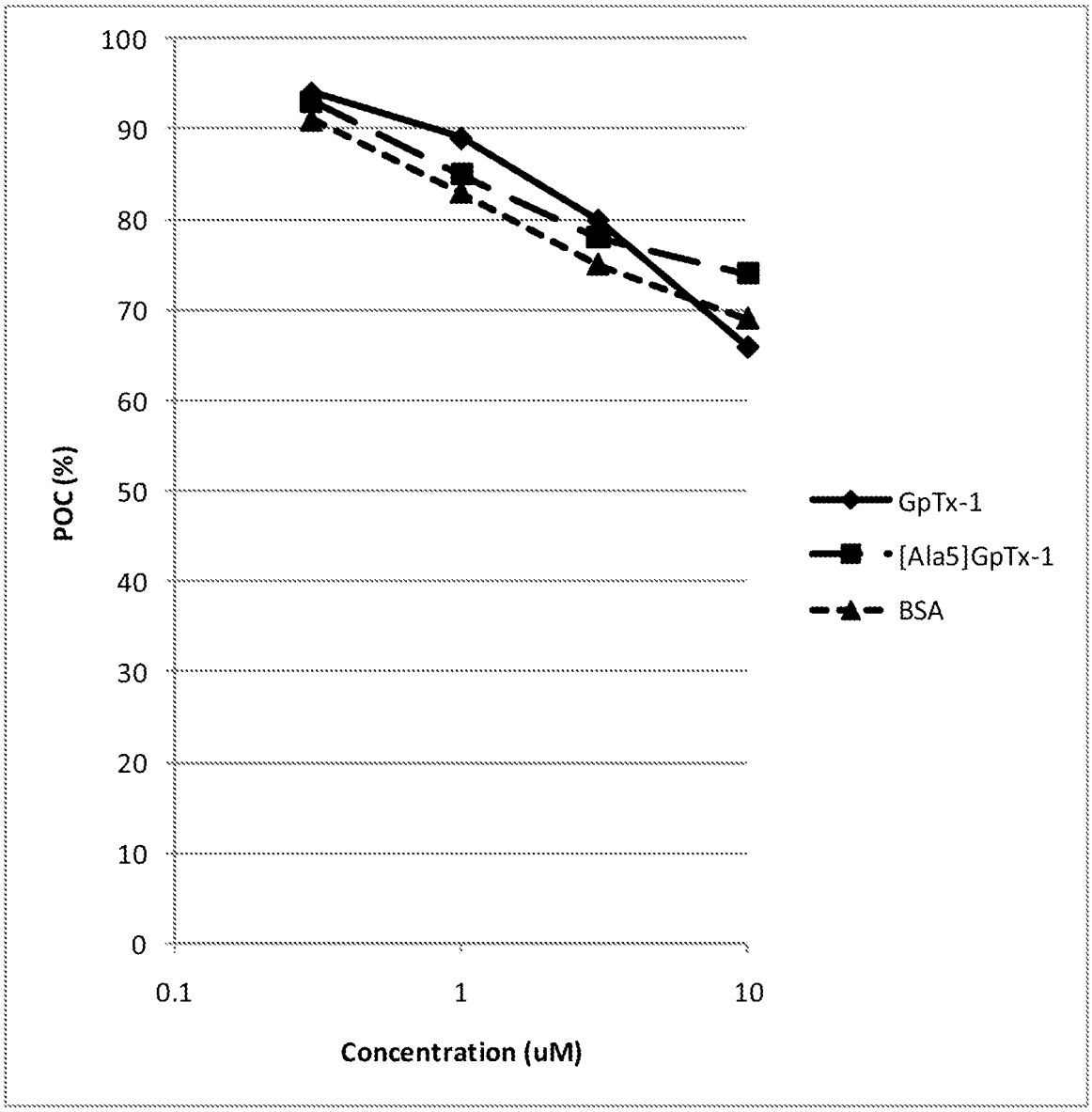

100
90
80
70
60
50
40
30
20
10
0
POC (%)
0.1
1
10
Concentration (uM)
GpTx-1
[Ala5]GpTx-1
BSA

FIG. 18

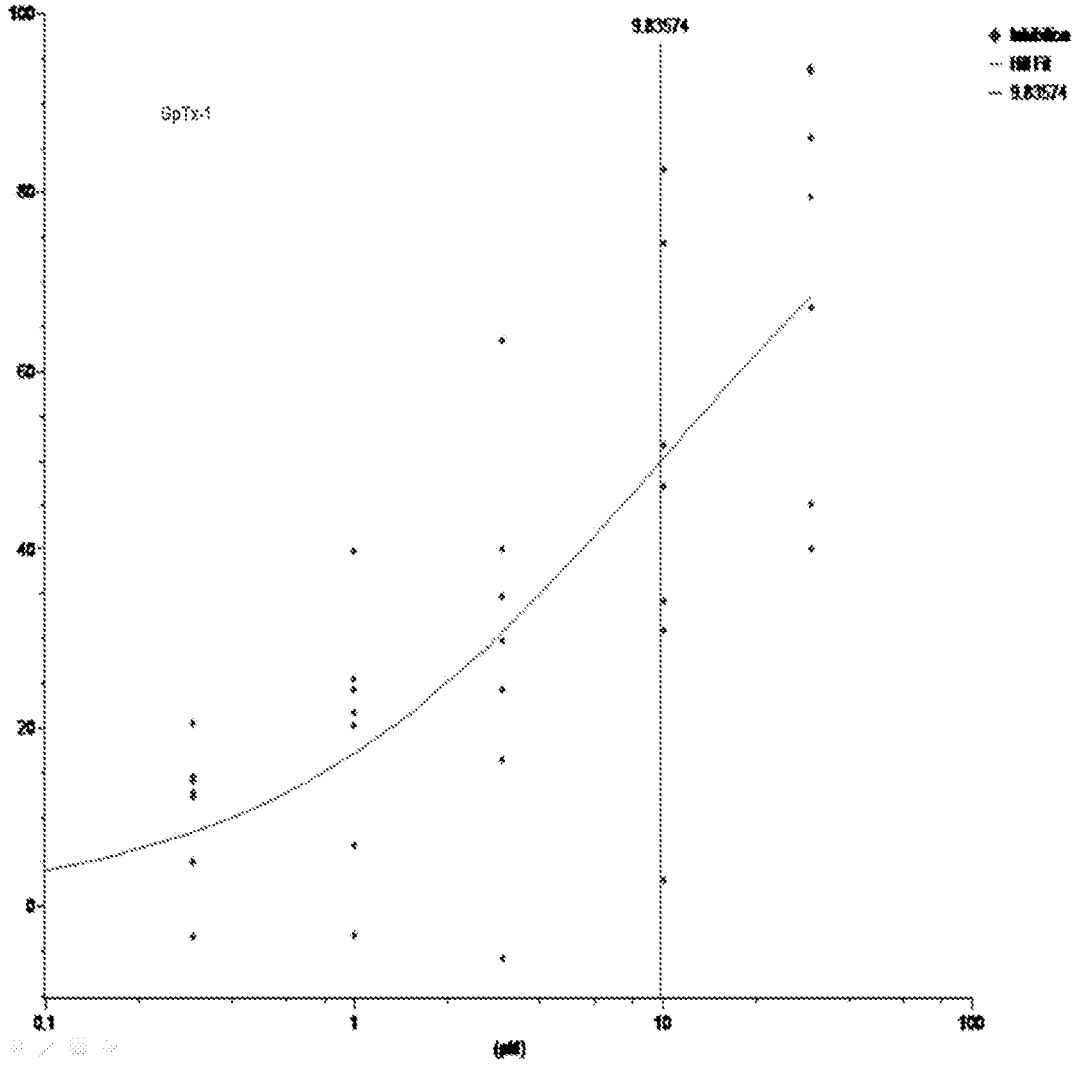


FIG. 19A

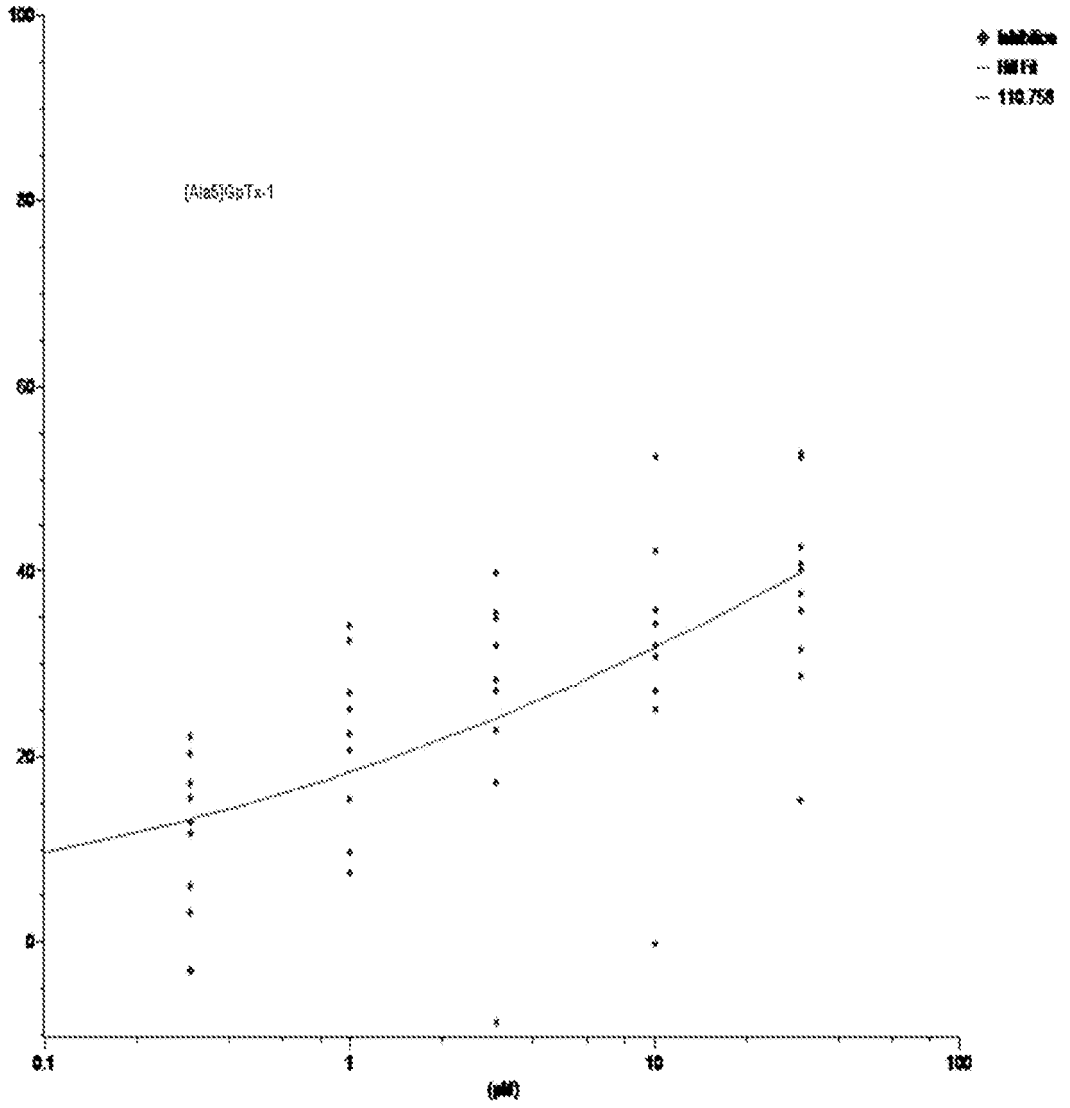


FIG. 19B

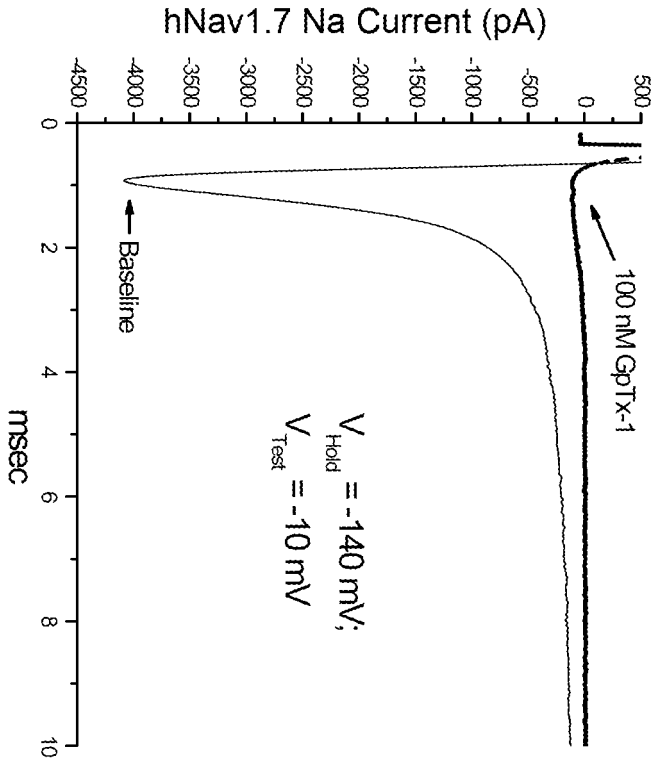

hNav1.7 Na Current (pA)
500
0
-500
-1000
-1500
-2000
-2500
-3000
-3500
-4000
-4500
100 nM GpTx-1
Baseline
V_{Hold} = -140 mV;
V_{Test} = -10 mV
0
2
4
6
8
10
msec

FIG. 20

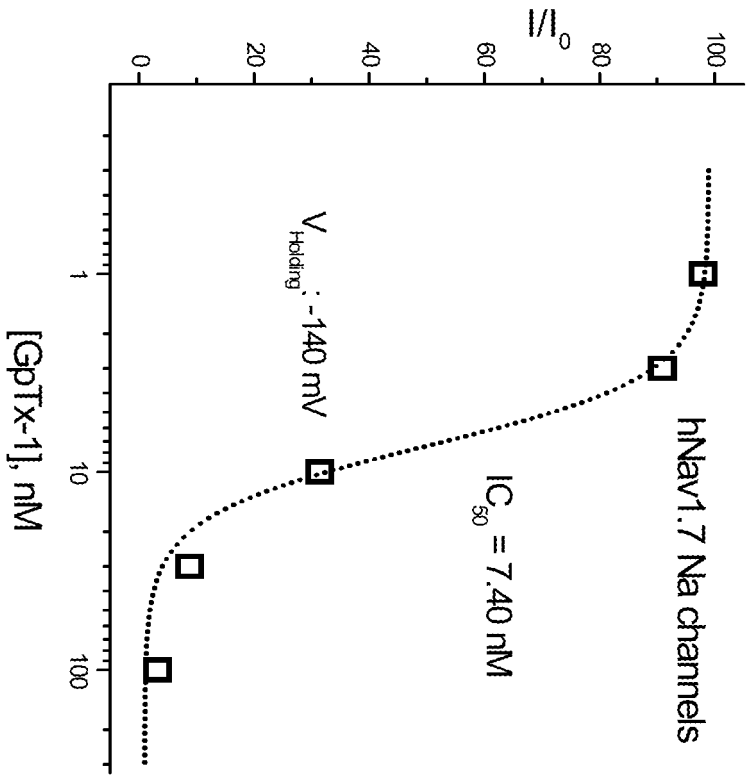

I/I0
100
80
60
40
20
0
1
10
100
[GpTx-1], nM
hNav1.7 Na channels
IC50 = 7.40 nM
VHolding: -140 mV

FIG. 21

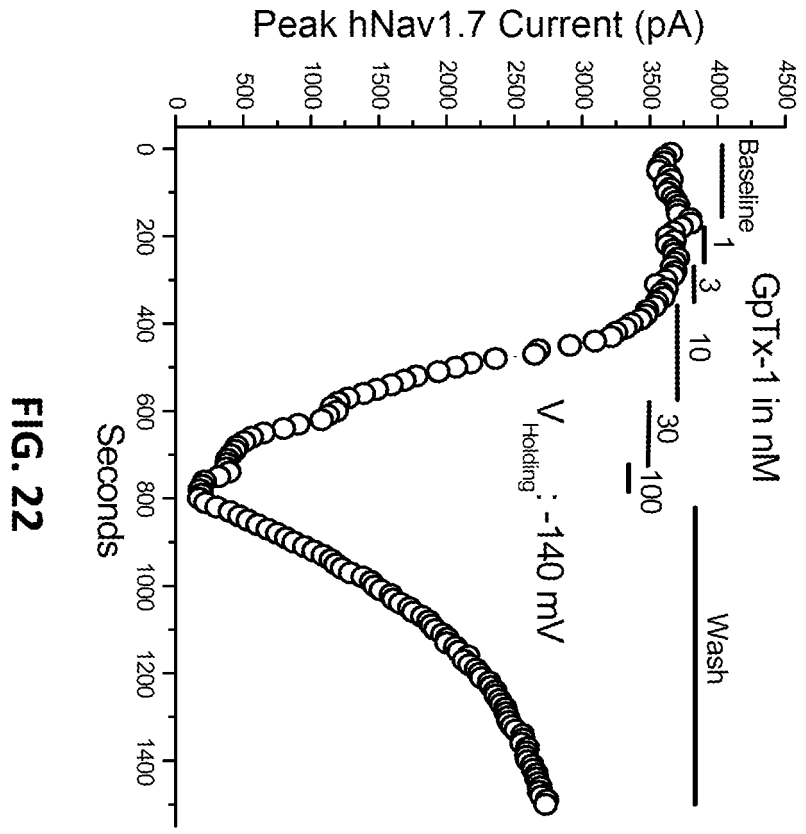

Peak hNav1.7 Current (pA)
0
500
1000
1500
2000
2500
3000
3500
4000
4500
Seconds
0
200
400
600
800
1000
1200
1400
Baseline
1
3
10
30
100
Wash
GpTx-1 in nM
V Holding: -140 mV

FIG. 22

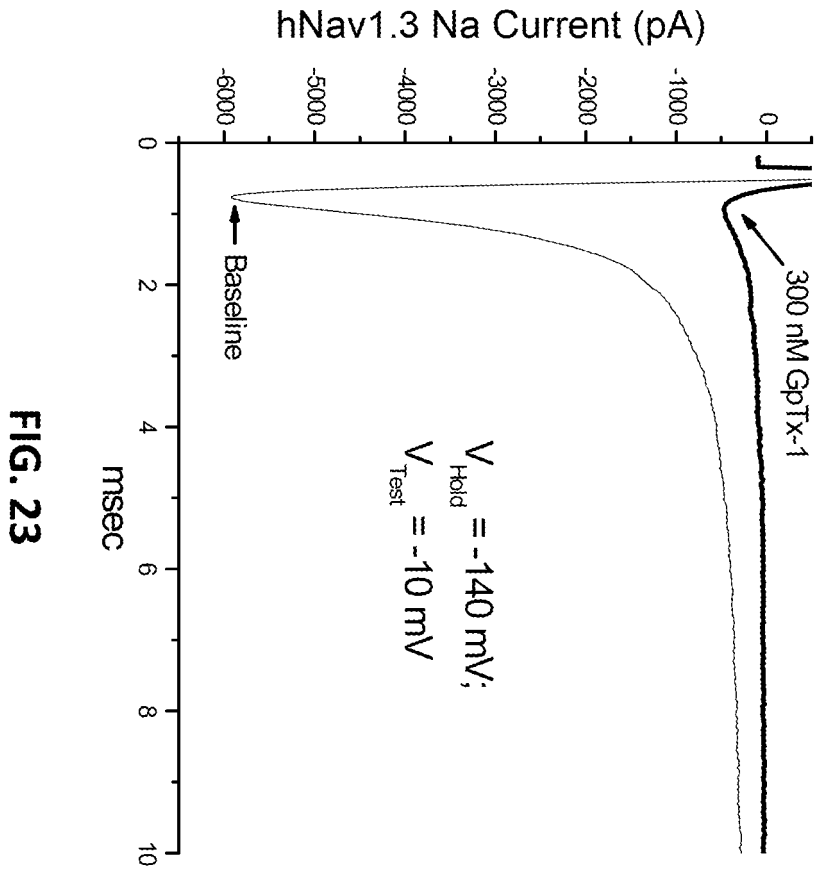

hNav1.3 Na Current (pA)
-6000
-5000
-4000
-3000
-2000
-1000
0
0
2
4
6
8
10
msec
Baseline
300 nM GpTx-1
V Hold = -140 mV;
V Test = -10 mV

FIG. 23

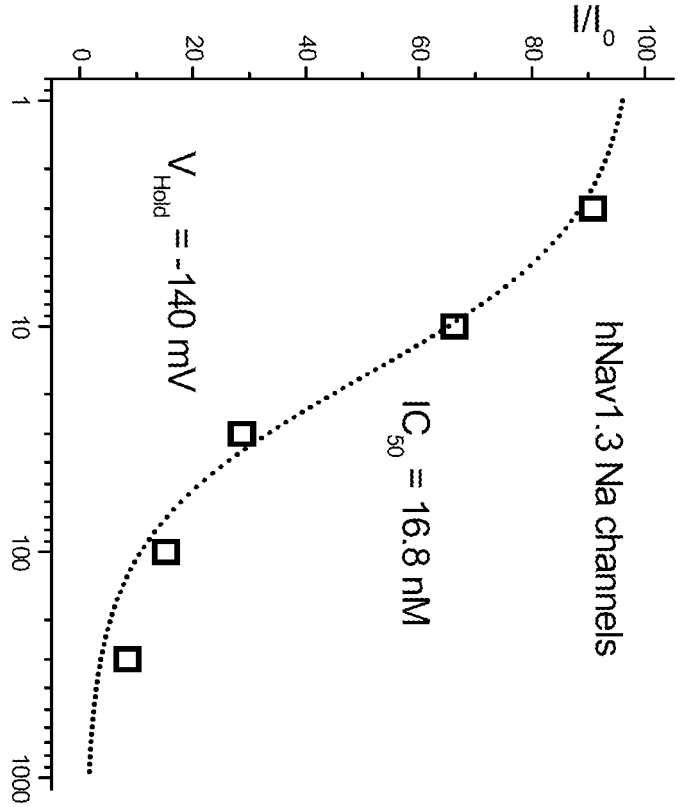

I/I0
100
80
60
40
20
0
1
10
100
1000
[GpTx-1], nM
hNav1.3 Na channels
IC50 = 16.8 nM
VHold = -140 mV

FIG. 24

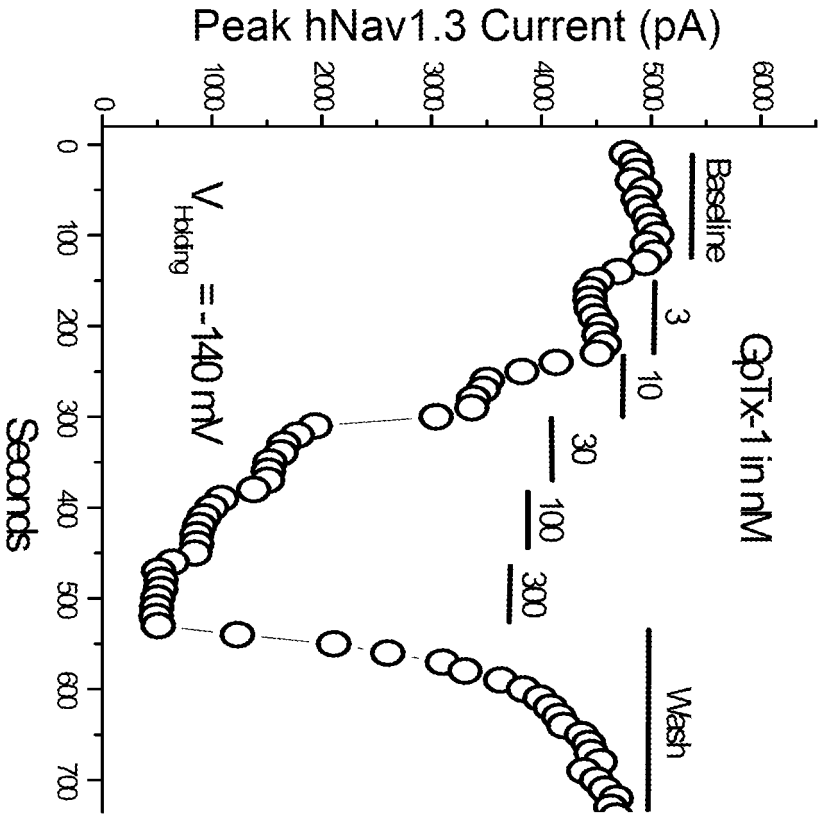

Peak hNav1.3 Current (pA)
0
1000
2000
3000
4000
5000
6000
Seconds
0
100
200
300
400
500
600
700
V Holding = -140 mV
Baseline
3
10
30
100
300
Wash
GpTx-1 in nM

FIG. 25

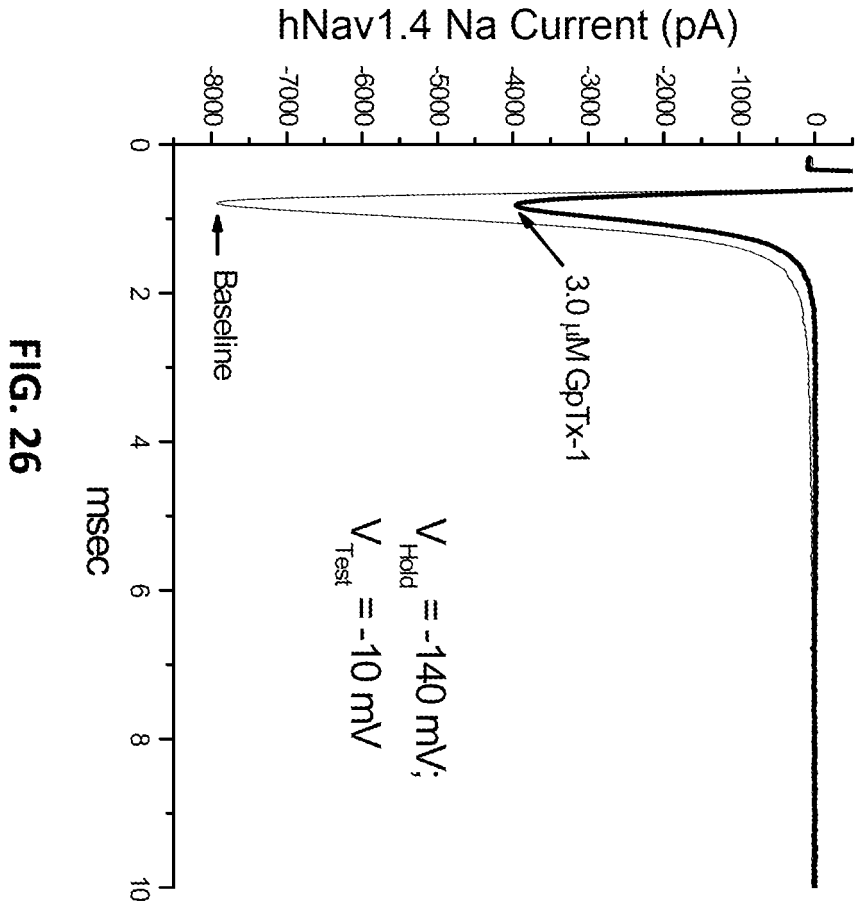

hNav1.4 Na Current (pA)
0
-1000
-2000
-3000
-4000
-5000
-6000
-7000
-8000
0
2
4
6
8
10
msec
Baseline
3.0 μM GpTx-1
V Hold = -140 mV;
V Test = -10 mV

FIG. 26

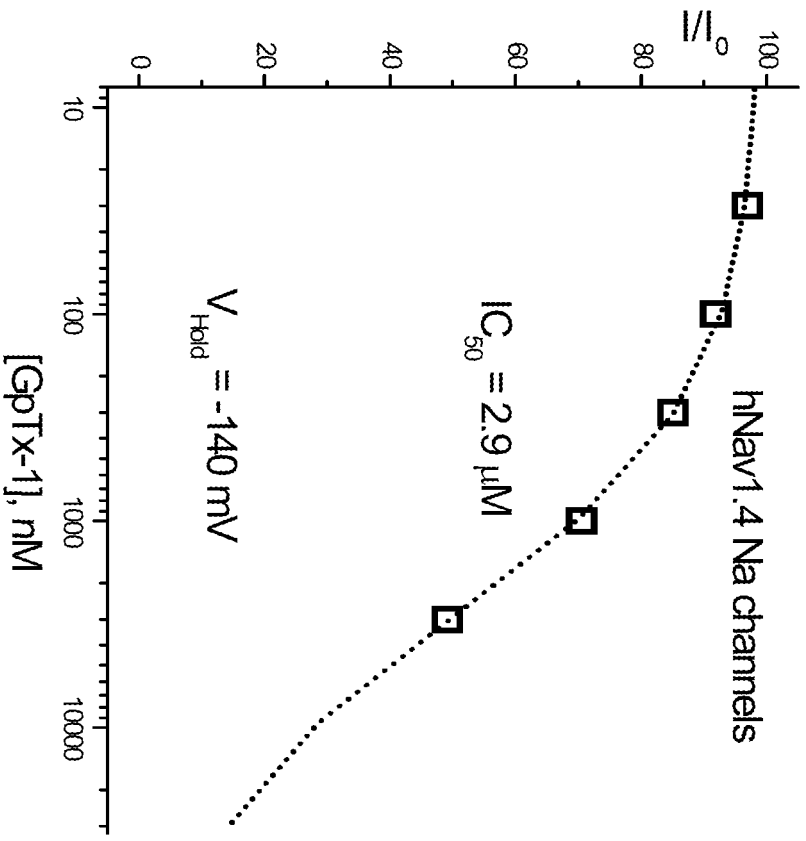

I/I0
100
80
60
40
20
0
10
100
1000
10000
[GpTx-1], nM
hNav1.4 Na channels
IC50 = 2.9 μM
VHold = -140 mV

FIG. 27

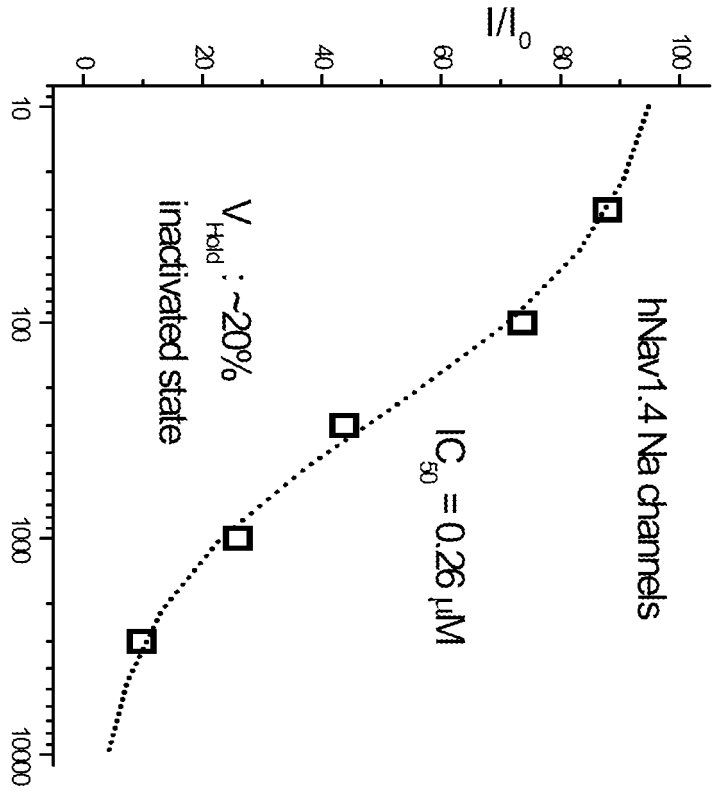

I/I0
0
20
40
60
80
100
10
100
1000
10000
[GpTx-1], nM
hNav1.4 Na channels
IC50 = 0.26 μM
VHold : ~20%
inactivated state

FIG. 28

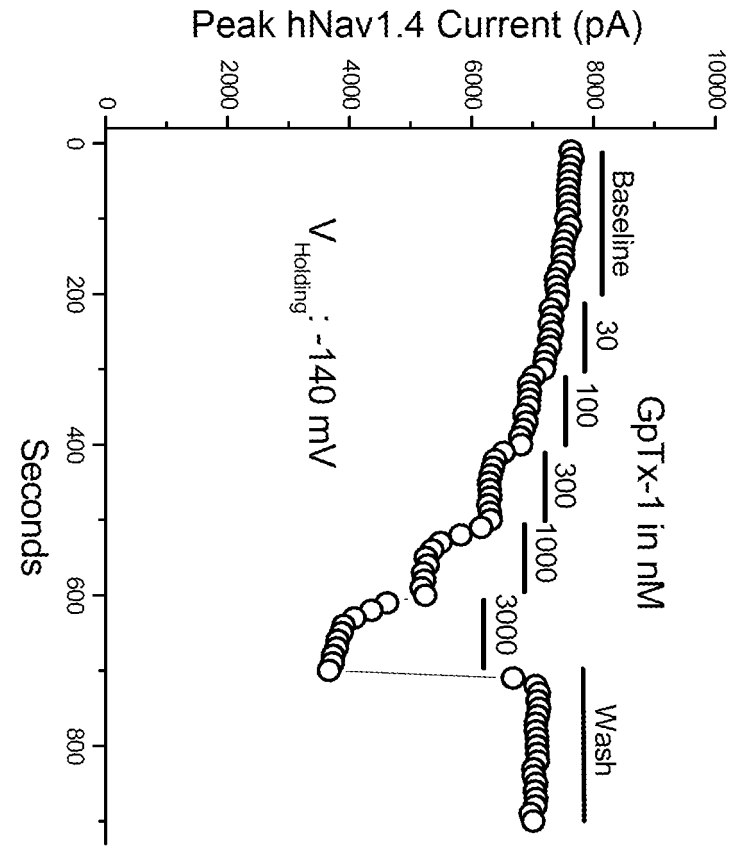

Peak hNav1.4 Current (pA)
0
2000
4000
6000
8000
10000
0
200
400
600
800
Seconds
$V_{Holding}$: -140 mV
Baseline
30
100
300
1000
3000
Wash
GpTx-1 in nM

FIG. 29

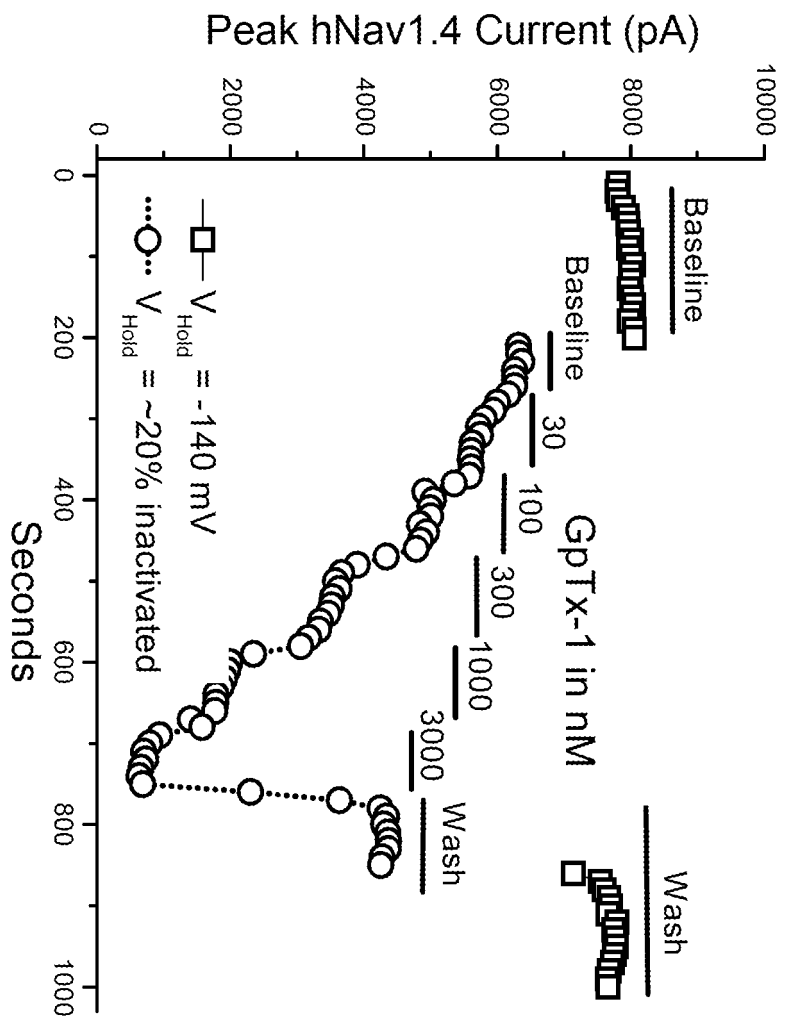

Peak hNav1.4 Current (pA)
0
2000
4000
6000
8000
10000
Baseline
Baseline
30
100
300
1000
3000
Wash
GpTx-1 in nM
Wash
V Hold = -140 mV
V Hold = ~20% inactivated
0
200
400
600
800
1000
Seconds

FIG. 30

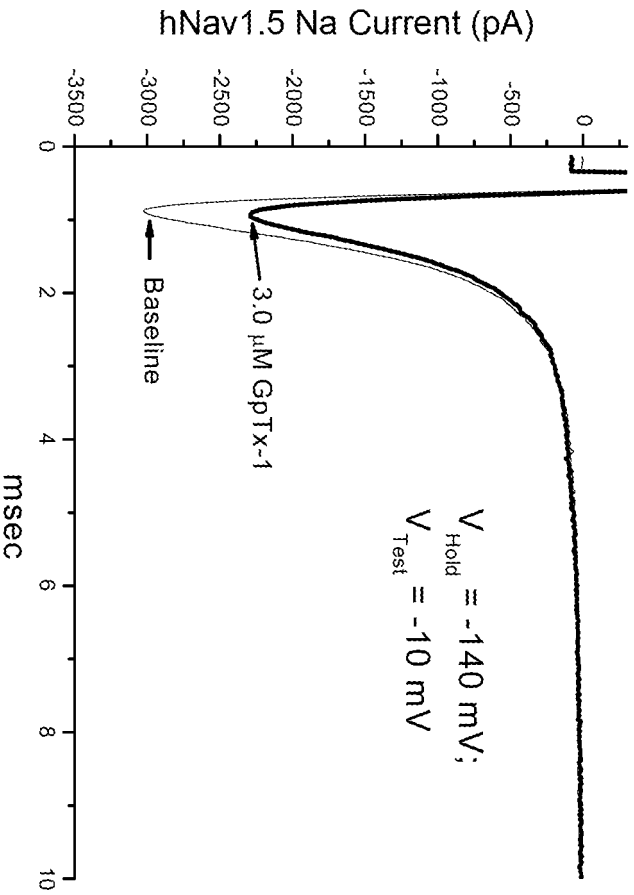

hNav1.5 Na Current (pA)
-3500
-3000
-2500
-2000
-1500
-1000
-500
0
0
2
4
6
8
10
msec
Baseline
3.0 μM GpTx-1
V Hold = -140 mV;
V Test = -10 mV

FIG. 31

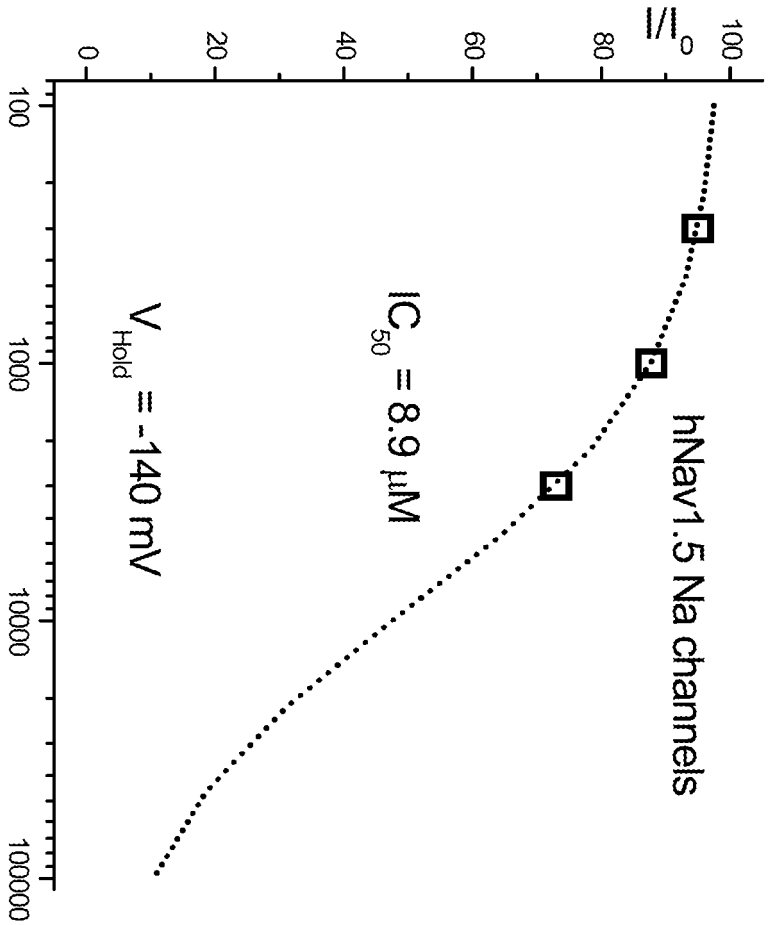

I/I0
100
80
60
40
20
0
100
1000
10000
100000
[GpTx-1], nM
hNav1.5 Na channels
IC50 = 8.9 μM
VHold = -140 mV

FIG. 32

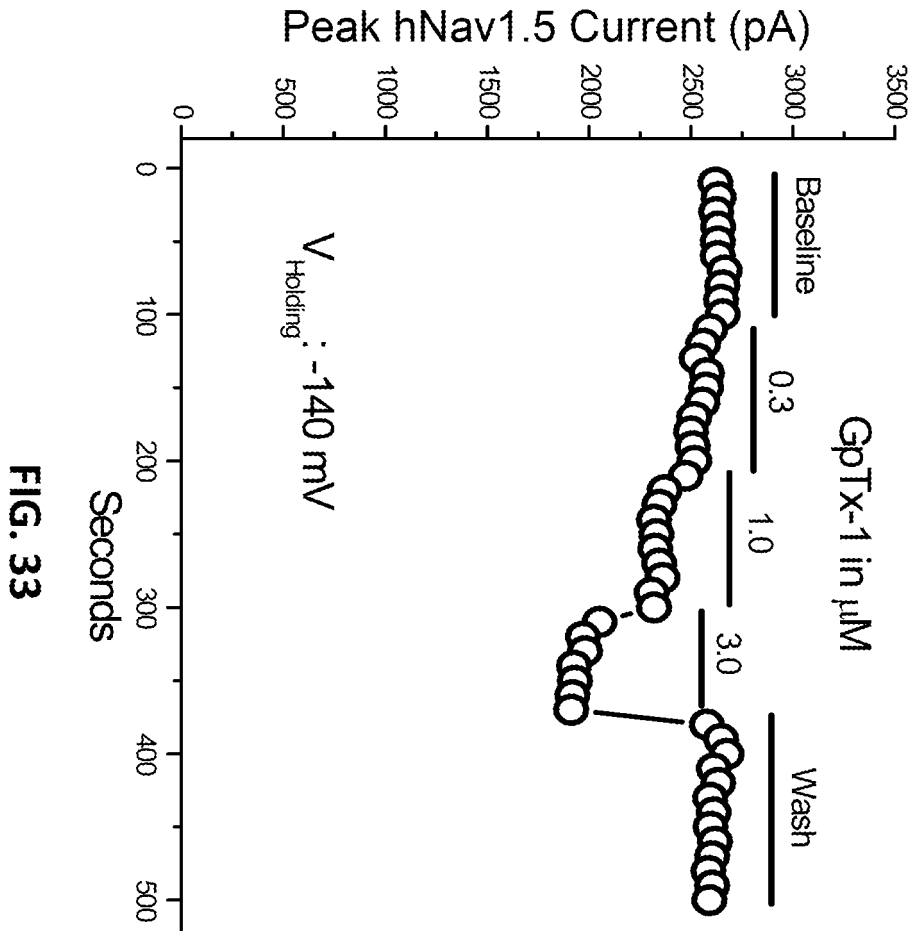

Peak hNav1.5 Current (pA)
0
500
1000
1500
2000
2500
3000
3500
0
100
200
300
400
500
Seconds
$V_{Holding}$: -140 mV
Baseline
0.3
1.0
3.0
Wash
GpTx-1 in μM

FIG. 33

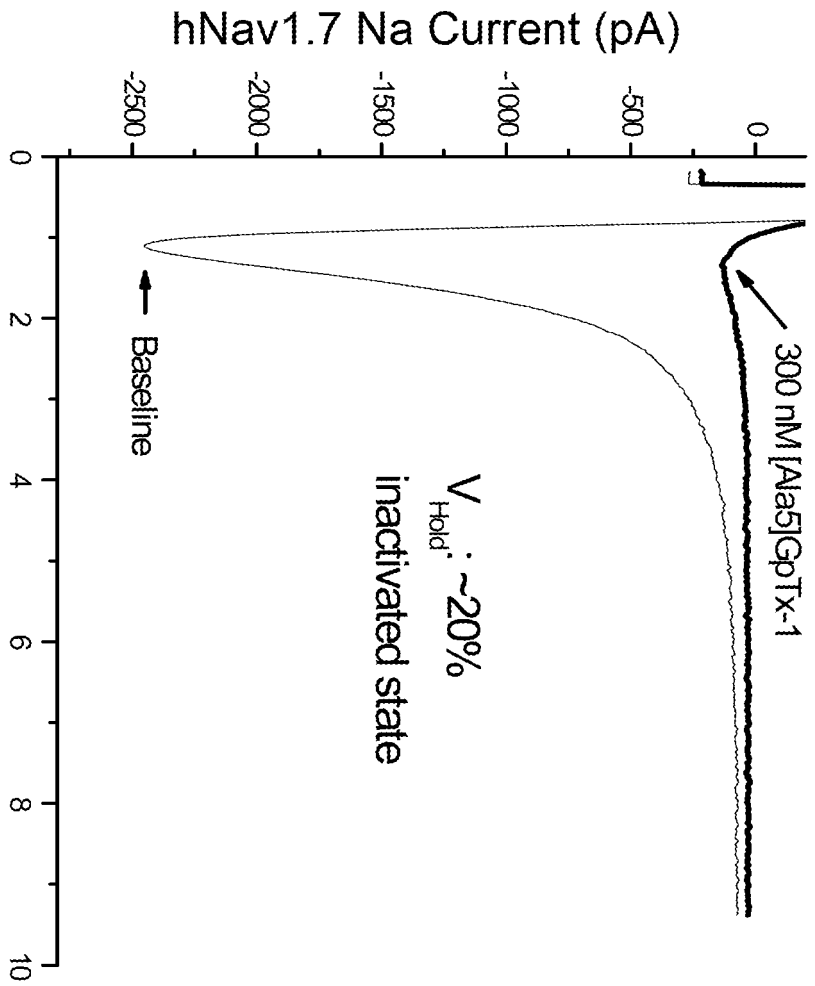

hNav1.7 Na Current (pA)
-2500
-2000
-1500
-1000
-500
0
0
2
4
6
8
10
msec
Baseline
300 nM [Ala5]GpTx-1
V_{Hold}: ~20%
inactivated state

FIG. 34

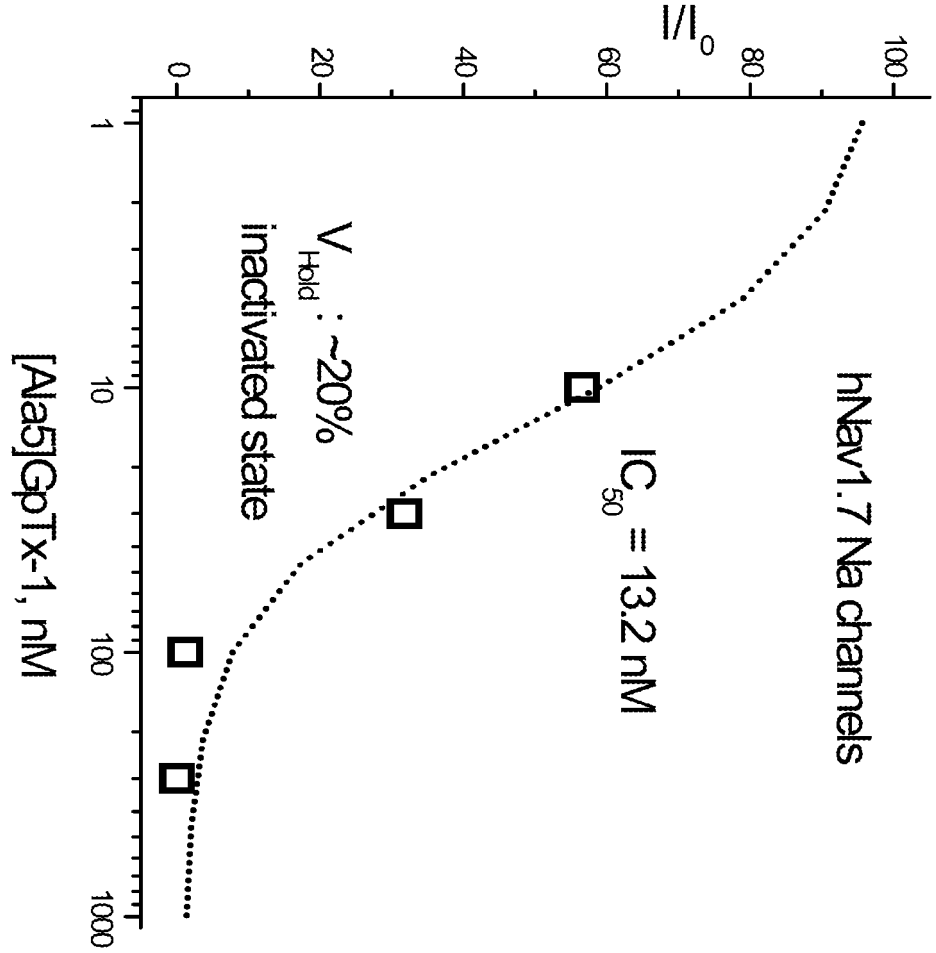

I/I0
100
80
60
40
20
0
1
10
100
1000
[Ala5]GpTx-1, nM
hNav1.7 Na channels
IC50 = 13.2 nM
VHold : ~20%
inactivated state

FIG. 35

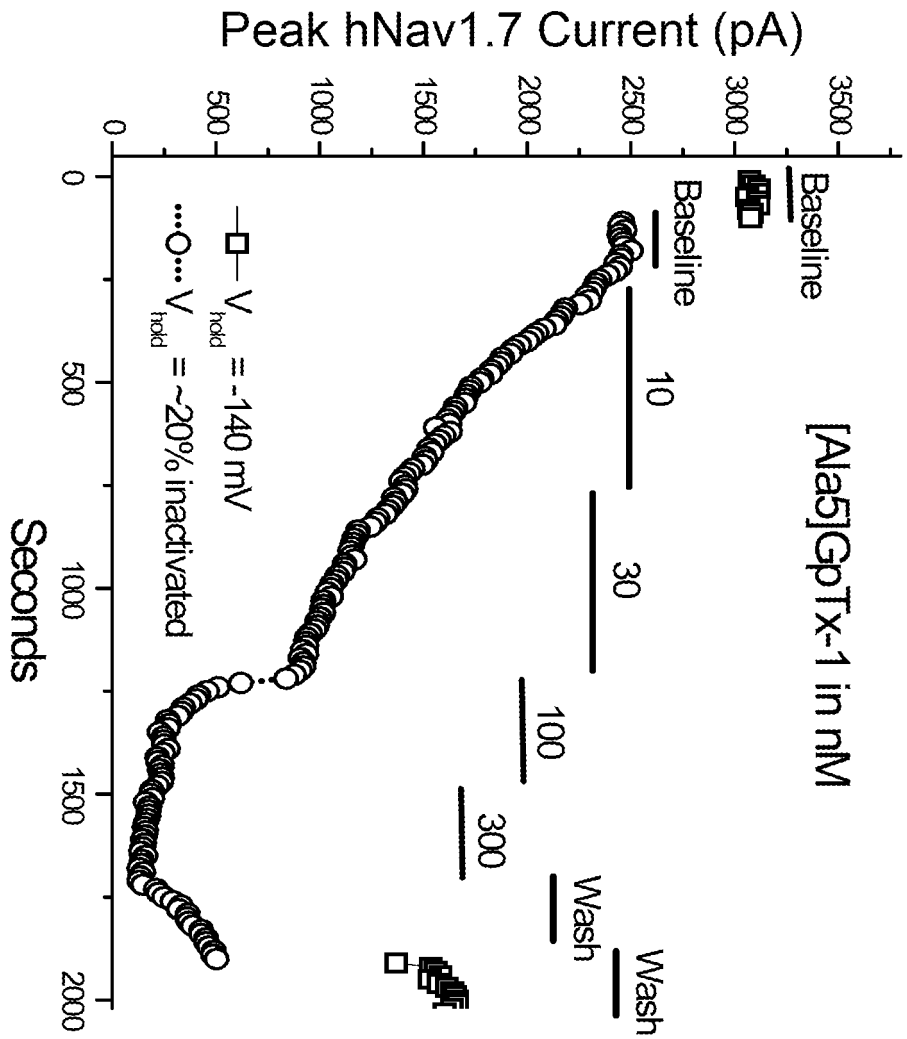

Peak hNav1.7 Current (pA)
0
500
1000
1500
2000
2500
3000
3500
Seconds
0
500
1000
1500
2000
Baseline
Baseline
10
30
100
300
Wash
Wash
[Ala5]GpTx-1 in nM
V hold = -140 mV
V hold = ~20% inactivated

FIG. 36

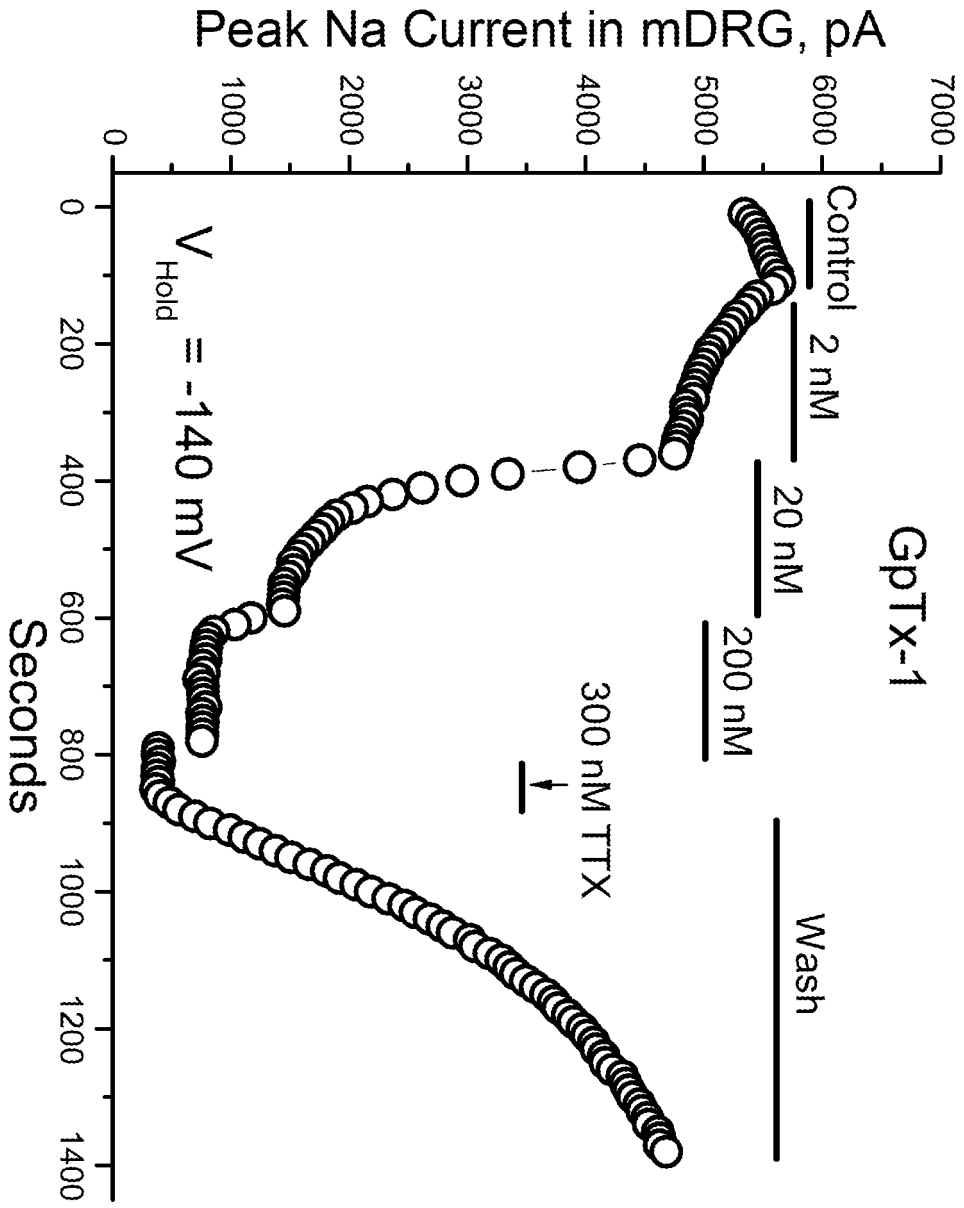

Peak Na Current in mDRG, pA
0
1000
2000
3000
4000
5000
6000
7000
0
200
400
600
800
1000
1200
1400
Seconds
V Hold = -140 mV
Control
2 nM
20 nM
200 nM
300 nM TTX
Wash
GpTx-1

FIG. 37

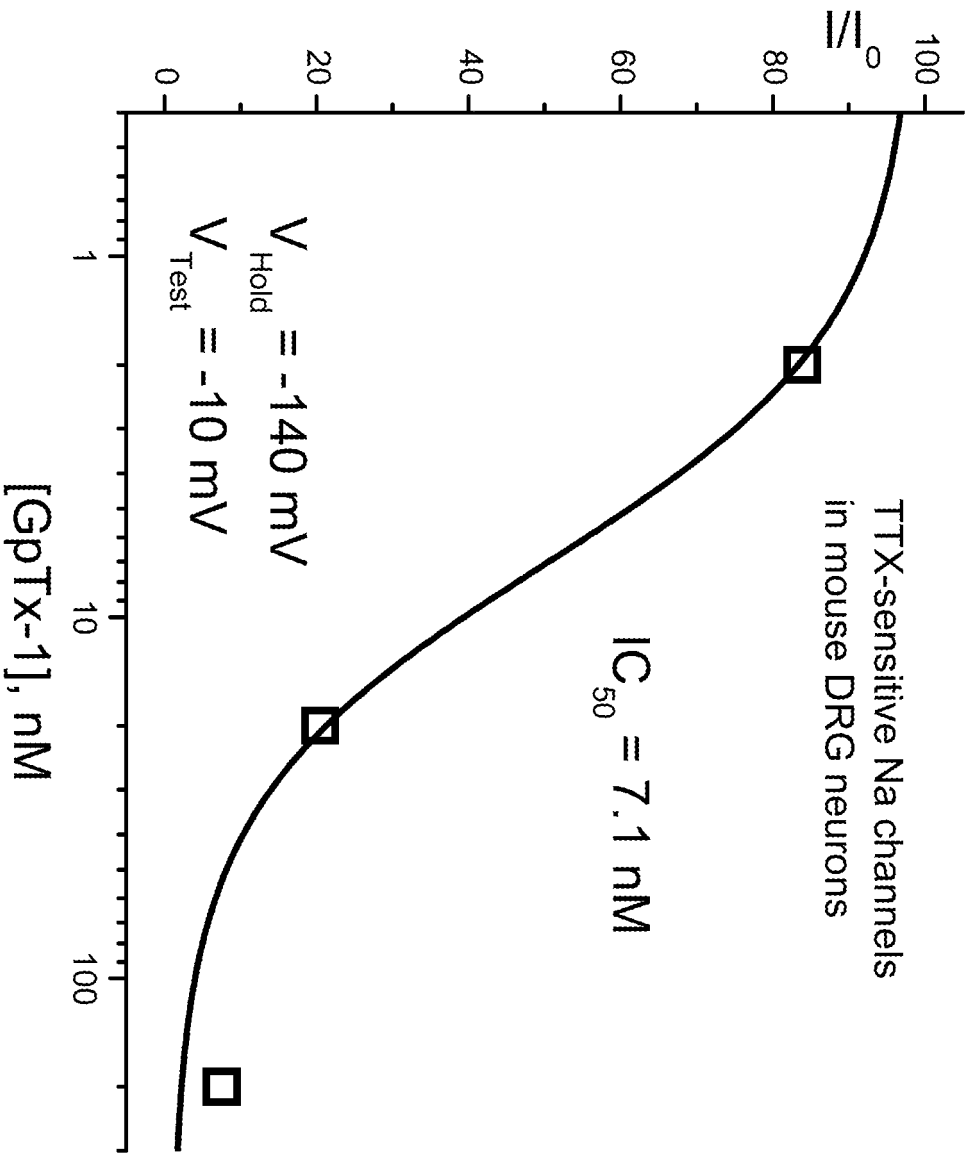

I/I0
100
80
60
40
20
0
1
10
100
[GpTx-1], nM
TTX-sensitive Na channels
in mouse DRG neurons
IC50 = 7.1 nM
VHold = -140 mV
VTest = -10 mV

FIG. 38

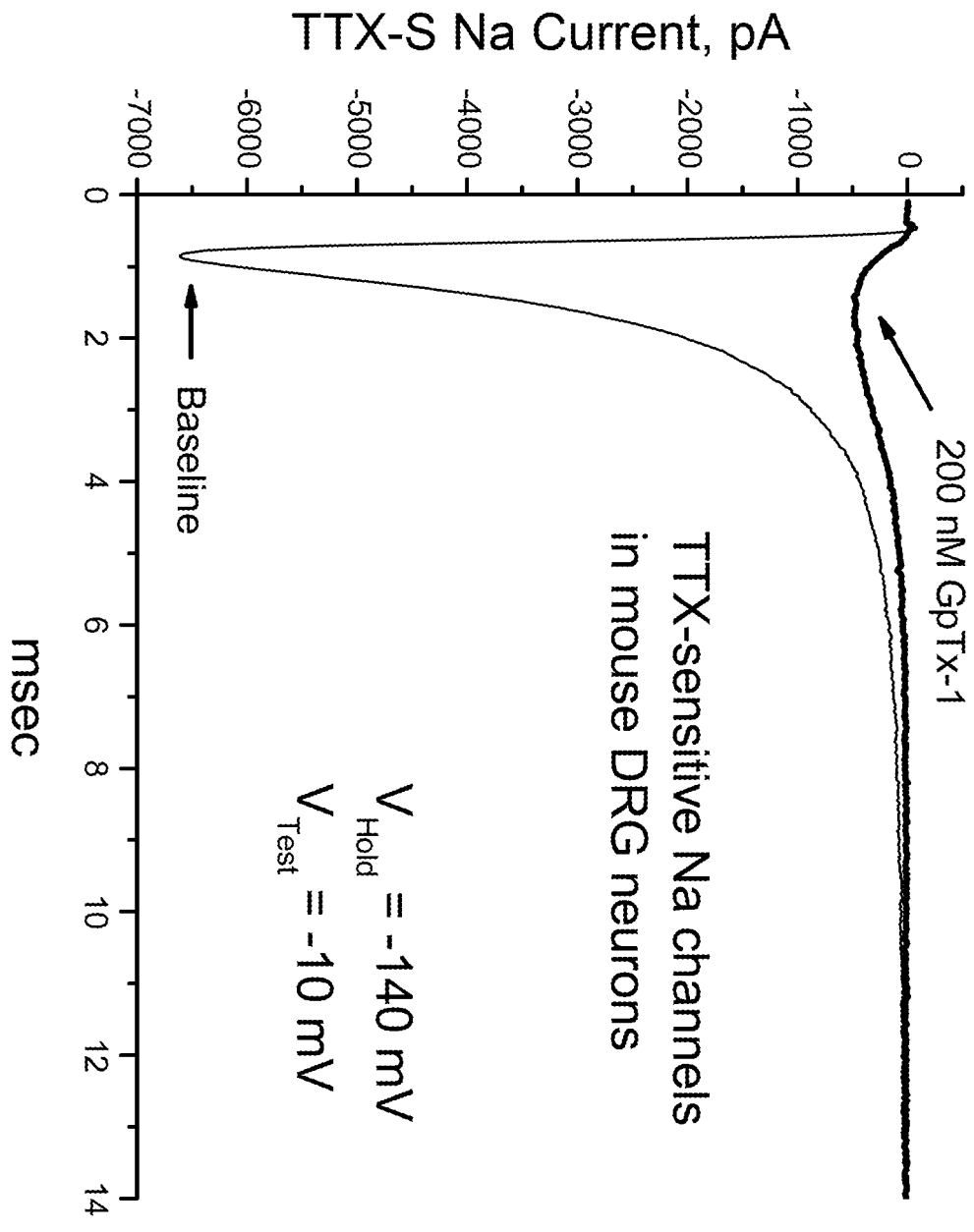

TTX-S Na Current, pA
-7000
-6000
-5000
-4000
-3000
-2000
-1000
0
0
2
4
6
8
10
12
14
msec
Baseline
200 nM GpTx-1
TTX-sensitive Na channels
in mouse DRG neurons
V Hold = -140 mV
V Test = -10 mV

FIG. 39

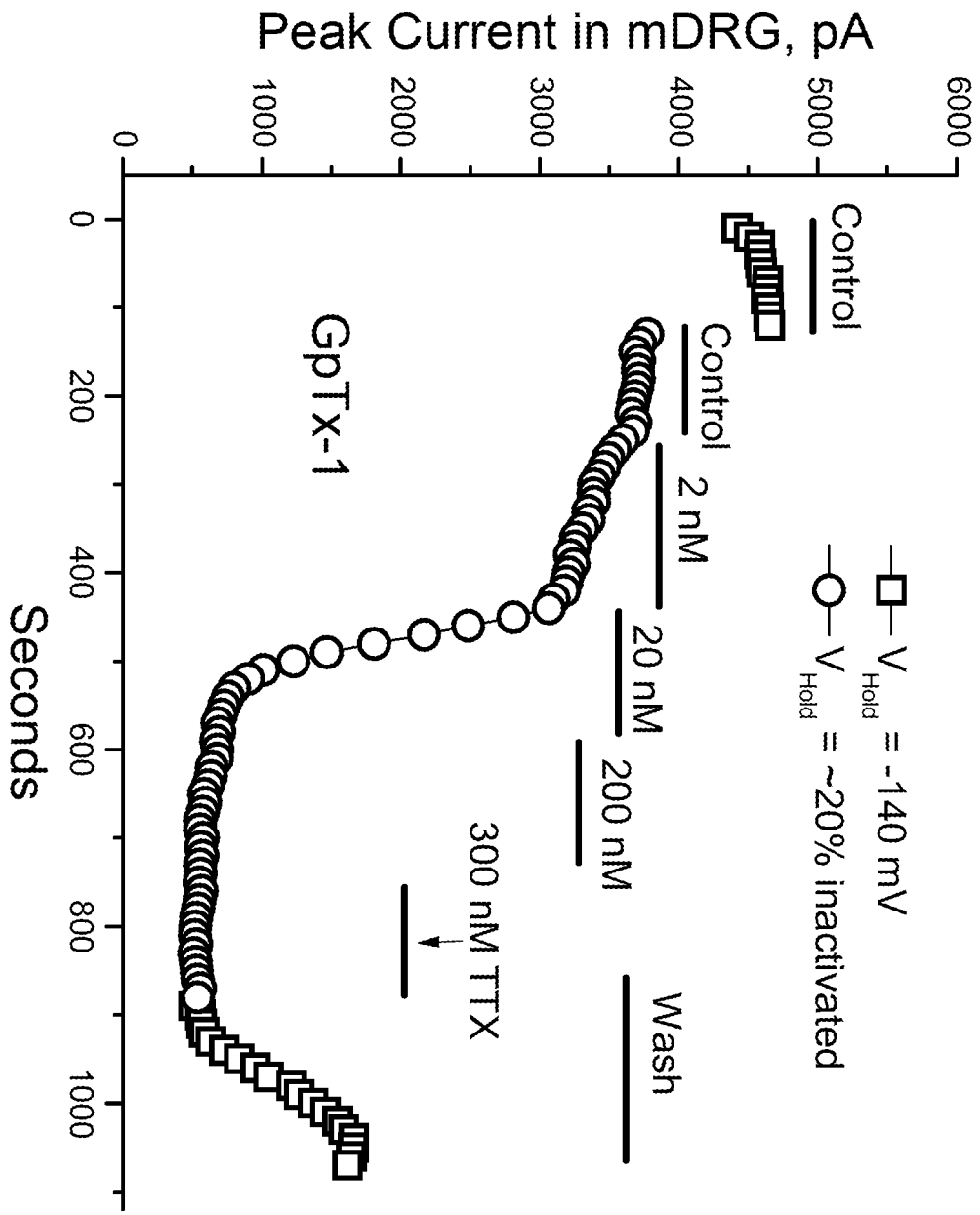

Peak Current in mDRG, pA
0
1000
2000
3000
4000
5000
6000
Seconds
0
200
400
600
800
1000
GpTx-1
Control
Control
2 nM
20 nM
200 nM
300 nM TTX
Wash
V Hold = -140 mV
V Hold = ~20% inactivated

FIG. 40

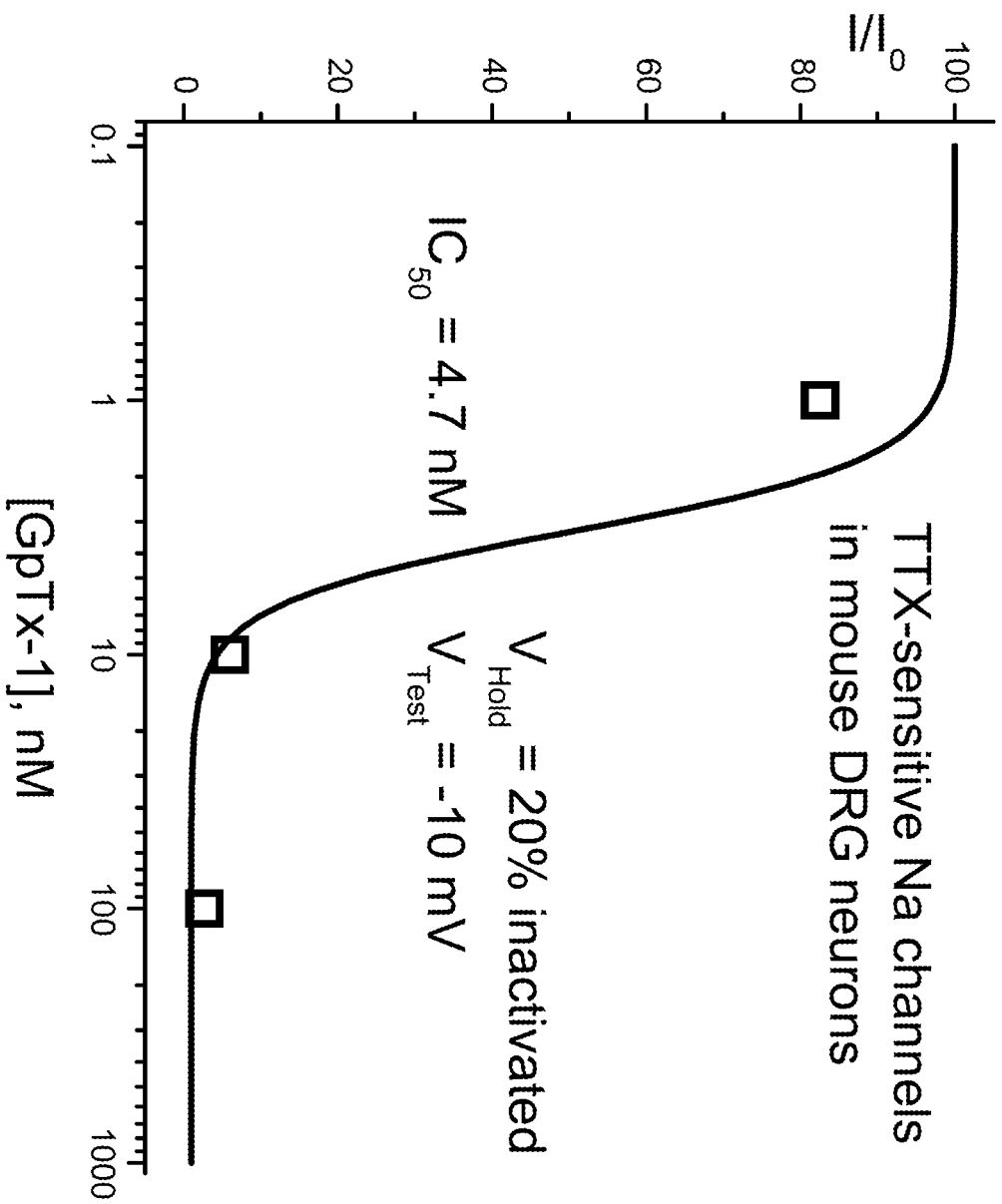

TTX-sensitive Na channels
in mouse DRG neurons
V_{Hold} = 20% inactivated
V_{Test} = -10 mV
IC_{50} = 4.7 nM
I/I$_0$
100
80
60
40
20
0
0.1
1
10
100
1000
[GpTx-1], nM

FIG. 41

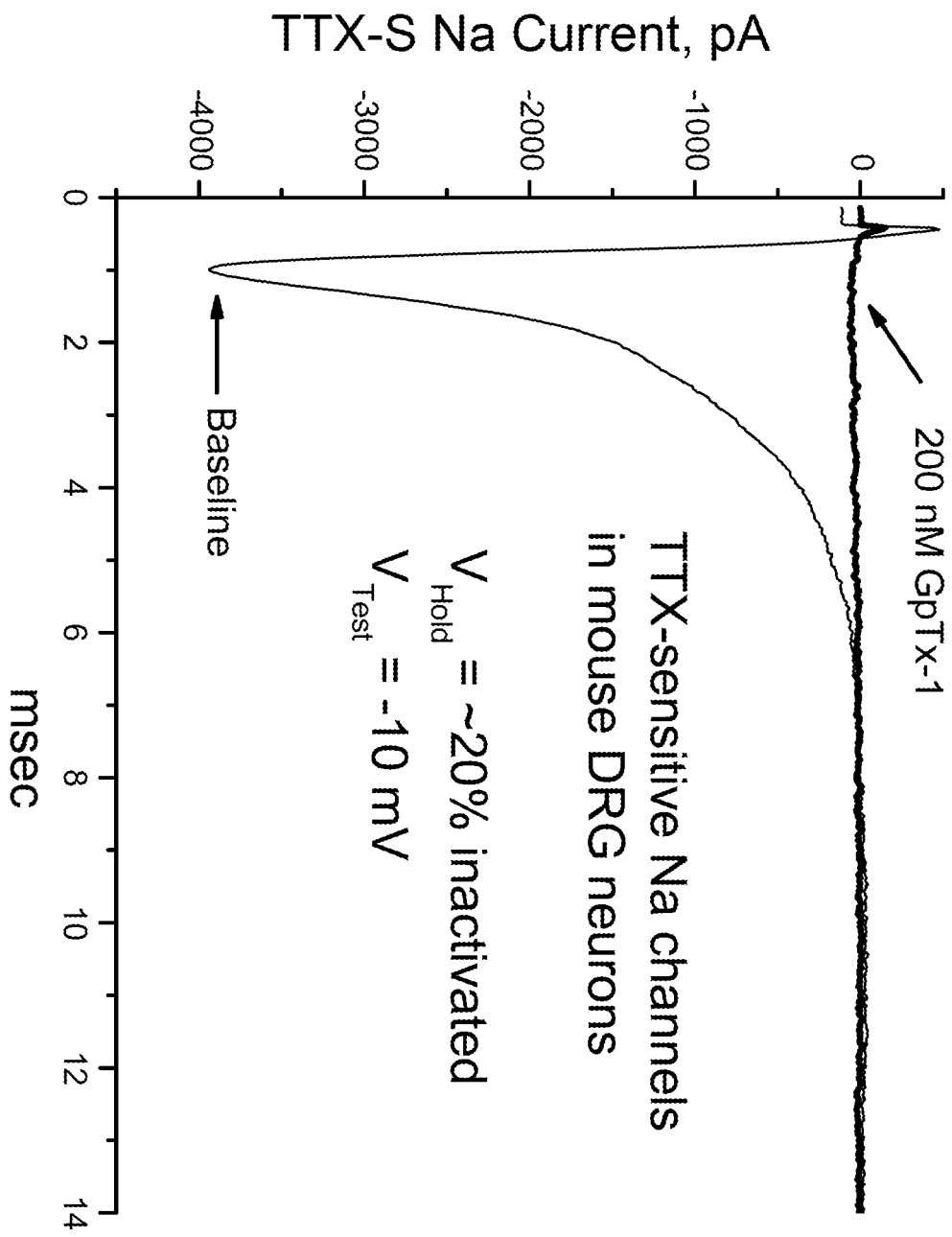

TTX-S Na Current, pA
0
-1000
-2000
-3000
-4000
0
2
4
6
8
10
12
14
msec
200 nM GpTx-1
Baseline
TTX-sensitive Na channels
in mouse DRG neurons
V Hold = ~20% inactivated
V Test = -10 mV

FIG. 42

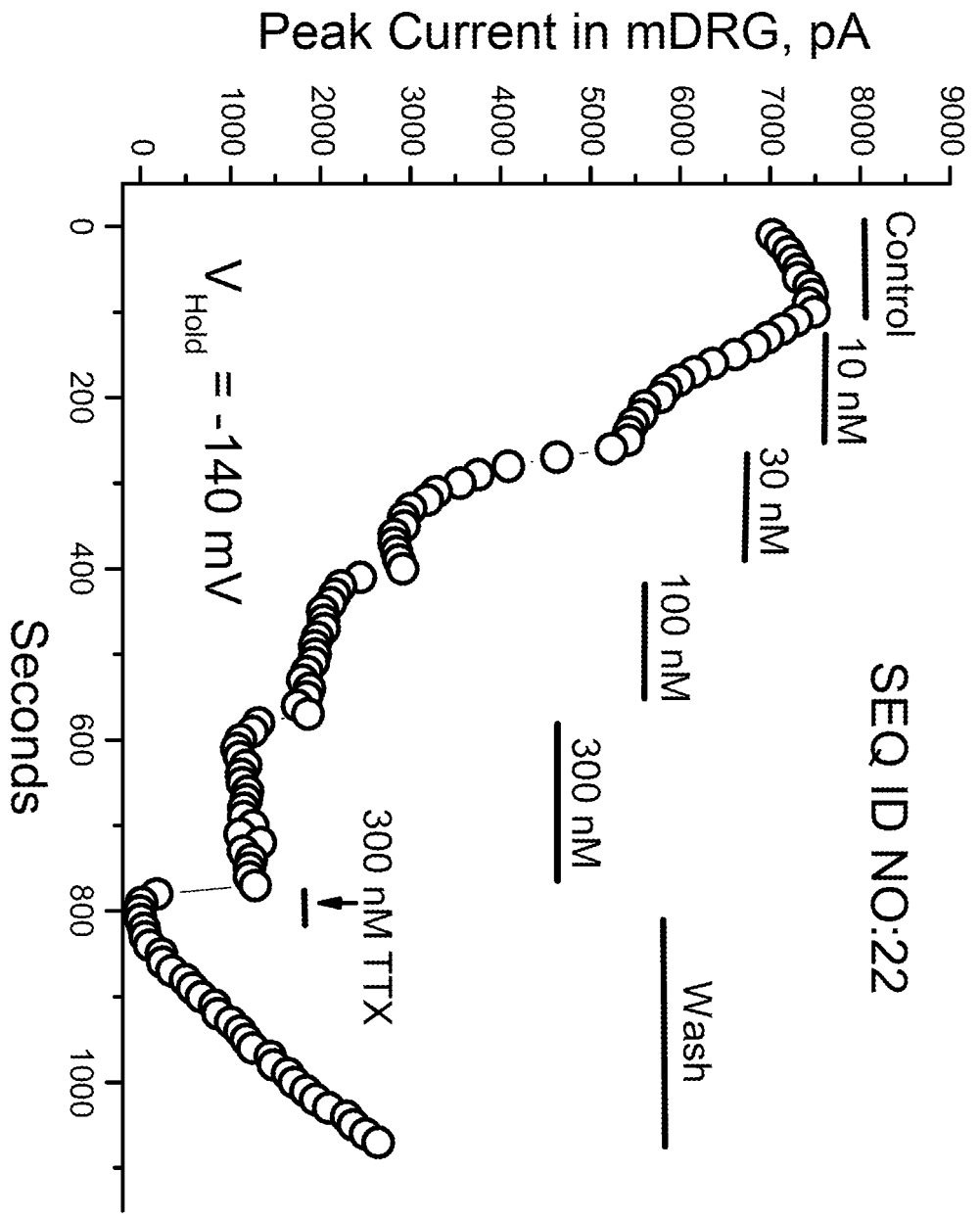

Peak Current in mDRG, pA
0
1000
2000
3000
4000
5000
6000
7000
8000
9000
Seconds
0
200
400
600
800
1000
V Hold = -140 mV
Control
10 nM
30 nM
100 nM
300 nM
Wash
300 nM TTX
SEQ ID NO:22

FIG. 43

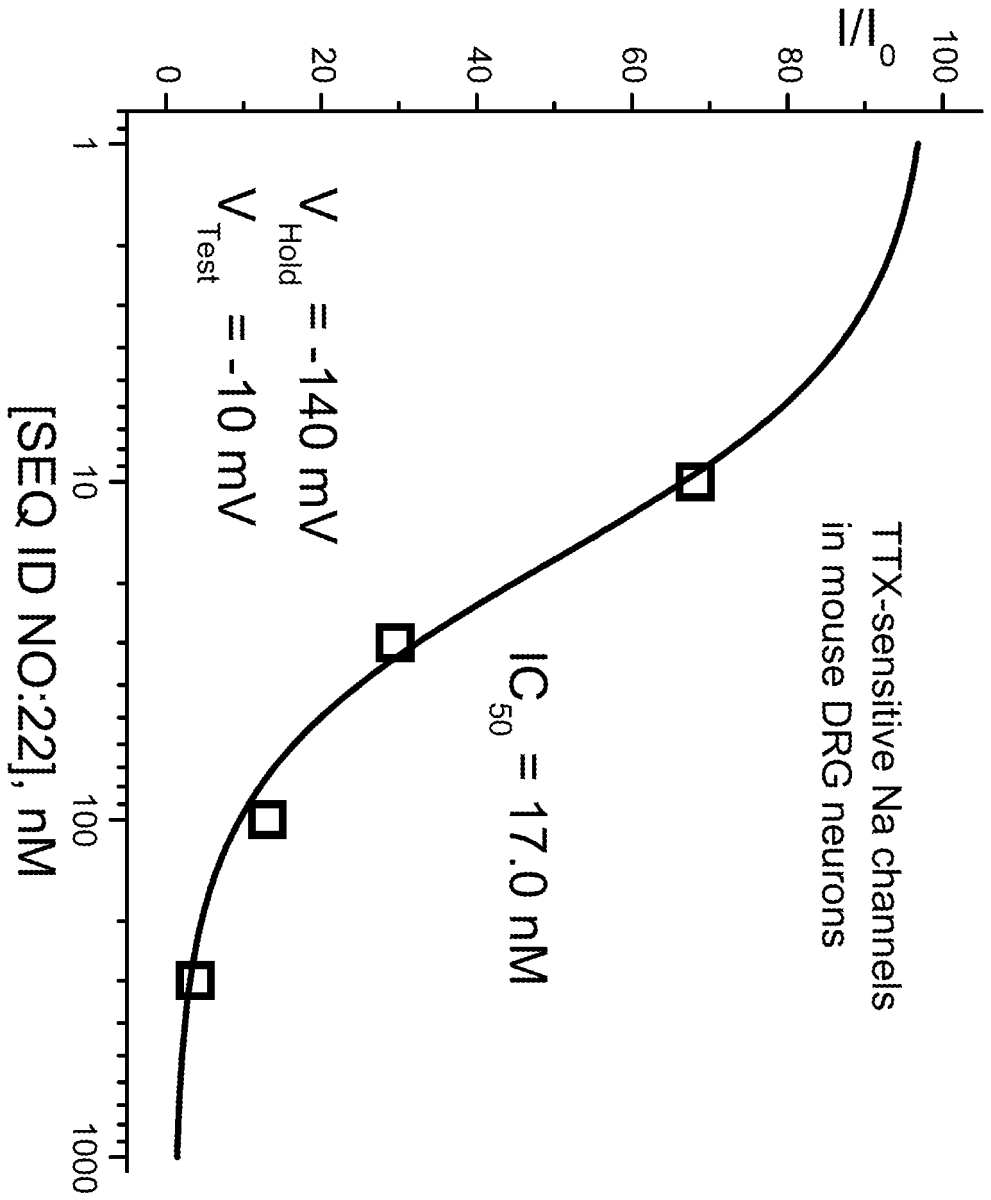

I/I0
100
80
60
40
20
0
1
10
100
1000
[SEQ ID NO:22], nM
VHold = -140 mV
VTest = -10 mV
IC50 = 17.0 nM
TTX-sensitive Na channels
in mouse DRG neurons

FIG. 44

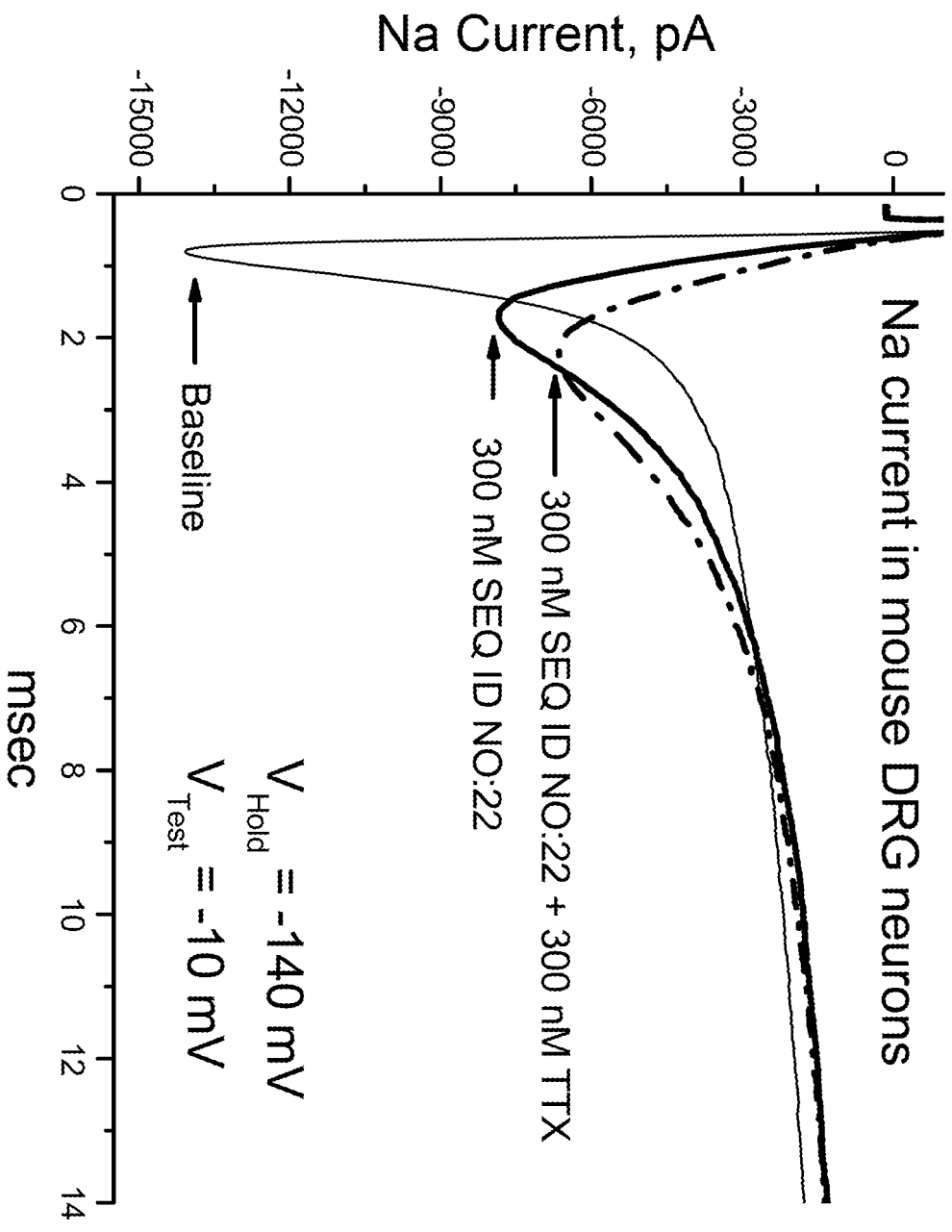

Na Current, pA
0
-3000
-6000
-9000
-12000
-15000
0
2
4
6
8
10
12
14
msec
Na current in mouse DRG neurons
Baseline
300 nM SEQ ID NO:22
300 nM SEQ ID NO:22 + 300 nM TTX
V Hold = -140 mV
V Test = -10 mV

FIG. 45

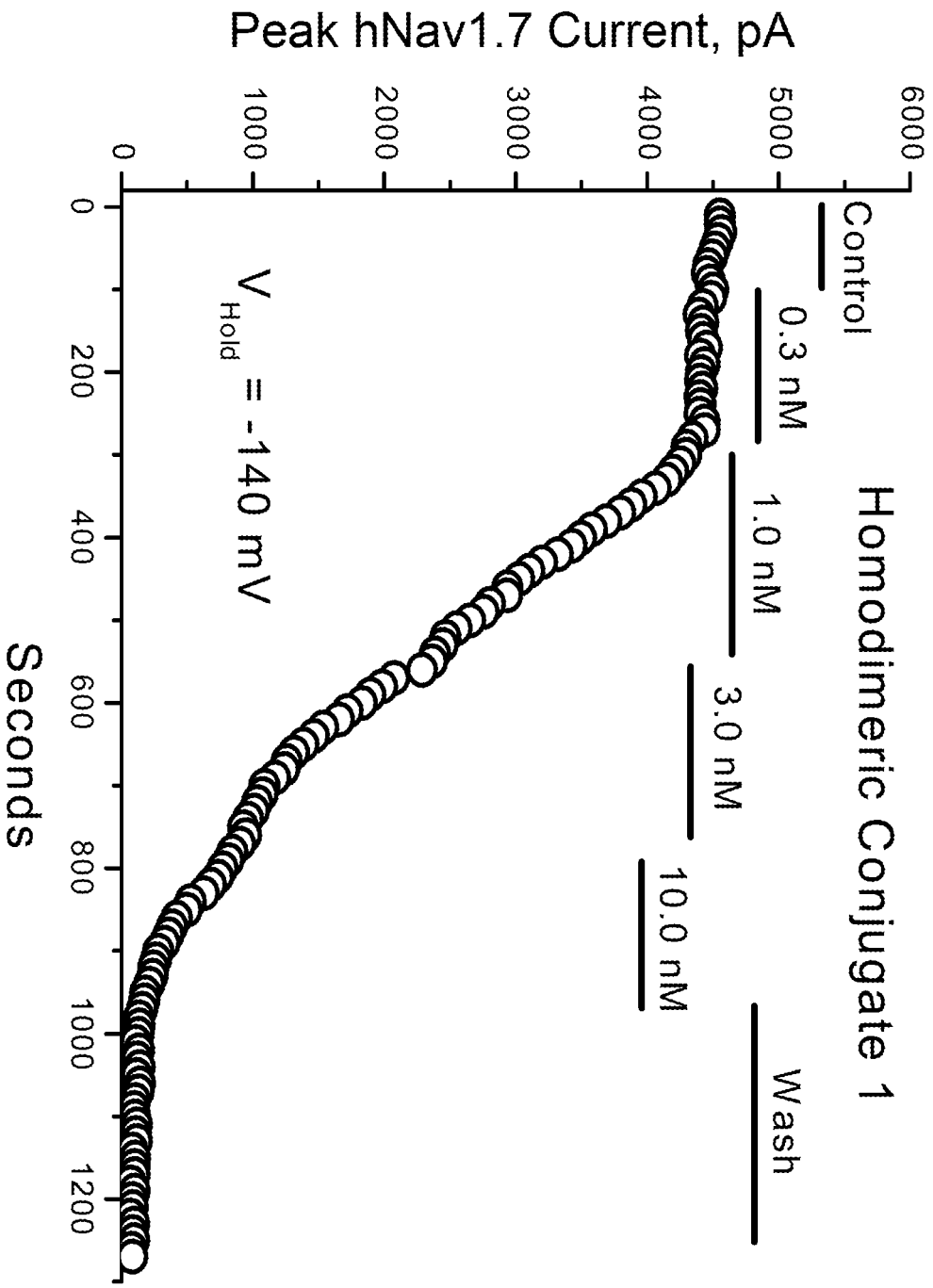

Peak hNav1.7 Current, pA
0
1000
2000
3000
4000
5000
6000
Seconds
0
200
400
600
800
1000
1200
V_{Hold} = -140 mV
Control
0.3 nM
1.0 nM
3.0 nM
10.0 nM
Wash
Homodimeric Conjugate 1

FIG. 46

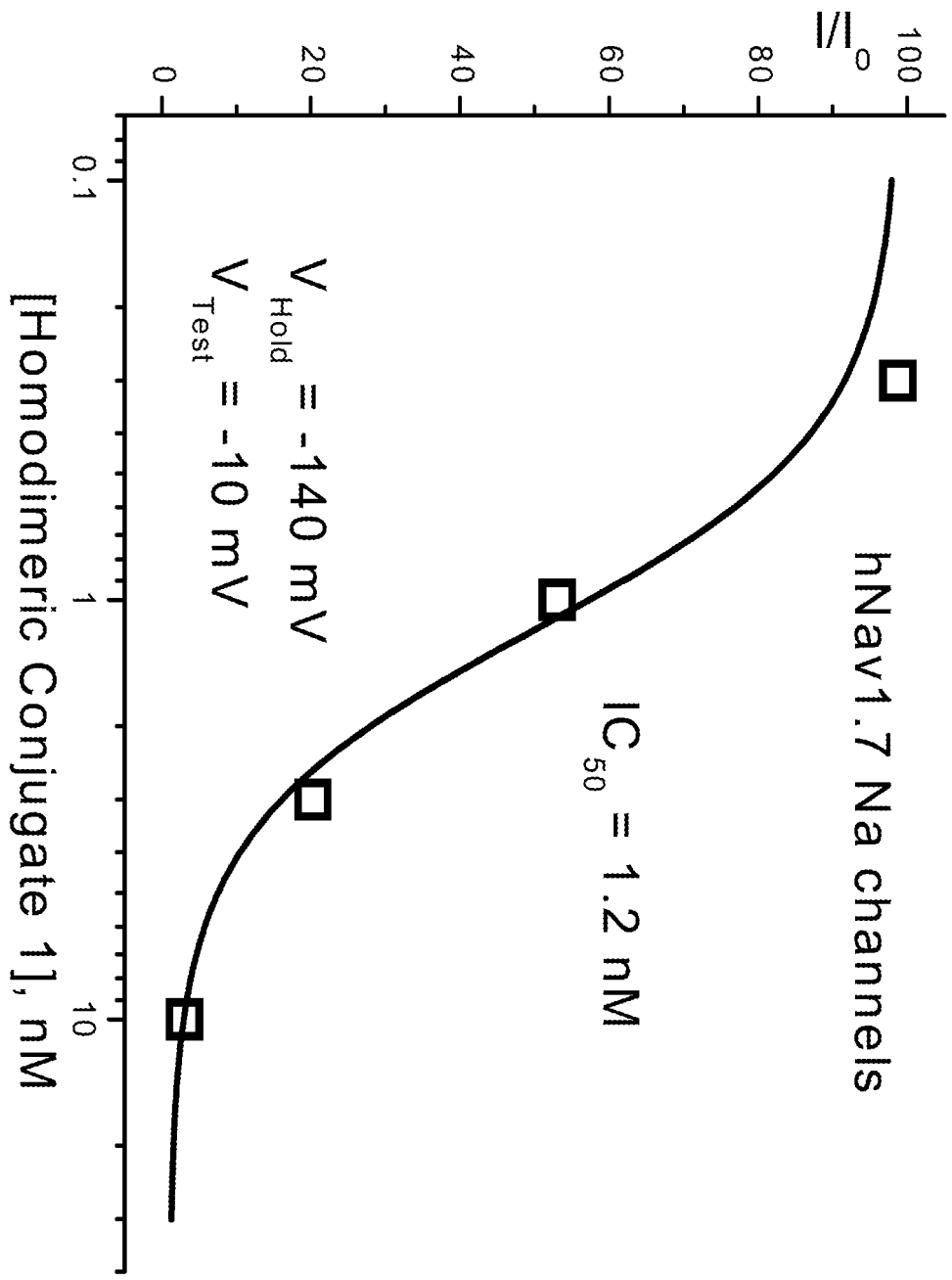

I/I0
100
80
60
40
20
0
0.1
1
10
[Homodimeric Conjugate 1], nM
hNav1.7 Na channels
IC50 = 1.2 nM
VHold = -140 mV
VTest = -10 mV

FIG. 47

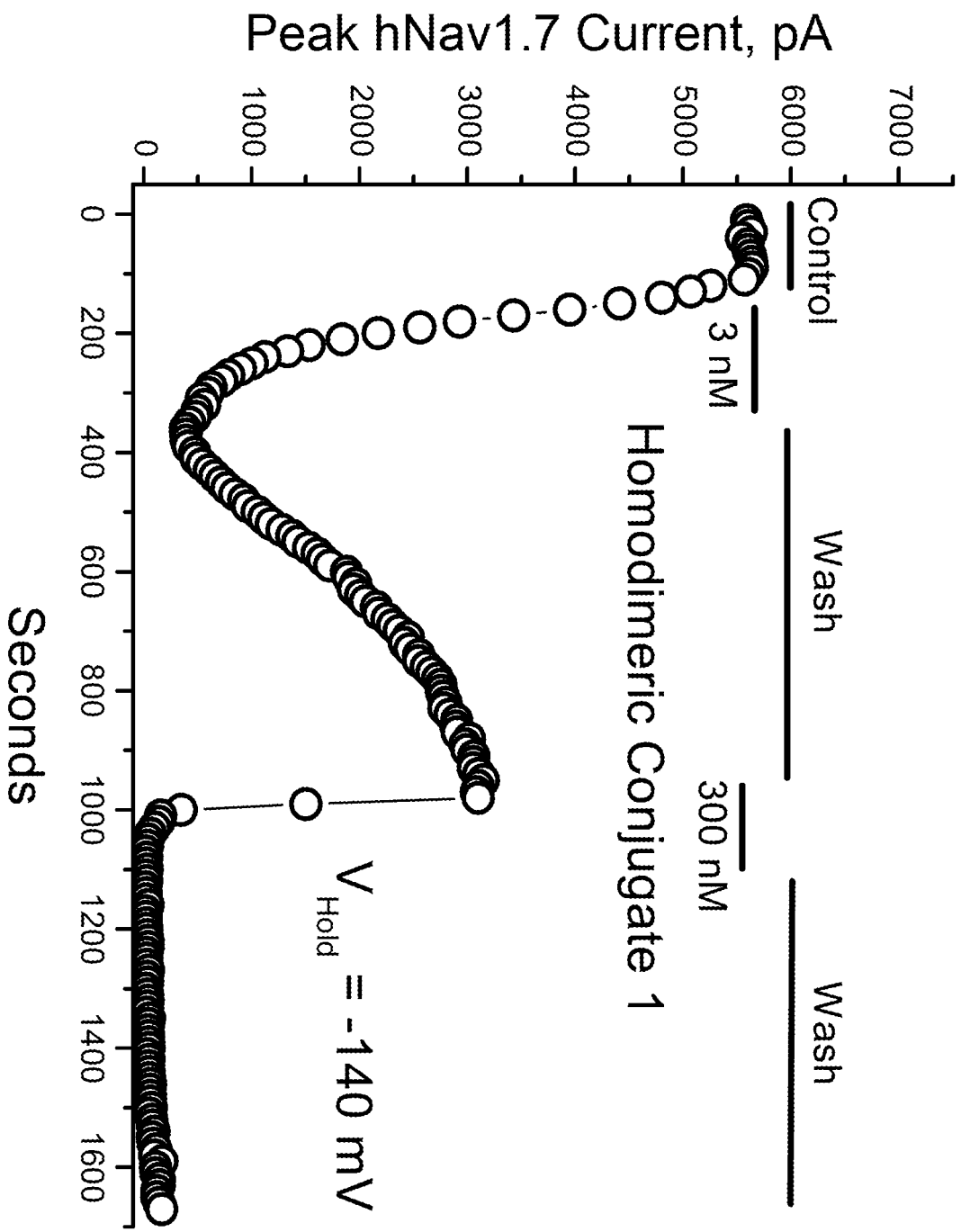

Peak hNav1.7 Current, pA
0
1000
2000
3000
4000
5000
6000
7000
Seconds
0
200
400
600
800
1000
1200
1400
1600
Control
3 nM
Wash
300 nM
Wash
Homodimeric Conjugate 1
V Hold = -140 mV

FIG. 48

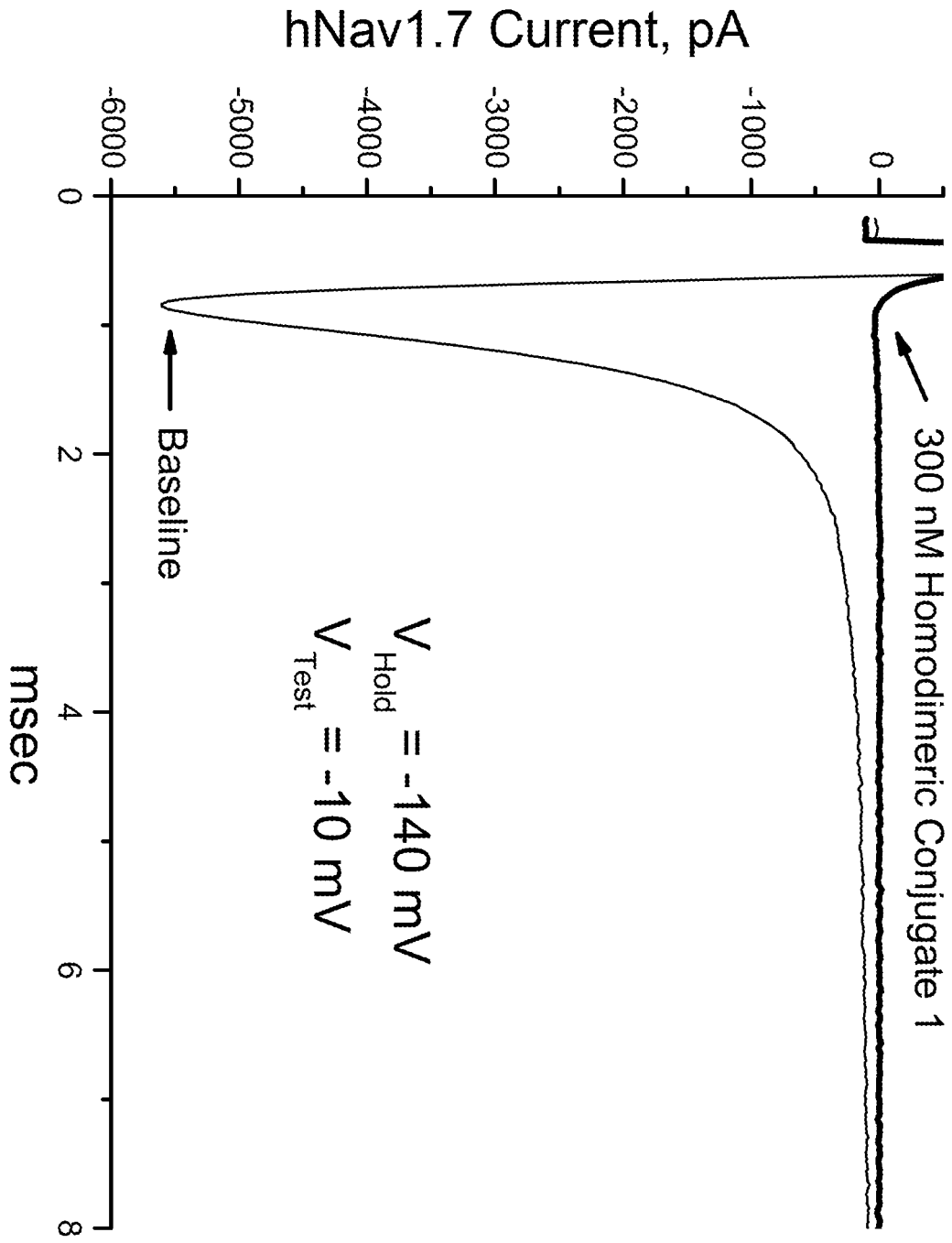

hNav1.7 Current, pA
-6000
-5000
-4000
-3000
-2000
-1000
0
0
2
4
6
8
msec
Baseline
300 nM Homodimeric Conjugate 1
V Hold = -140 mV
V Test = -10 mV

FIG. 49

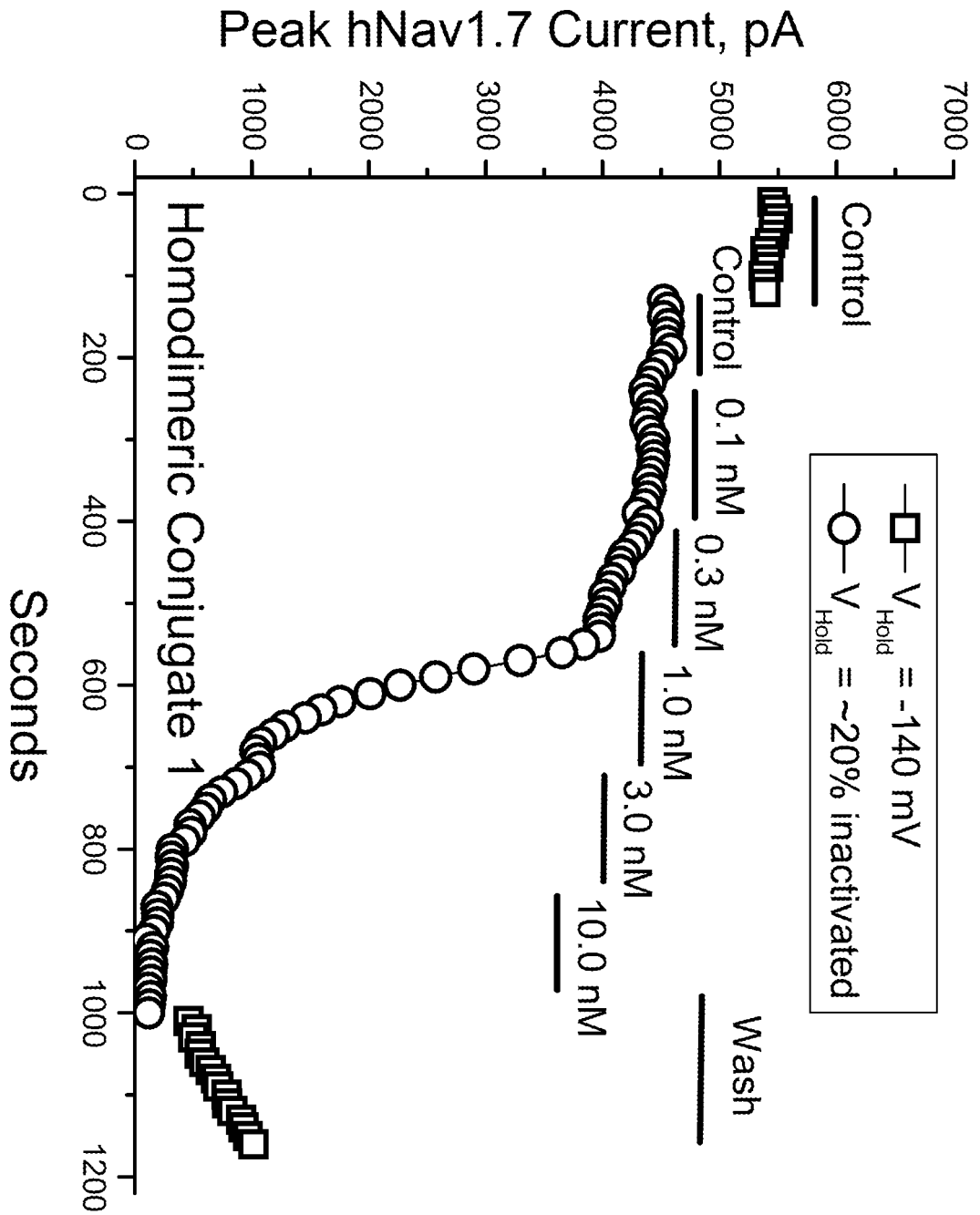

Peak hNav1.7 Current, pA
0
1000
2000
3000
4000
5000
6000
7000
Seconds
0
200
400
600
800
1000
1200
Homodimeric Conjugate 1
Control
Control
0.1 nM
0.3 nM
1.0 nM
3.0 nM
10.0 nM
Wash
V Hold = -140 mV
V Hold = ~20% inactivated

FIG. 50

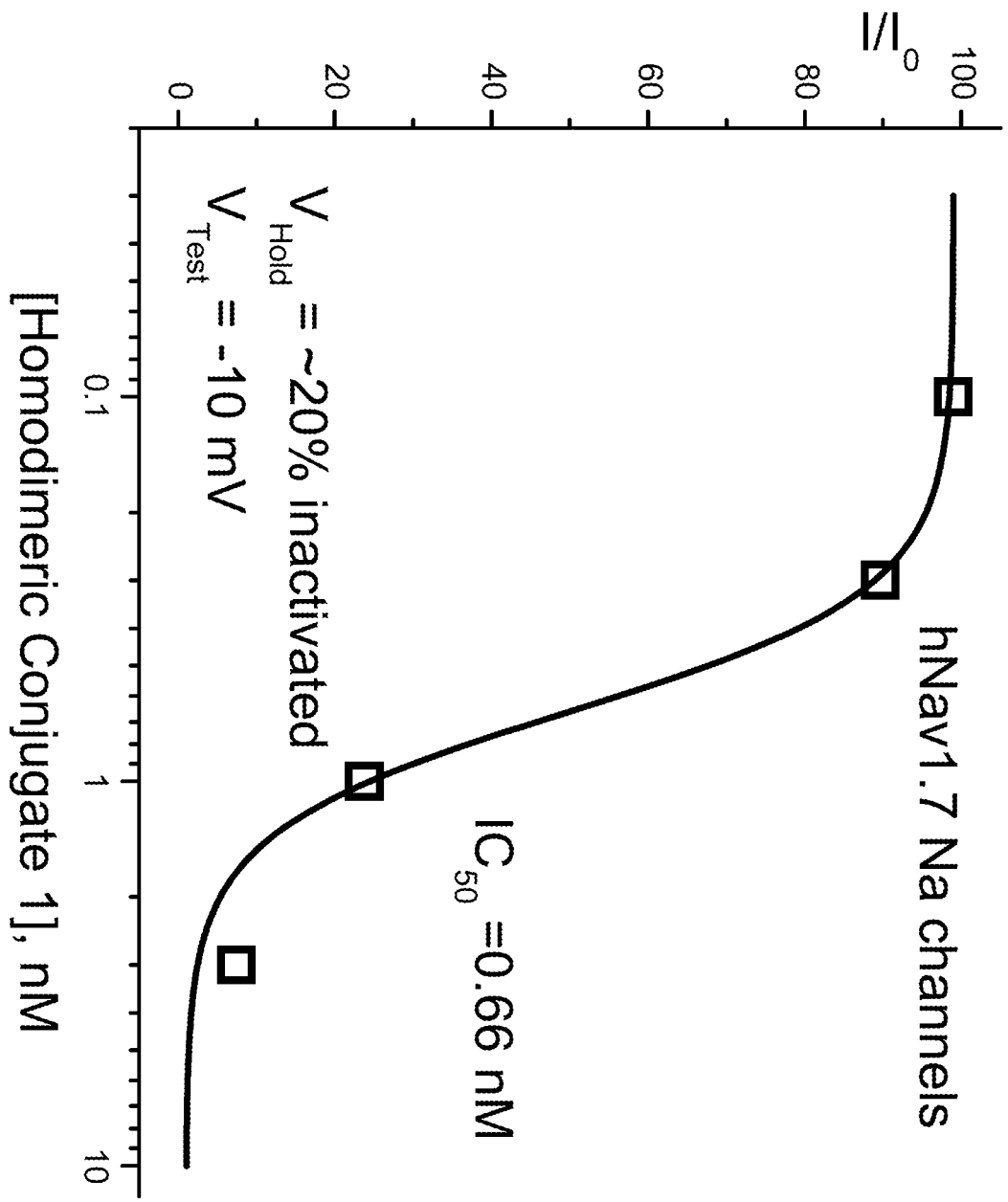

I/I0
100
80
60
40
20
0
hNav1.7 Na channels
IC50 =0.66 nM
VHold = ~20% inactivated
VTest = -10 mV
0.1
1
10
[Homodimeric Conjugate 1], nM

FIG. 51

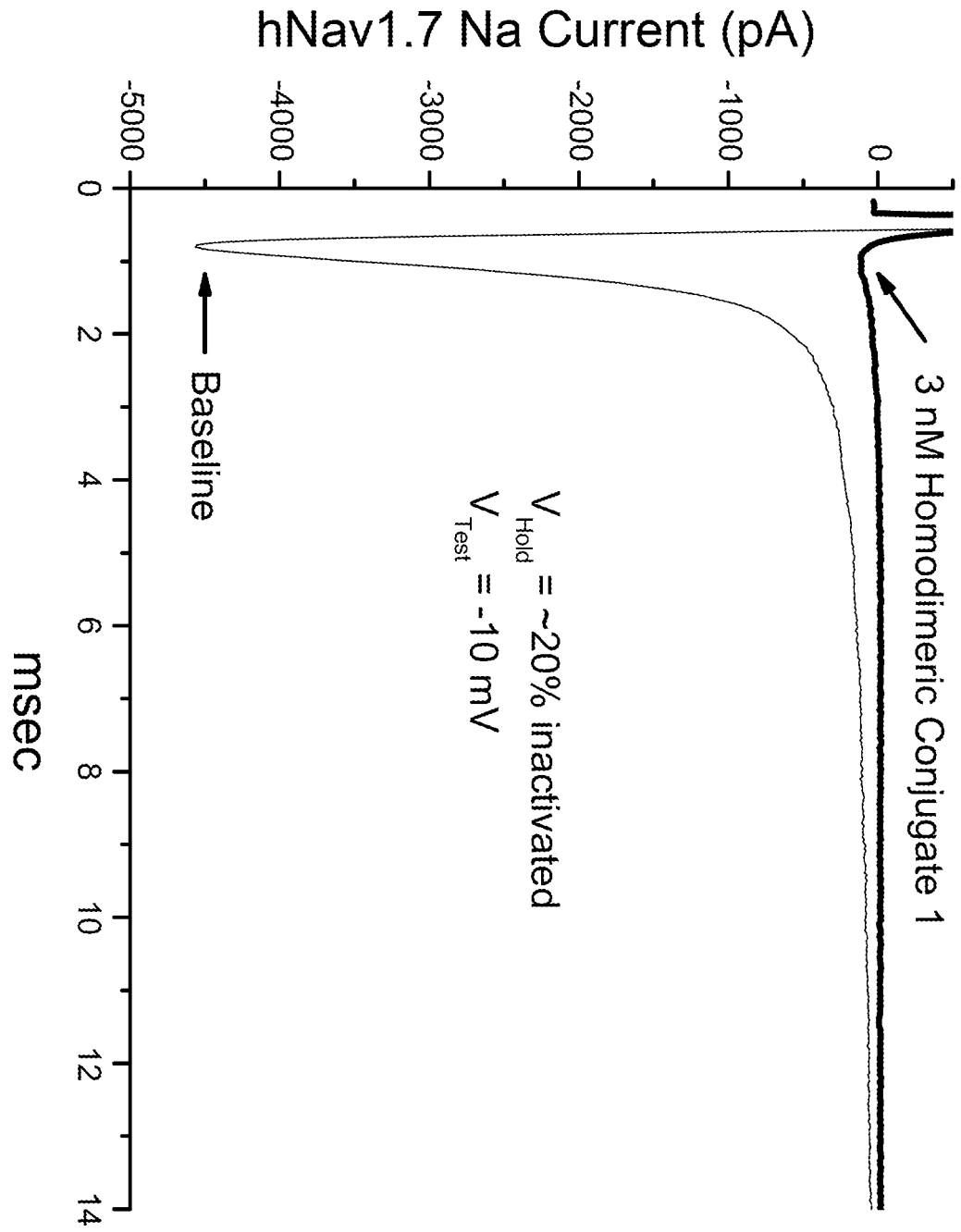

hNav1.7 Na Current (pA)
0
-1000
-2000
-3000
-4000
-5000
0
2
4
6
8
10
12
14
msec
3 nM Homodimeric Conjugate 1
Baseline
V Hold = ~20% inactivated
V Test = -10 mV

FIG. 52

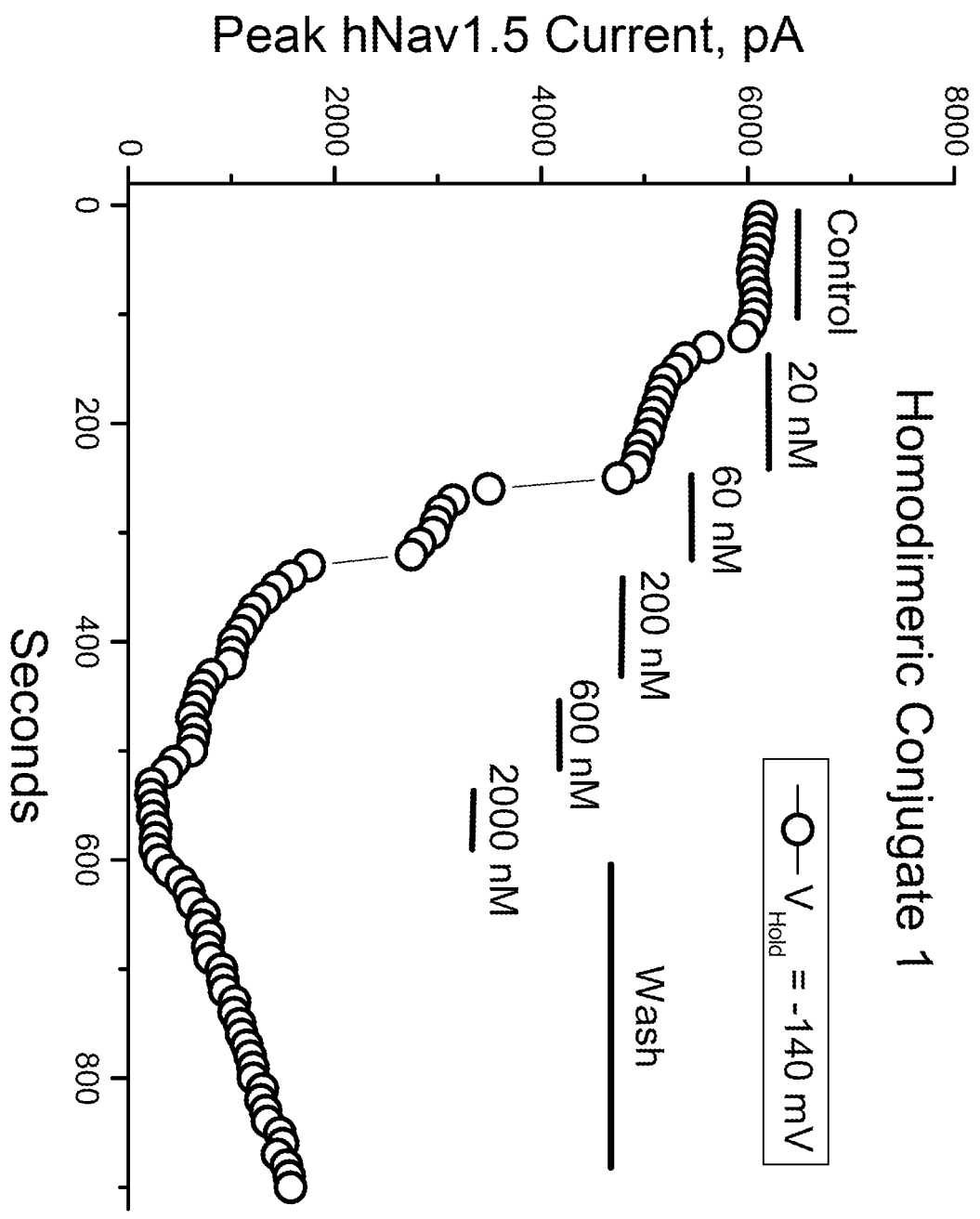

Peak hNav1.5 Current, pA
0
2000
4000
6000
8000
Seconds
0
200
400
600
800
Homodimeric Conjugate 1
Control
20 nM
60 nM
200 nM
600 nM
2000 nM
Wash
V Hold = -140 mV

FIG. 53

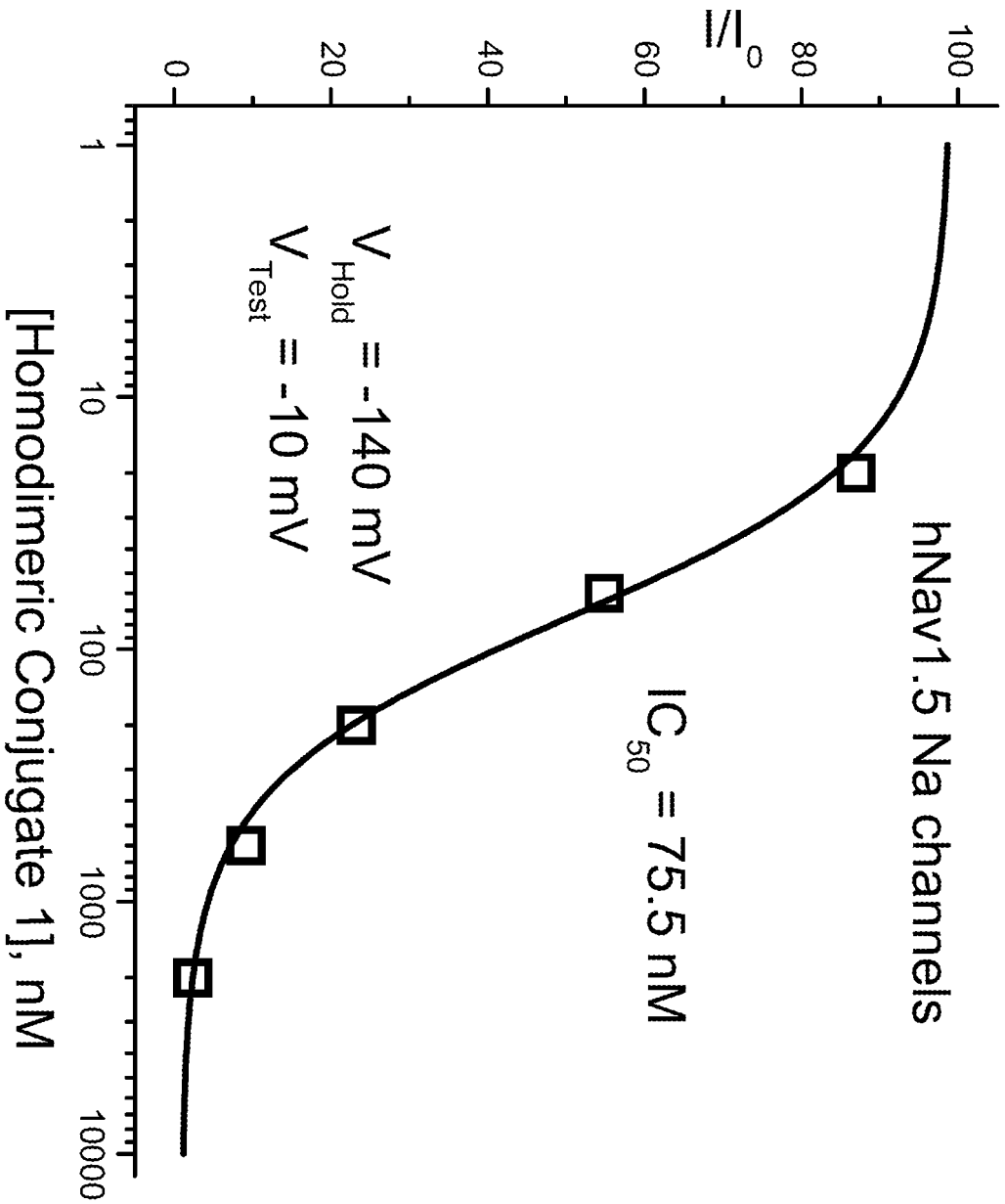

I/I0
100
80
60
40
20
0
1
10
100
1000
10000
[Homodimeric Conjugate 1], nM
hNav1.5 Na channels
IC50 = 75.5 nM
VHold = -140 mV
VTest = -10 mV

FIG. 54

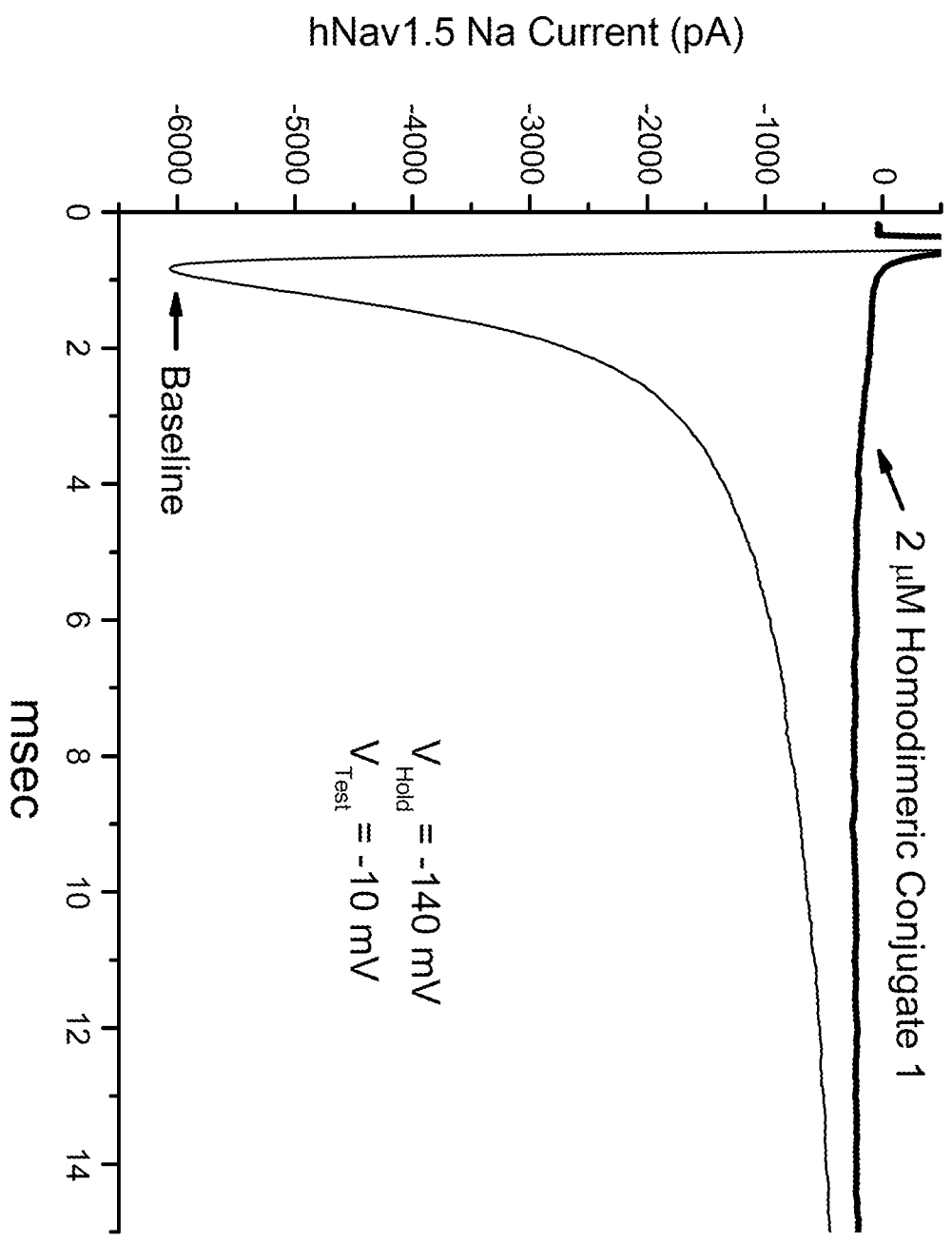

hNav1.5 Na Current (pA)
-6000
-5000
-4000
-3000
-2000
-1000
0
0
2
4
6
8
10
12
14
msec
Baseline
2 μM Homodimeric Conjugate 1
V Hold = -140 mV
V Test = -10 mV

FIG. 55

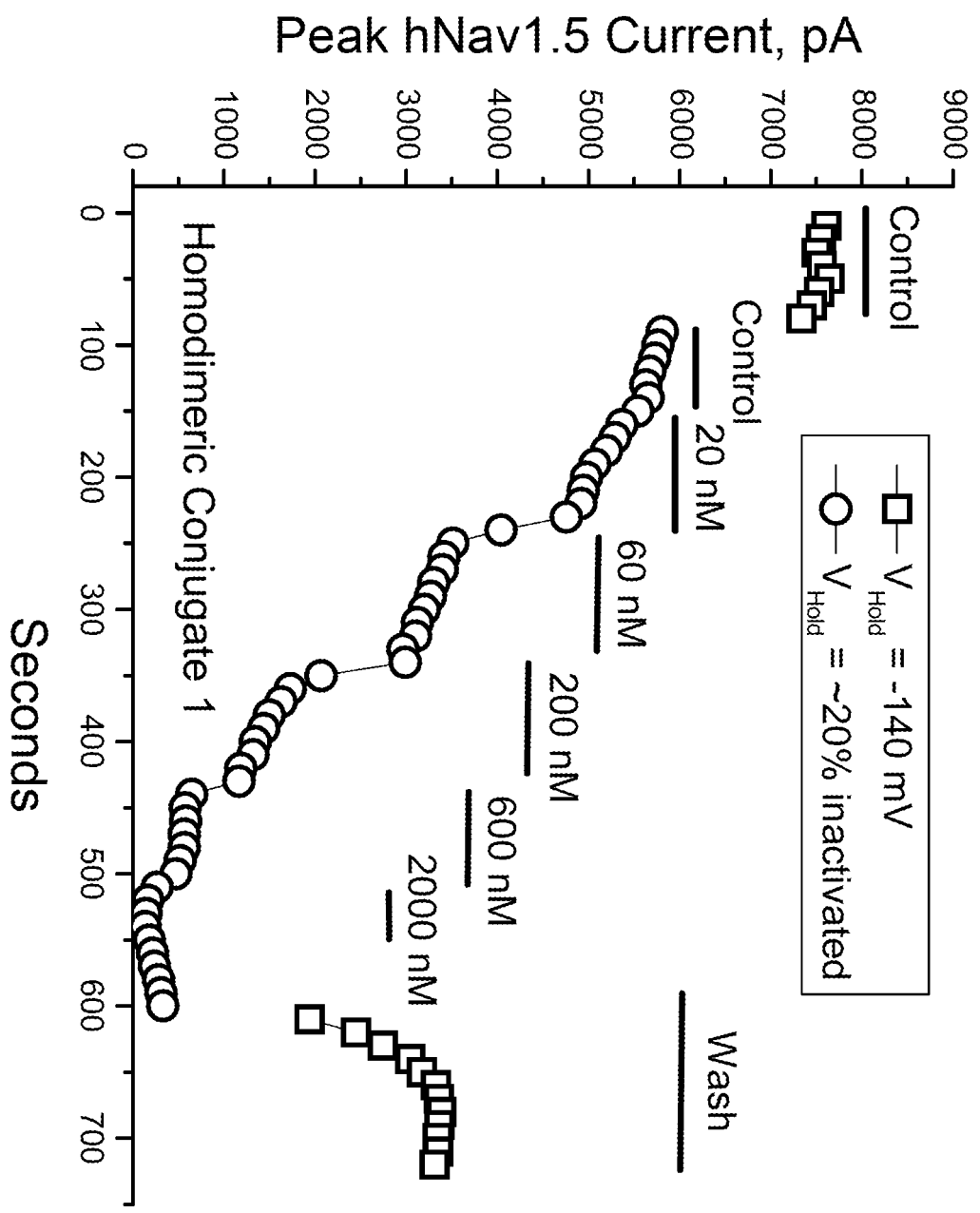

Peak hNav1.5 Current, pA
0
1000
2000
3000
4000
5000
6000
7000
8000
9000
Seconds
0
100
200
300
400
500
600
700
Homodimeric Conjugate 1
Control
20 nM
60 nM
200 nM
600 nM
2000 nM
Wash
Control
V Hold = -140 mV
V Hold = ~20% inactivated

FIG. 56

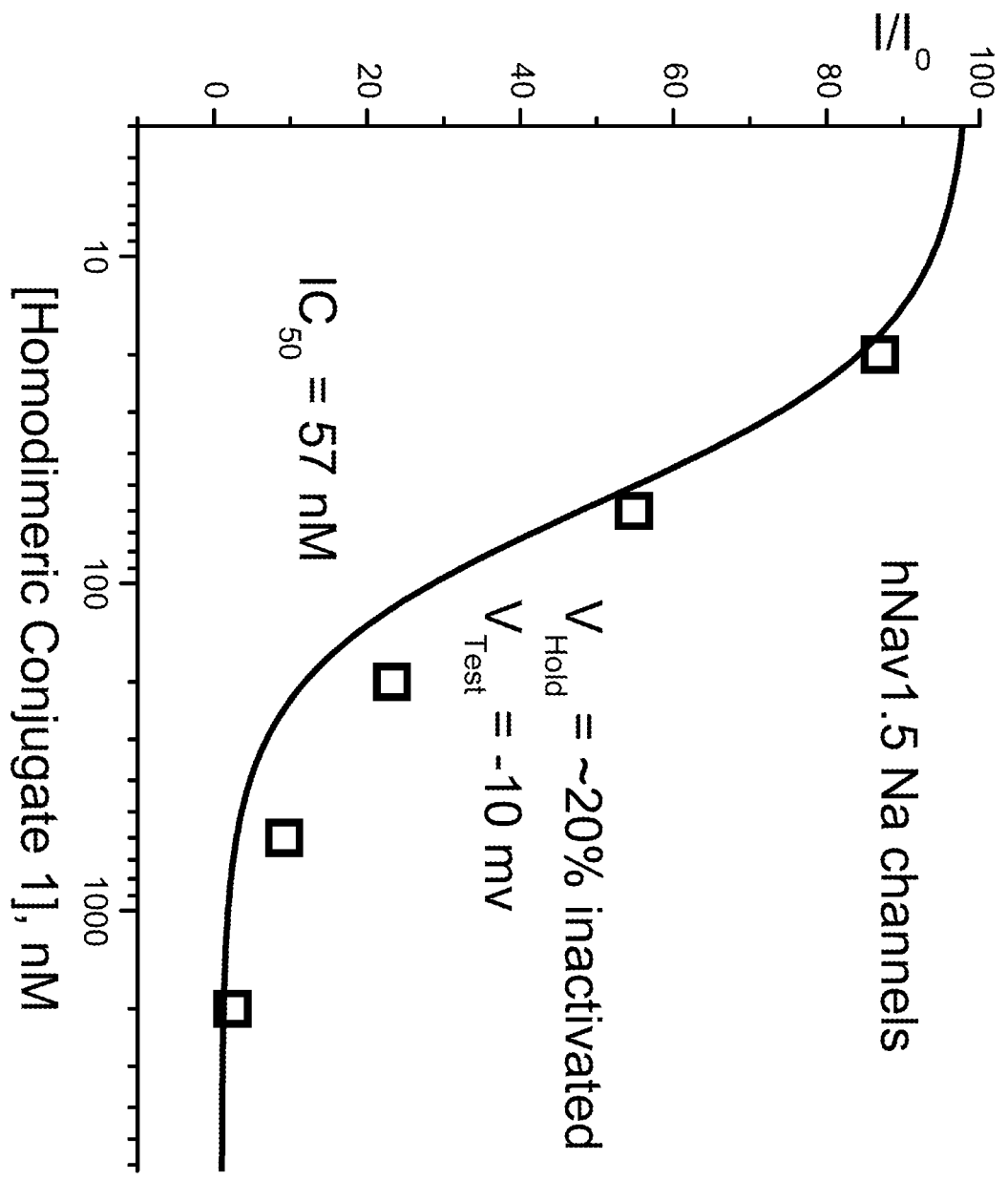

I/I0
100
80
60
40
20
0
10
100
1000
[Homodimeric Conjugate 1], nM
IC50 = 57 nM
VHold = ~20% inactivated
VTest = -10 mv
hNav1.5 Na channels

FIG. 57

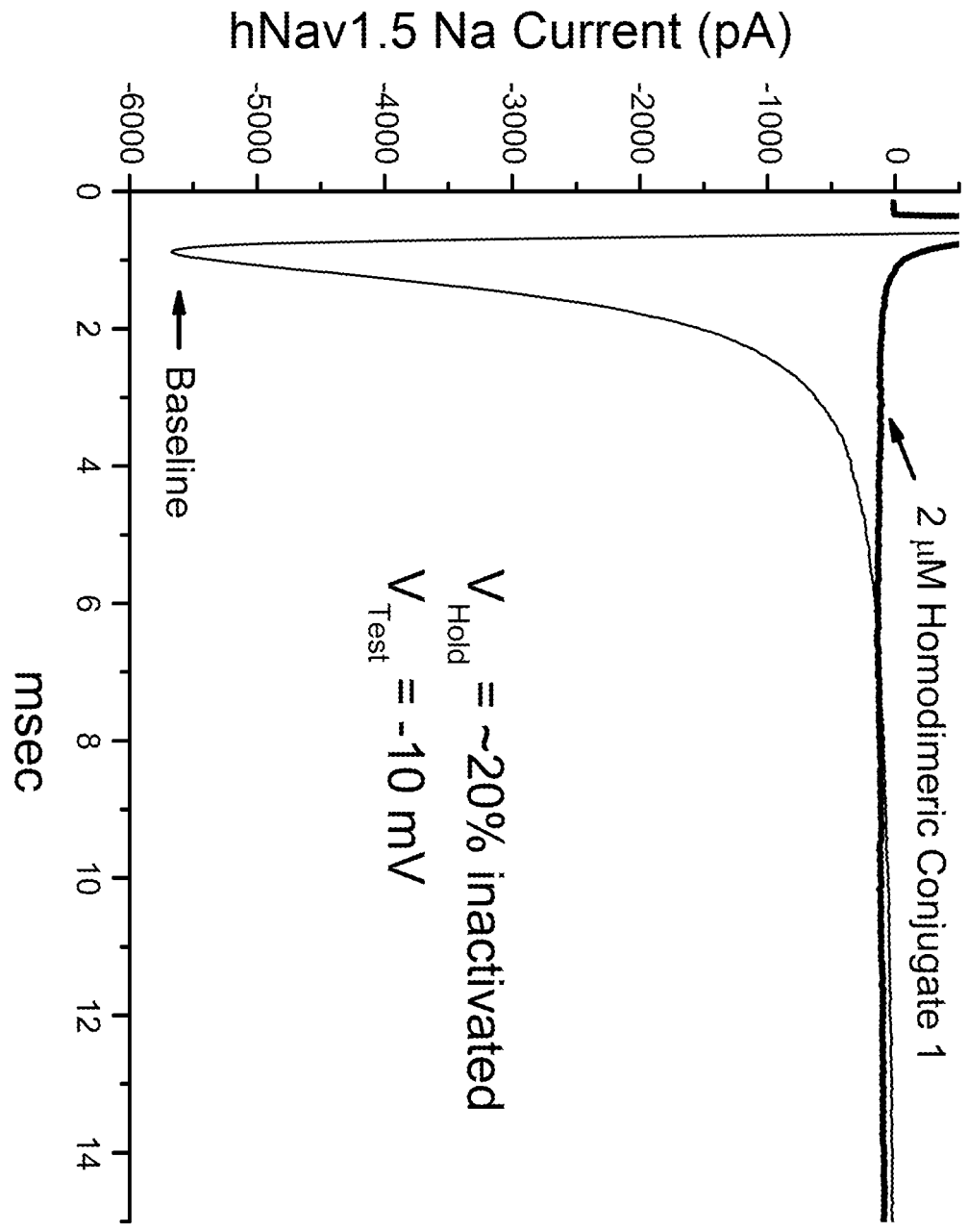

hNav1.5 Na Current (pA)
-6000
-5000
-4000
-3000
-2000
-1000
0
0
2
4
6
8
10
12
14
msec
Baseline
2 μM Homodimeric Conjugate 1
V Hold = ~20% inactivated
V Test = -10 mV

FIG. 58

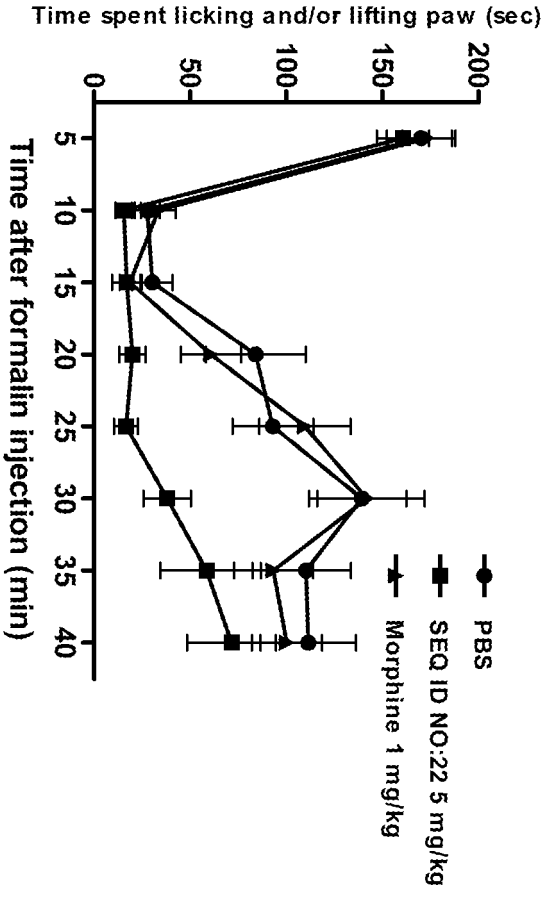

Time spent licking and/or lifting paw (sec)
0
50
100
150
200
Time after formalin injection (min)
5
10
15
20
25
30
35
40
PBS
SEQ ID NO:22 5 mg/kg
Morphine 1 mg/kg

FIG. 59

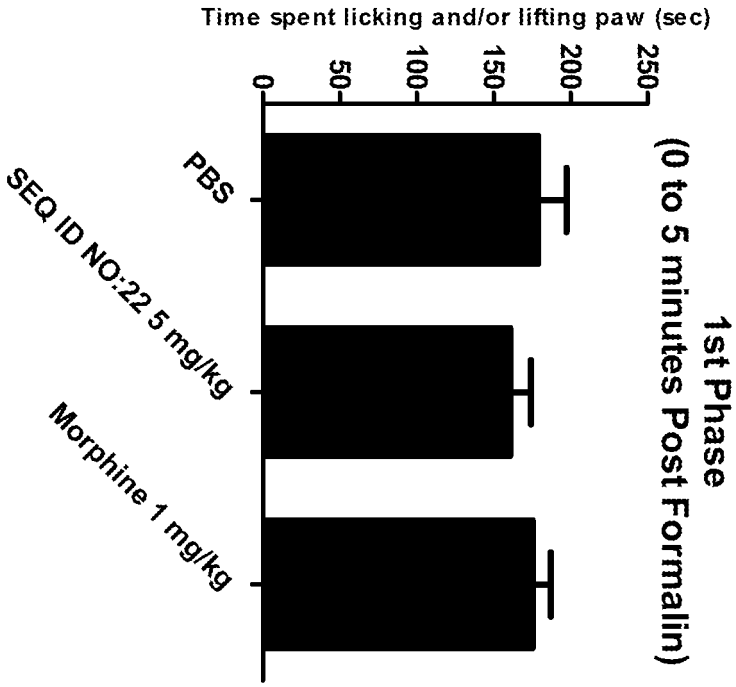

Time spent licking and/or lifting paw (sec)
0
50
100
150
200
250
PBS
SEQ ID NO:22 5 mg/kg
Morphine 1 mg/kg
1st Phase
(0 to 5 minutes Post Formalin)

FIG. 60

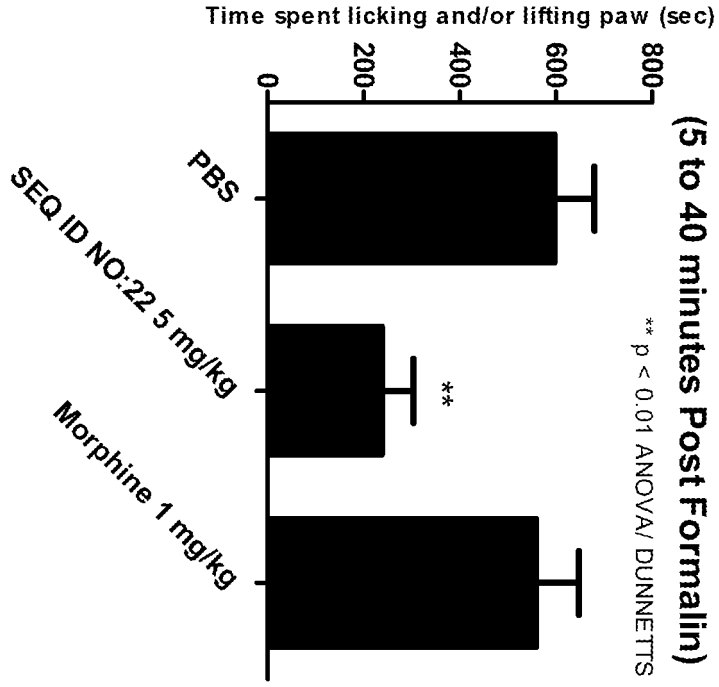

Time spent licking and/or lifting paw (sec)
0
200
400
600
800
PBS
SEQ ID NO:22 5 mg/kg
Morphine 1 mg/kg
**
2nd Phase
(5 to 40 minutes Post Formalin)
** p < 0.01 ANOVA/ DUNNETTS

FIG. 61

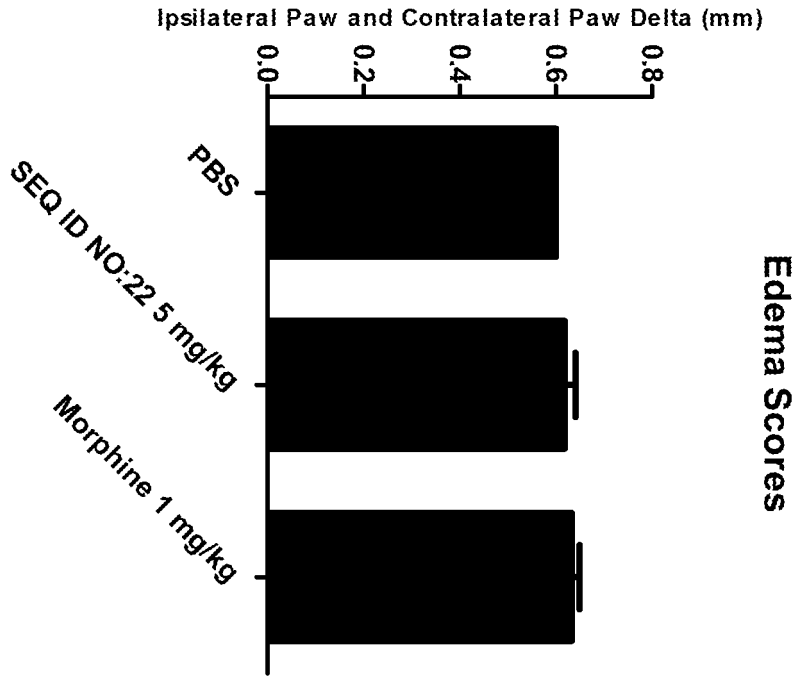

Ipsilateral Paw and Contralateral Paw Delta (mm)
0.0
0.2
0.4
0.6
0.8
PBS
SEQ ID NO:22 5 mg/kg
Morphine 1 mg/kg
Edema Scores

FIG. 62

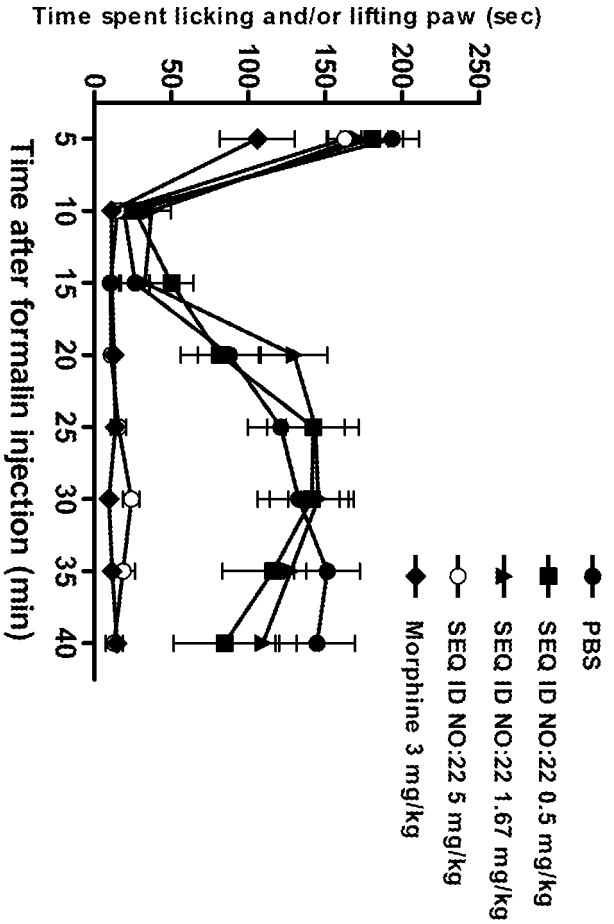

Time spent licking and/or lifting paw (sec)
0
50
100
150
200
250
Time after formalin injection (min)
5
10
15
20
25
30
35
40
PBS
SEQ ID NO:22 0.5 mg/kg
SEQ ID NO:22 1.67 mg/kg
SEQ ID NO:22 5 mg/kg
Morphine 3 mg/kg

FIG. 63

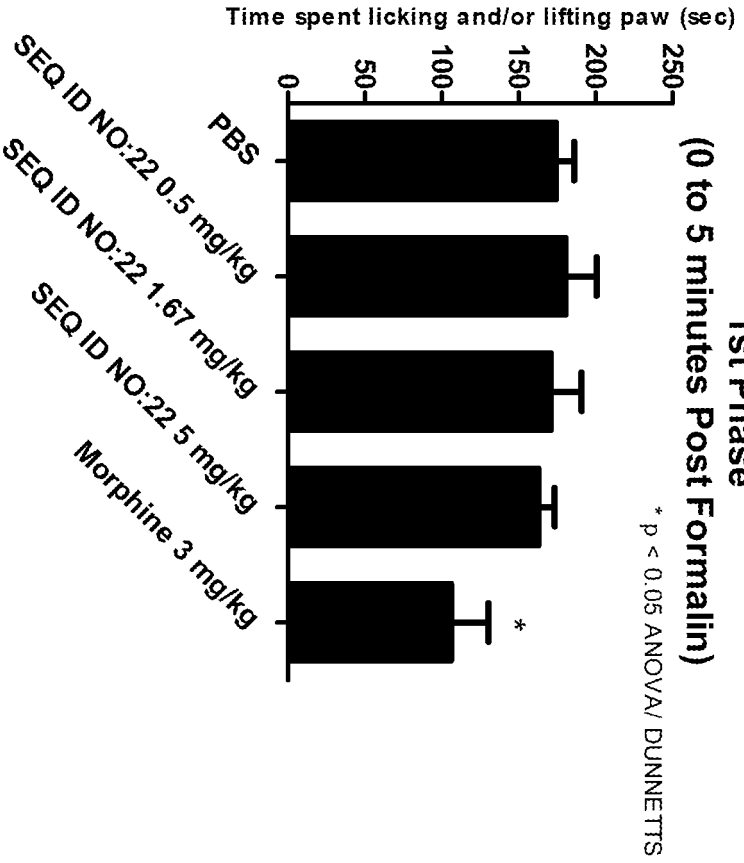

Time spent licking and/or lifting paw (sec)
0
50
100
150
200
250
PBS
SEQ ID NO:22 0.5 mg/kg
SEQ ID NO:22 1.67 mg/kg
SEQ ID NO:22 5 mg/kg
Morphine 3 mg/kg
*
1st Phase
(0 to 5 minutes Post Formalin)
* p < 0.05 ANOVA/ DUNNETTS

FIG. 64

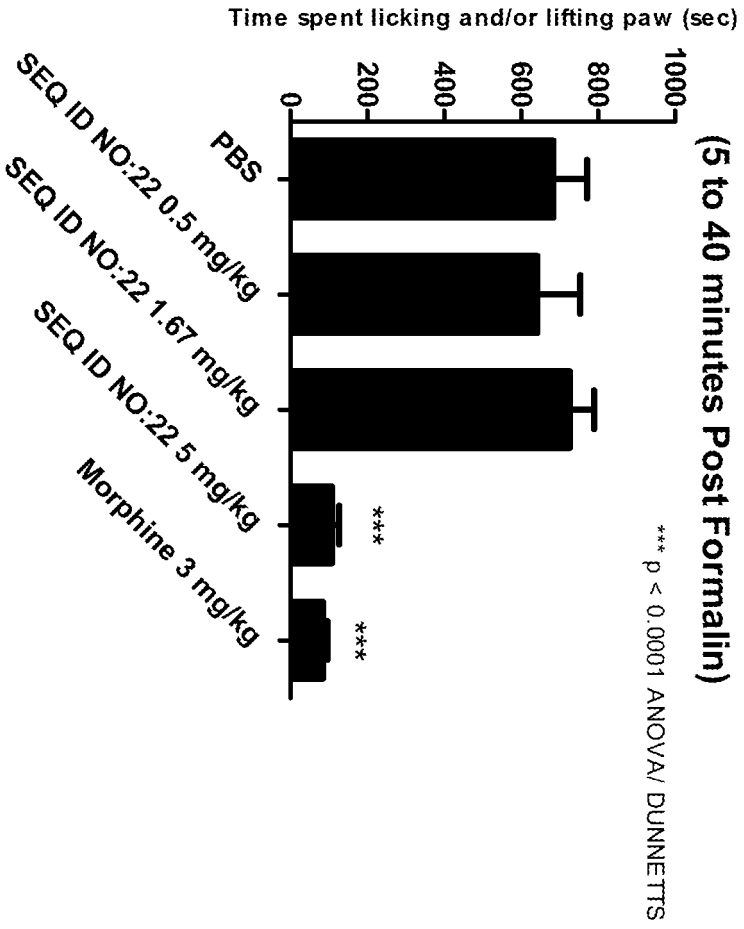

Time spent licking and/or lifting paw (sec)
0
200
400
600
800
1000
PBS
SEQ ID NO:22 0.5 mg/kg
SEQ ID NO:22 1.67 mg/kg
SEQ ID NO:22 5 mg/kg
Morphine 3 mg/kg
***
***
2nd Phase
(5 to 40 minutes Post Formalin)
*** p < 0.0001 ANOVA/ DUNNETTS

FIG. 65

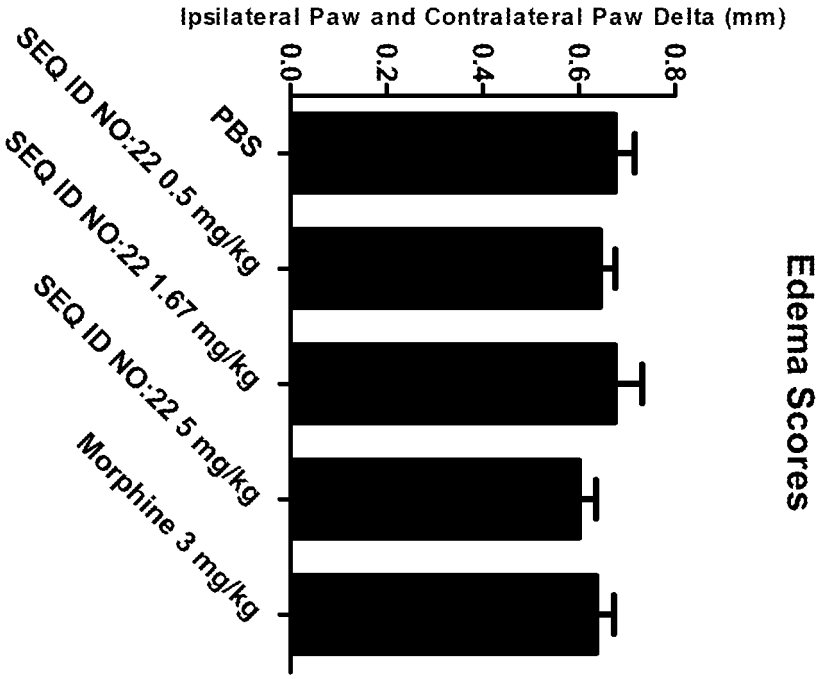

Ipsilateral Paw and Contralateral Paw Delta (mm)
0.0
0.2
0.4
0.6
0.8
PBS
SEQ ID NO:22 0.5 mg/kg
SEQ ID NO:22 1.67 mg/kg
SEQ ID NO:22 5 mg/kg
Morphine 3 mg/kg
Edema Scores

FIG. 66

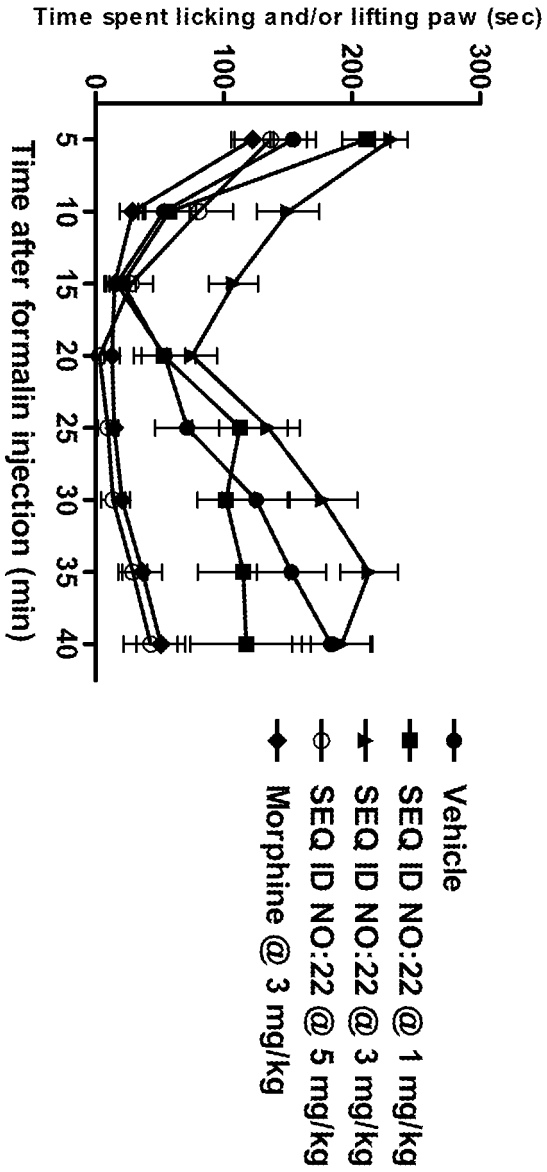

Time spent licking and/or lifting paw (sec)
0
100
200
300
Time after formalin injection (min)
5
10
15
20
25
30
35
40
Vehicle
SEQ ID NO:22 @ 1 mg/kg
SEQ ID NO:22 @ 3 mg/kg
SEQ ID NO:22 @ 5 mg/kg
Morphine @ 3 mg/kg

FIG. 67

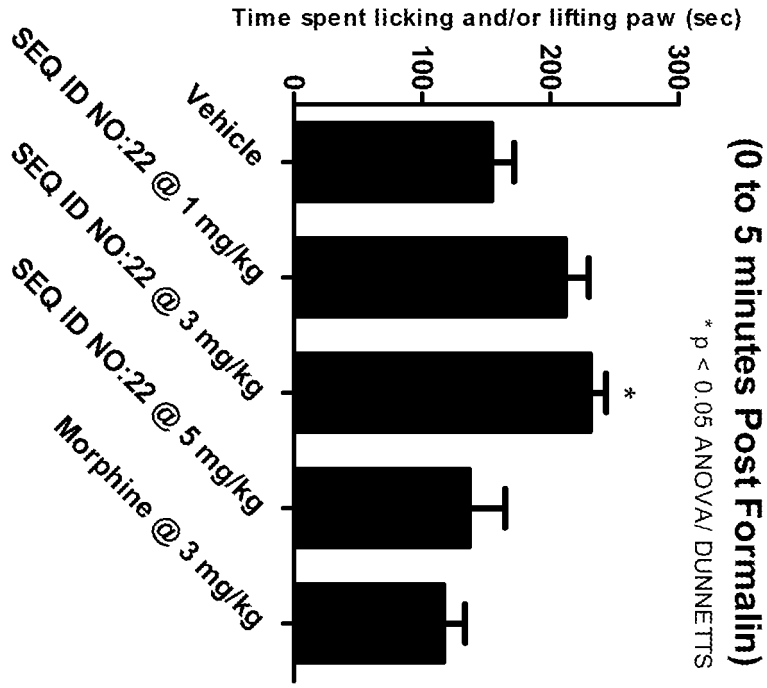

Time spent licking and/or lifting paw (sec)
0
100
200
300
Vehicle
SEQ ID NO:22 @ 1 mg/kg
SEQ ID NO:22 @ 3 mg/kg
SEQ ID NO:22 @ 5 mg/kg
Morphine @ 3 mg/kg
*
1st Phase
(0 to 5 minutes Post Formalin)
* p < 0.05 ANOVA/ DUNNETTS

FIG. 68

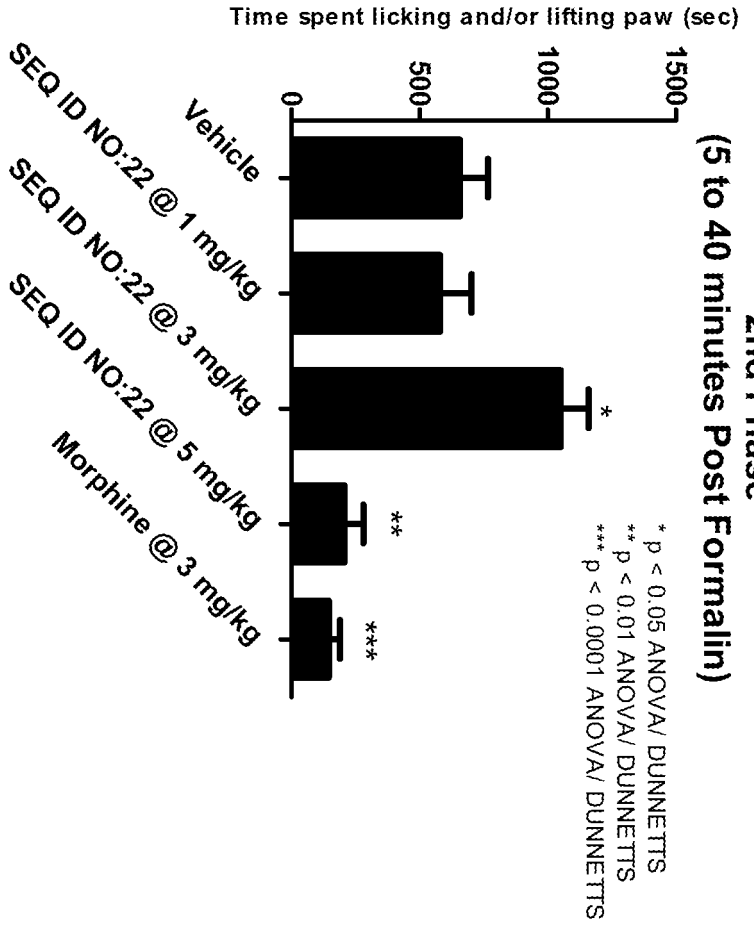

Time spent licking and/or lifting paw (sec)
0
500
1000
1500
2nd Phase
(5 to 40 minutes Post Formalin)
Vehicle
SEQ ID NO:22 @ 1 mg/kg
SEQ ID NO:22 @ 3 mg/kg
SEQ ID NO:22 @ 5 mg/kg
Morphine @ 3 mg/kg
*
**
***
* p < 0.05 ANOVA/ DUNNETTS
** p < 0.01 ANOVA/ DUNNETTS
*** p < 0.0001 ANOVA/ DUNNETTS

FIG. 69

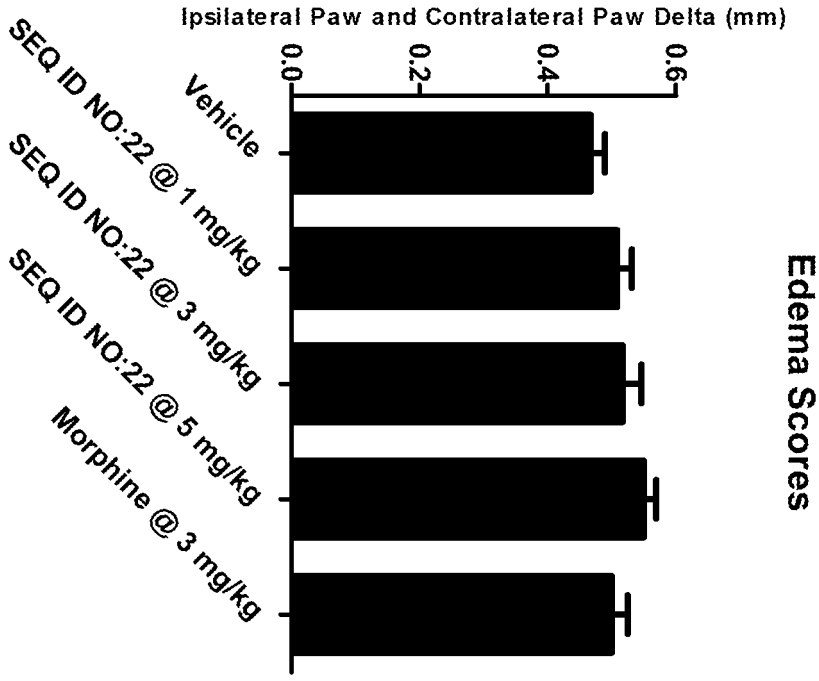

Ipsilateral Paw and Contralateral Paw Delta (mm)
0.0
0.2
0.4
0.6
Vehicle
SEQ ID NO:22 @ 1 mg/kg
SEQ ID NO:22 @ 3 mg/kg
SEQ ID NO:22 @ 5 mg/kg
Morphine @ 3 mg/kg
Edema Scores

FIG. 70

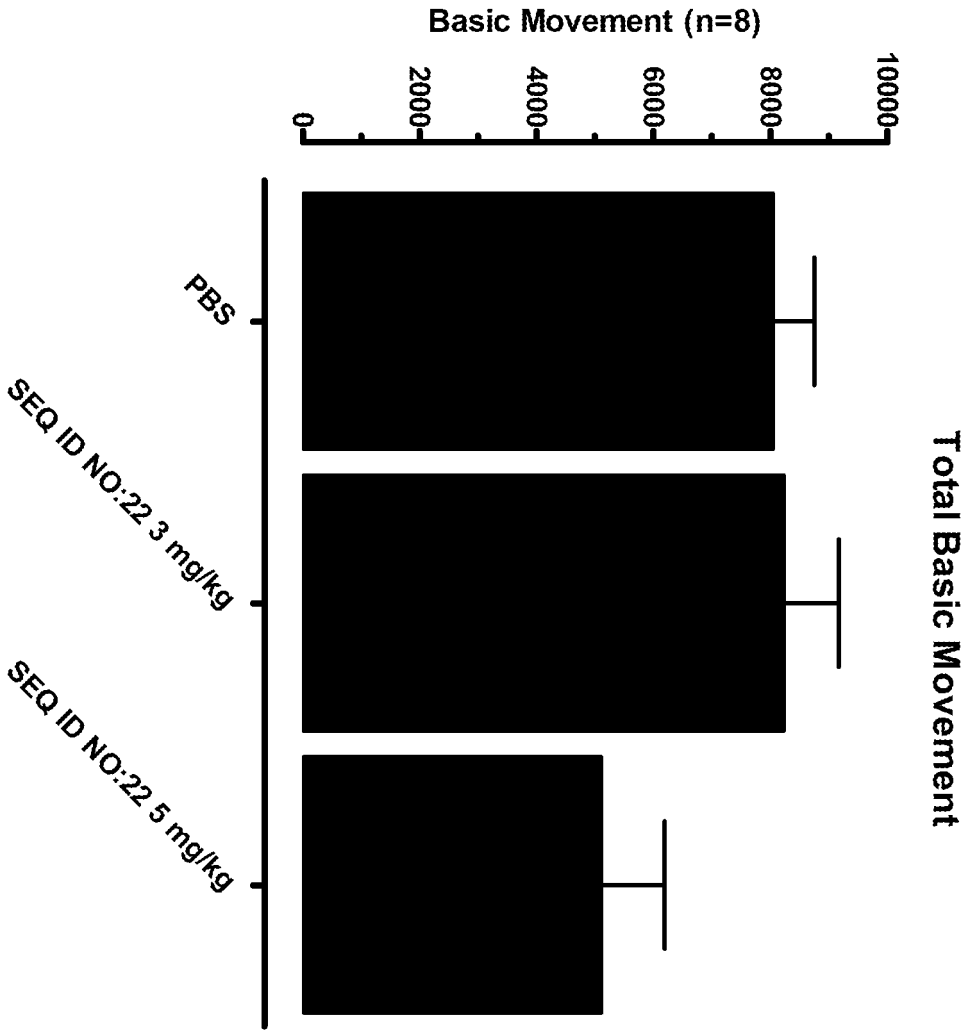

Basic Movement (n=8)
0
2000
4000
6000
8000
10000
PBS
SEQ ID NO:22 3 mg/kg
SEQ ID NO:22 5 mg/kg
Total Basic Movement

FIG. 71

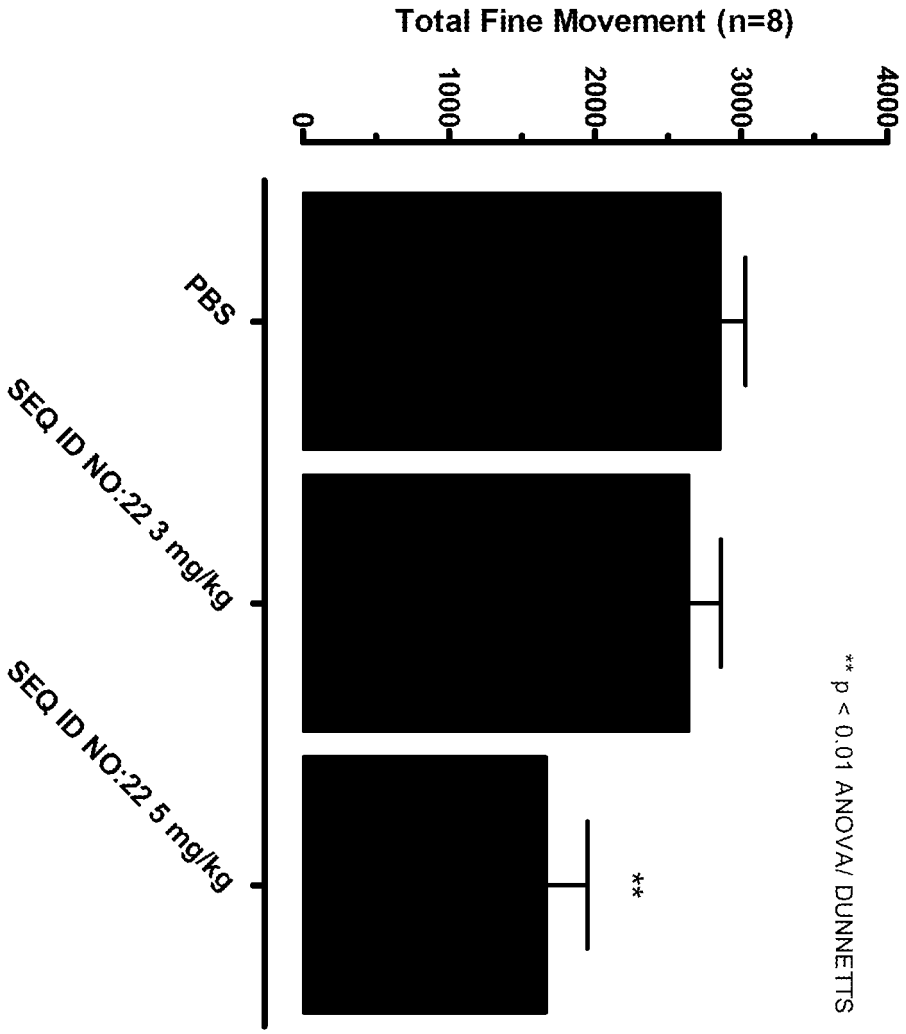

Total Fine Movement (n=8)
0
1000
2000
3000
4000
PBS
SEQ ID NO:22 3 mg/kg
SEQ ID NO:22 5 mg/kg
**
Total Fine Movement
** p < 0.01 ANOVA/ DUNNETTS

FIG. 72

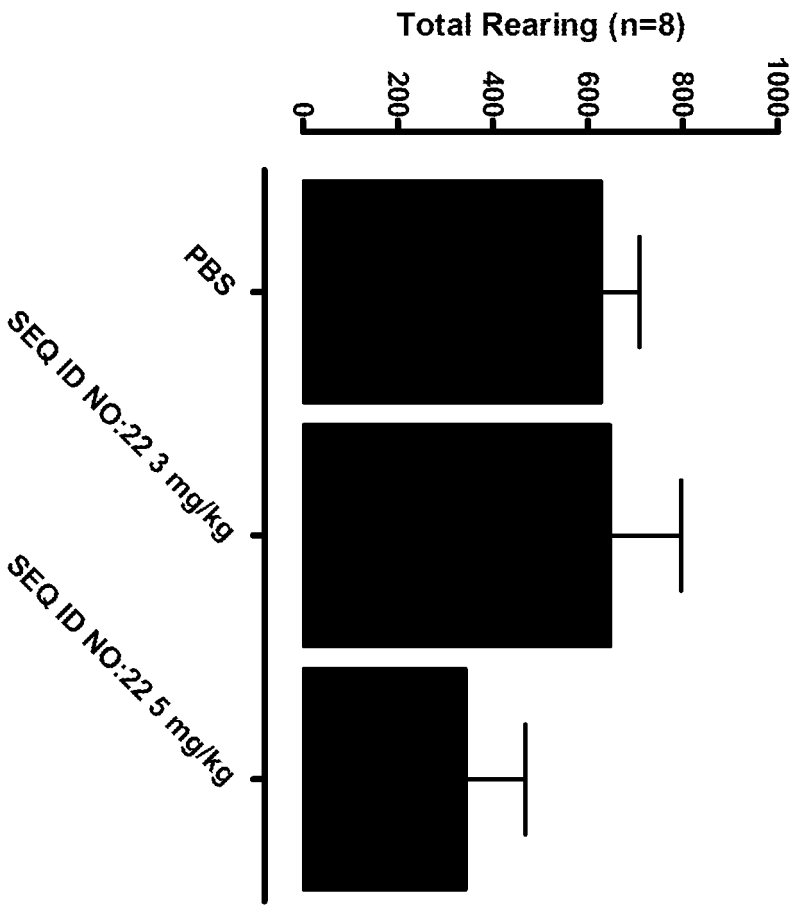

Total Rearing (n=8)
0
200
400
600
800
1000
PBS
SEQ ID NO:22 3 mg/kg
SEQ ID NO:22 5 mg/kg
Total Rearing

FIG. 73

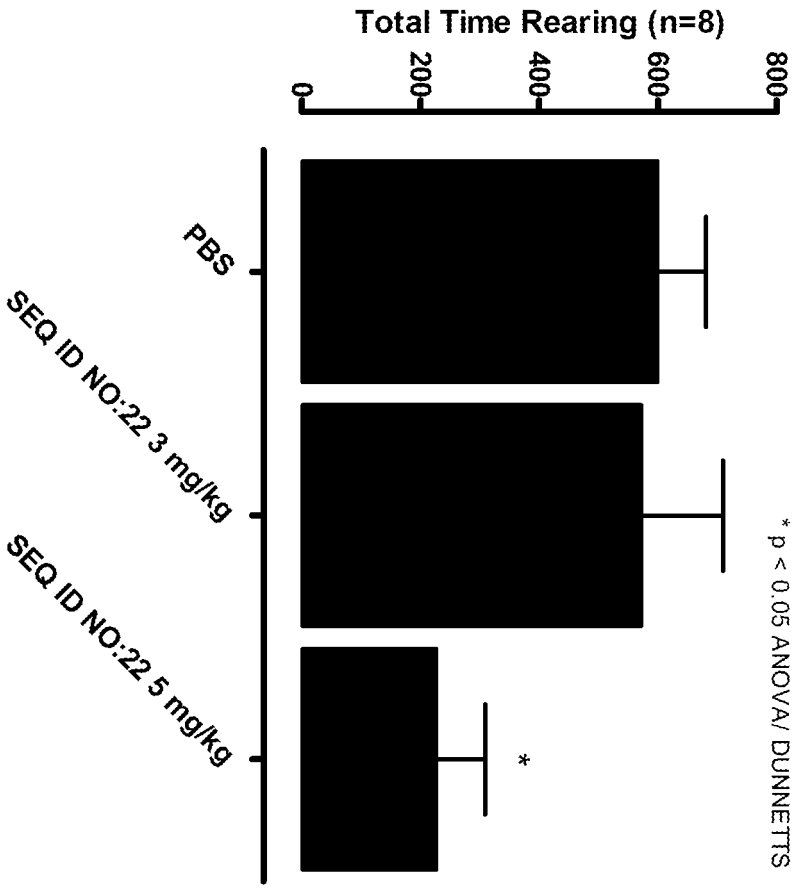

Total Time Rearing (n=8)
0
200
400
600
800
PBS
SEQ ID NO:22 3 mg/kg
SEQ ID NO:22 5 mg/kg
*
Total Time Rearing
* p < 0.05 ANOVA/ DUNNETTS

FIG. 74

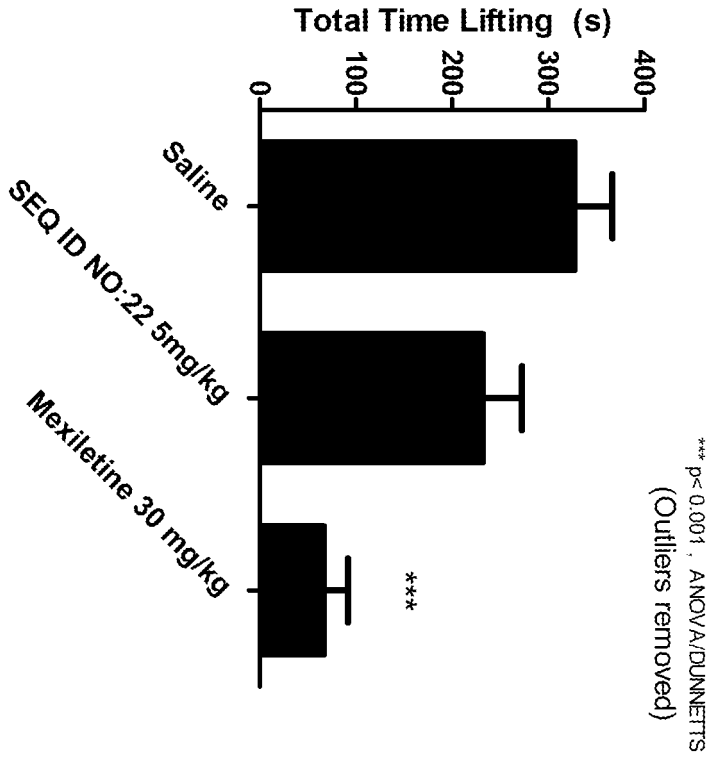

Total Time Lifting (s)
0
100
200
300
400
Saline
SEQ ID NO:22 5mg/kg
Mexiletine 30 mg/kg
***
*** p< 0.001 , ANOVA/DUNNETTS
(Outliers removed)

FIG. 75

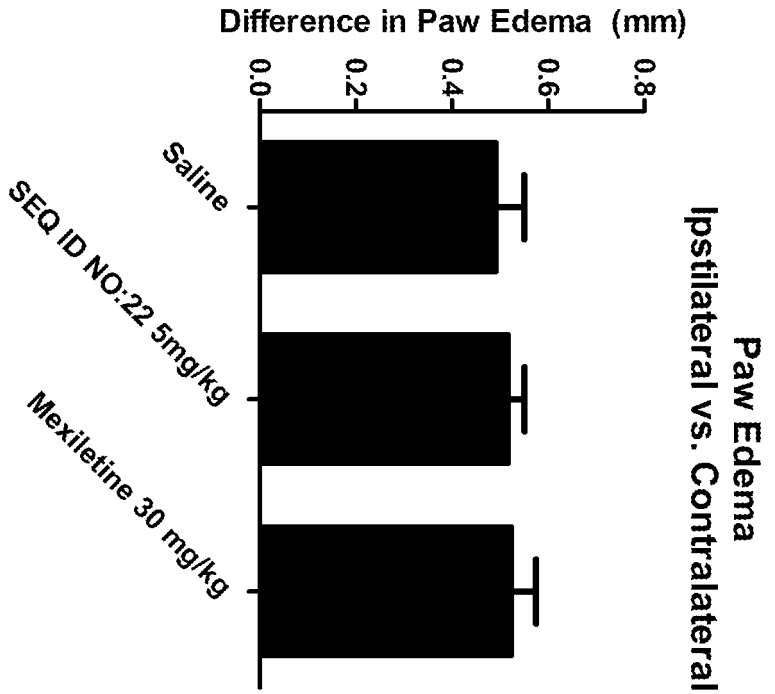

Difference in Paw Edema (mm)
0.0
0.2
0.4
0.6
0.8
Saline
SEQ ID NO:22 5mg/kg
Mexiletine 30 mg/kg
Paw Edema
Ipstilateral vs. Contralateral

FIG. 76

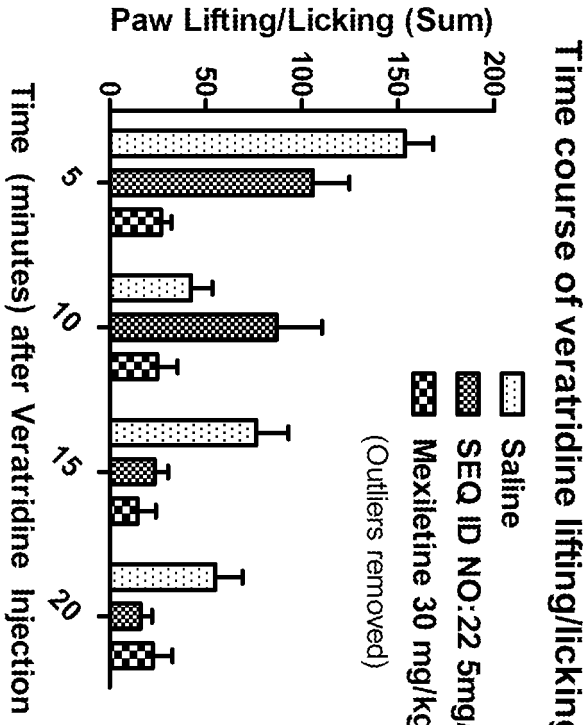

Time course of veratridine lifting/licking
Saline
SEQ ID NO:22 5mg/kg
Mexiletine 30 mg/kg
(Outliers removed)
Paw Lifting/Licking (Sum)
0
50
100
150
200
5
10
15
20
Time (minutes) after Veratridine Injection

FIG. 77

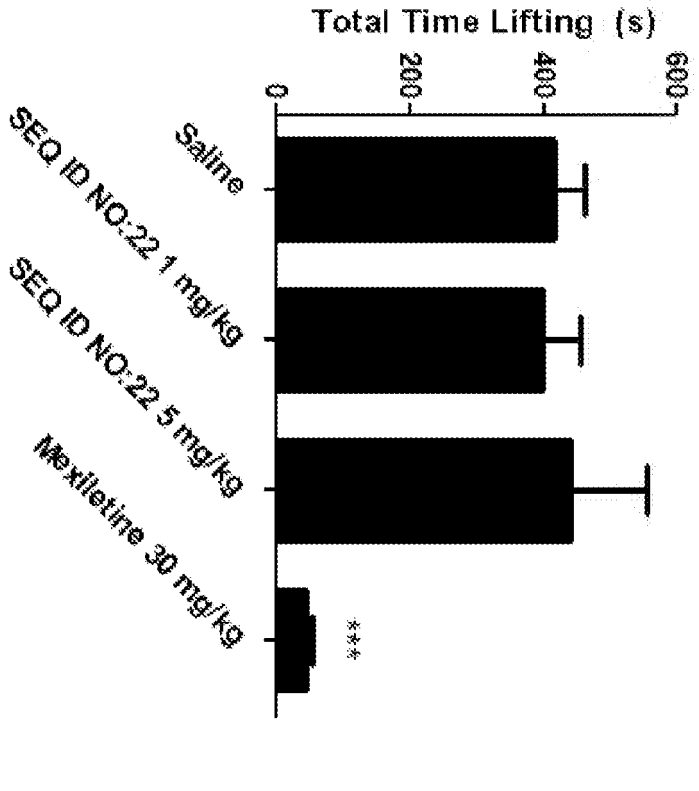

Total Time Lifting (s)
0
200
400
600
Saline
SEQ ID NO:22 1 mg/kg
SEQ ID NO:22 5 mg/kg
Mexiletine 30 mg/kg
***
*** p< 0.001, ANOVA/DUNNETTS

FIG. 78

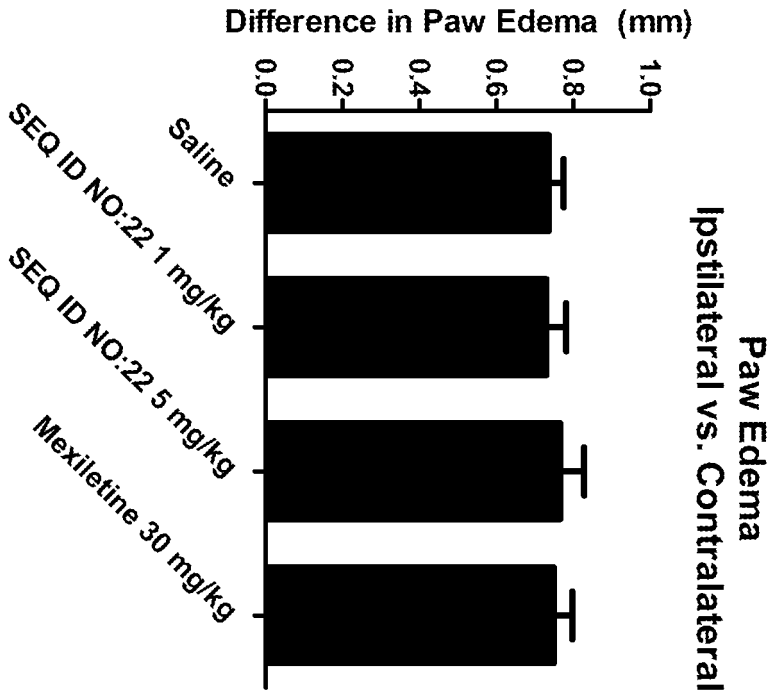

Paw Edema
Ipstilateral vs. Contralateral
Difference in Paw Edema (mm)
0.0
0.2
0.4
0.6
0.8
1.0
Saline
SEQ ID NO:22 1 mg/kg
SEQ ID NO:22 5 mg/kg
Mexiletine 30 mg/kg

FIG. 79

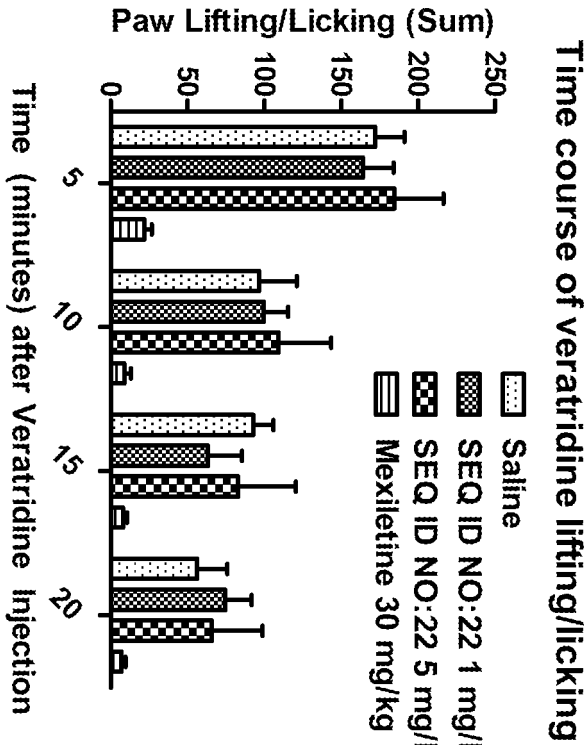

Time course of veratridine lifting/licking
Paw Lifting/Licking (Sum)
0
50
100
150
200
250
5
10
15
20
Time (minutes) after Veratridine Injection
Saline
SEQ ID NO:22 1 mg/kg
SEQ ID NO:22 5 mg/kg
Mexiletine 30 mg/kg

FIG. 80

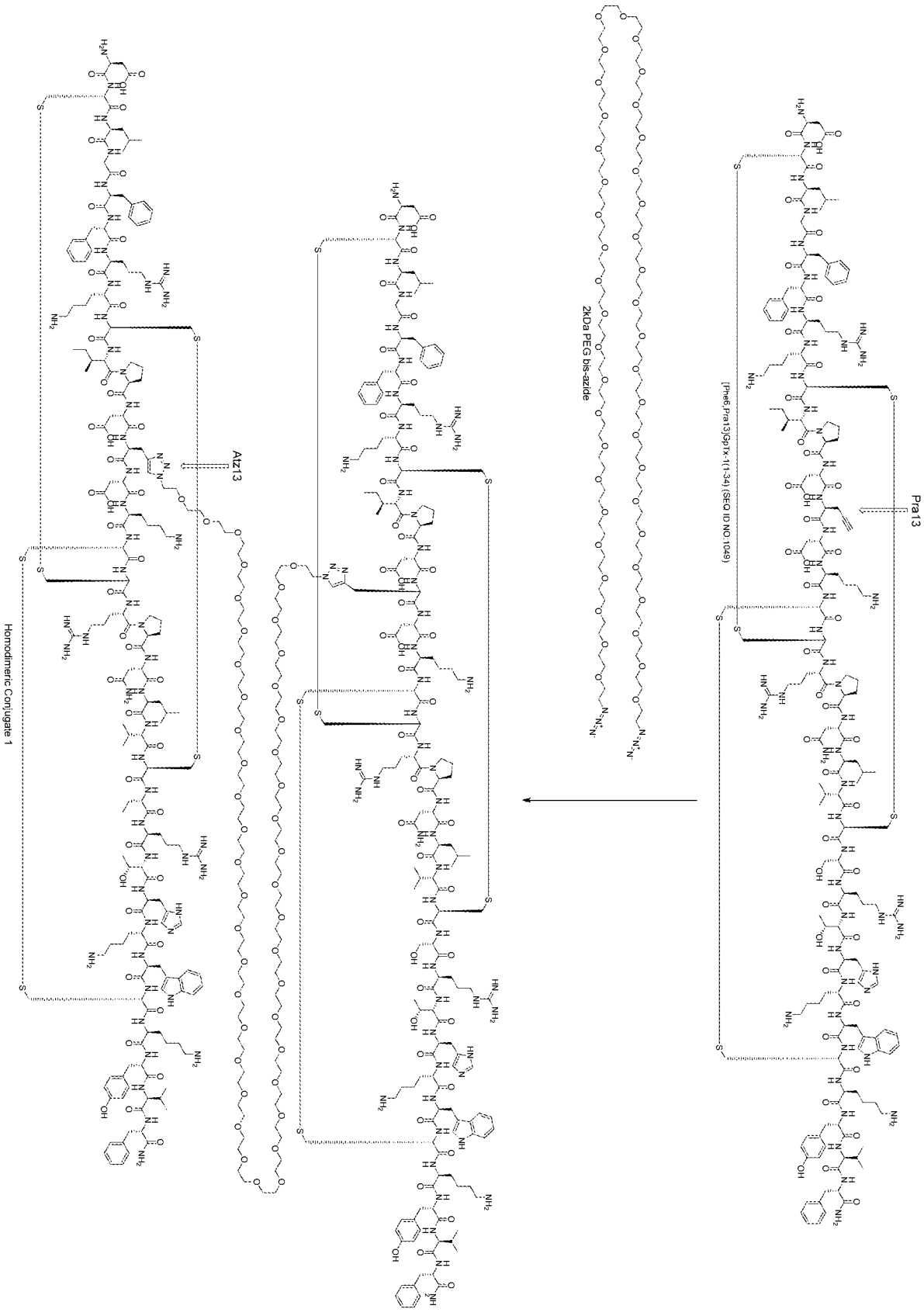

[Phe6,Pra13]GpTx-1(1-34) (SEQ ID NO:1049)
Pra13
2kDa PEG bis-azide
Aiz13
Homodimeric Conjugate 1

FIG. 81A

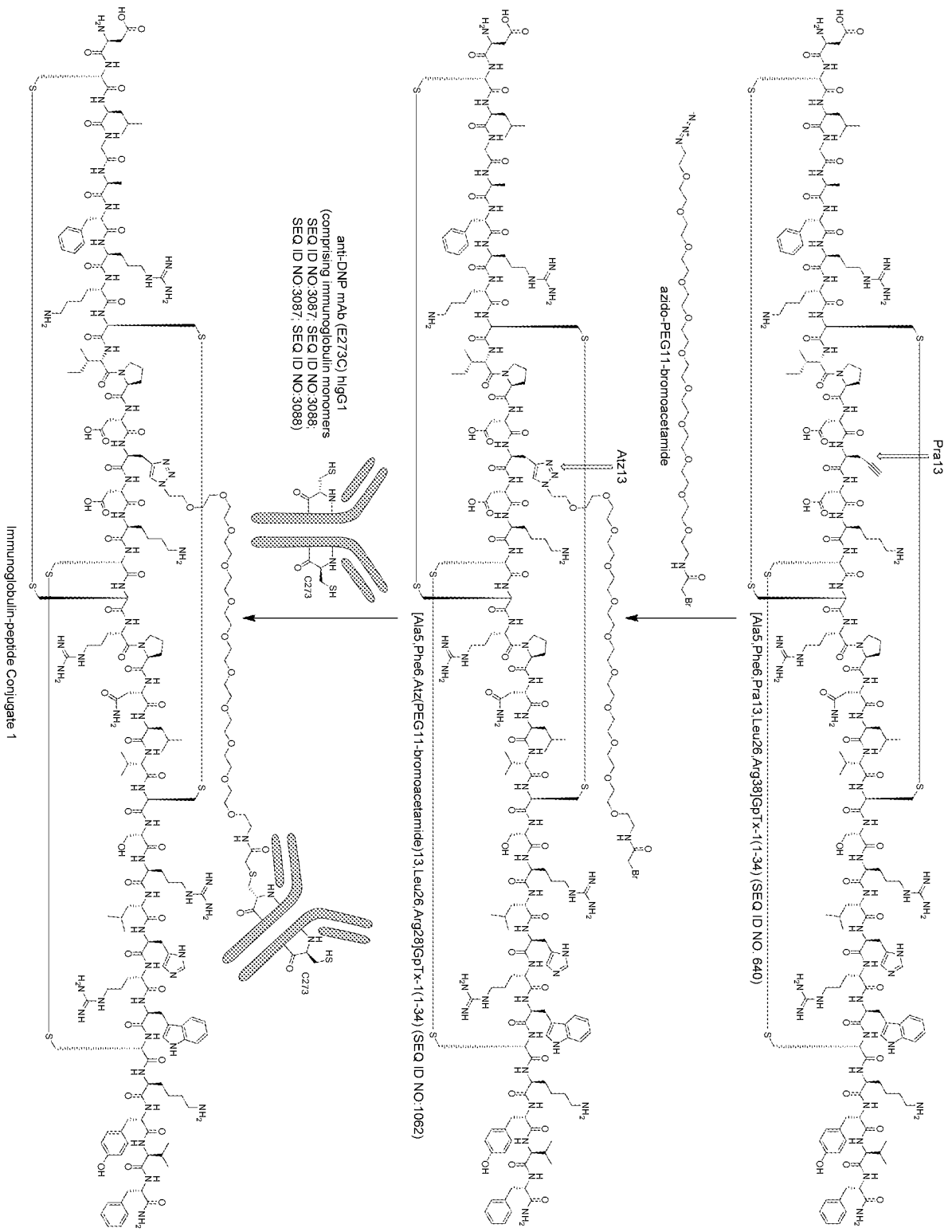

Pra13
[Ala5,Phe6,Pra13,Leu26,Arg38]GpTx-1(1-34) (SEQ ID NO: 640)
azido-PEG11-bromoacetamide
Atz13
[Ala5,Phe6,Atz(PEG11-bromoacetamide)13,Leu26,Arg28]GpTx-1(1-34) (SEQ ID NO:1062)
anti-DNP mAb (E273C) hIgG1
(comprising immunoglobulin monomers
SEQ ID NO:3087; SEQ ID NO:3088;
SEQ ID NO:3087; SEQ ID NO:3088)
C273
C273
Immunoglobulin-peptide Conjugate 1

FIG. 81B

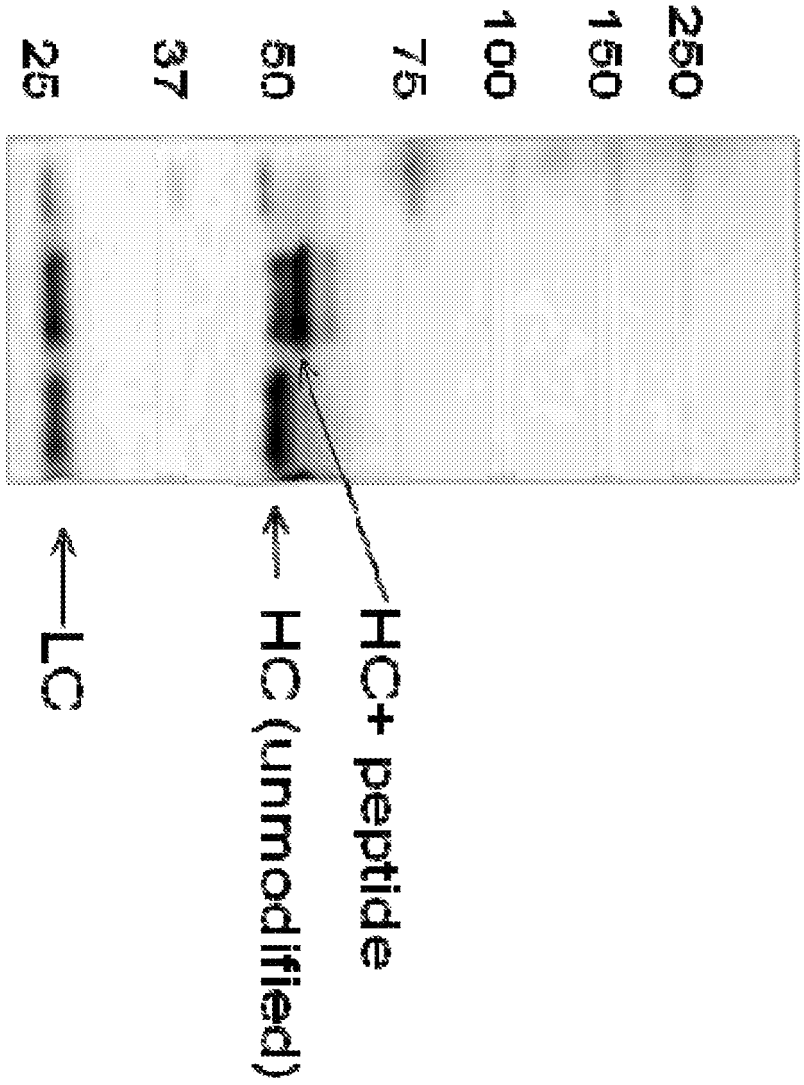

250
150
100
75
50
37
25
+ peptide
No peptide
HC+ peptide
HC (unmodified)
LC

FIG. 82

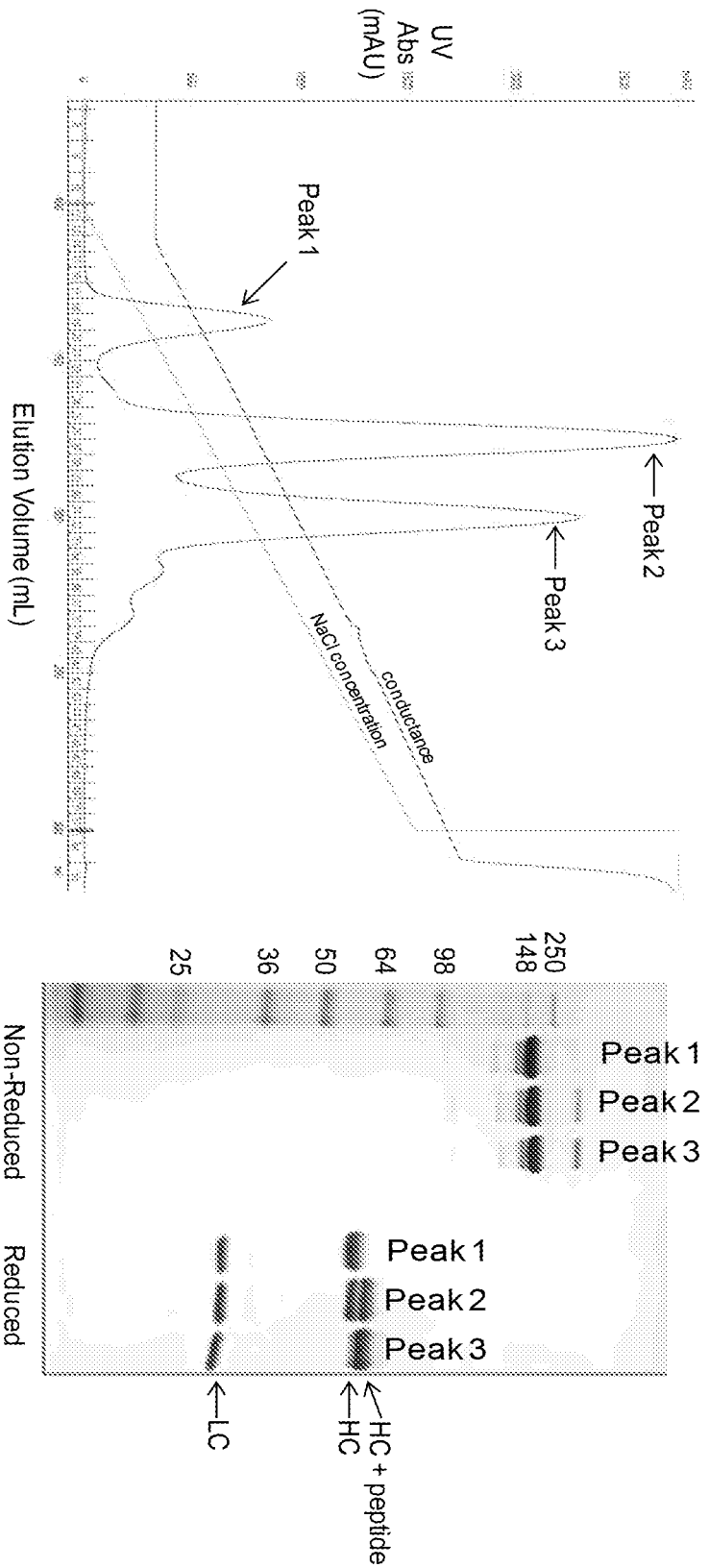

UV Abs (mAU)
Peak 1
Peak 2
Peak 3
Elution Volume (mL)
NaCl concentration
conductance
250
148
98
64
50
36
25
Non-Reduced
Peak 1
Peak 2
Peak 3
Reduced
Peak 1
Peak 2
Peak 3
LC
HC
HC + peptide

FIG. 83

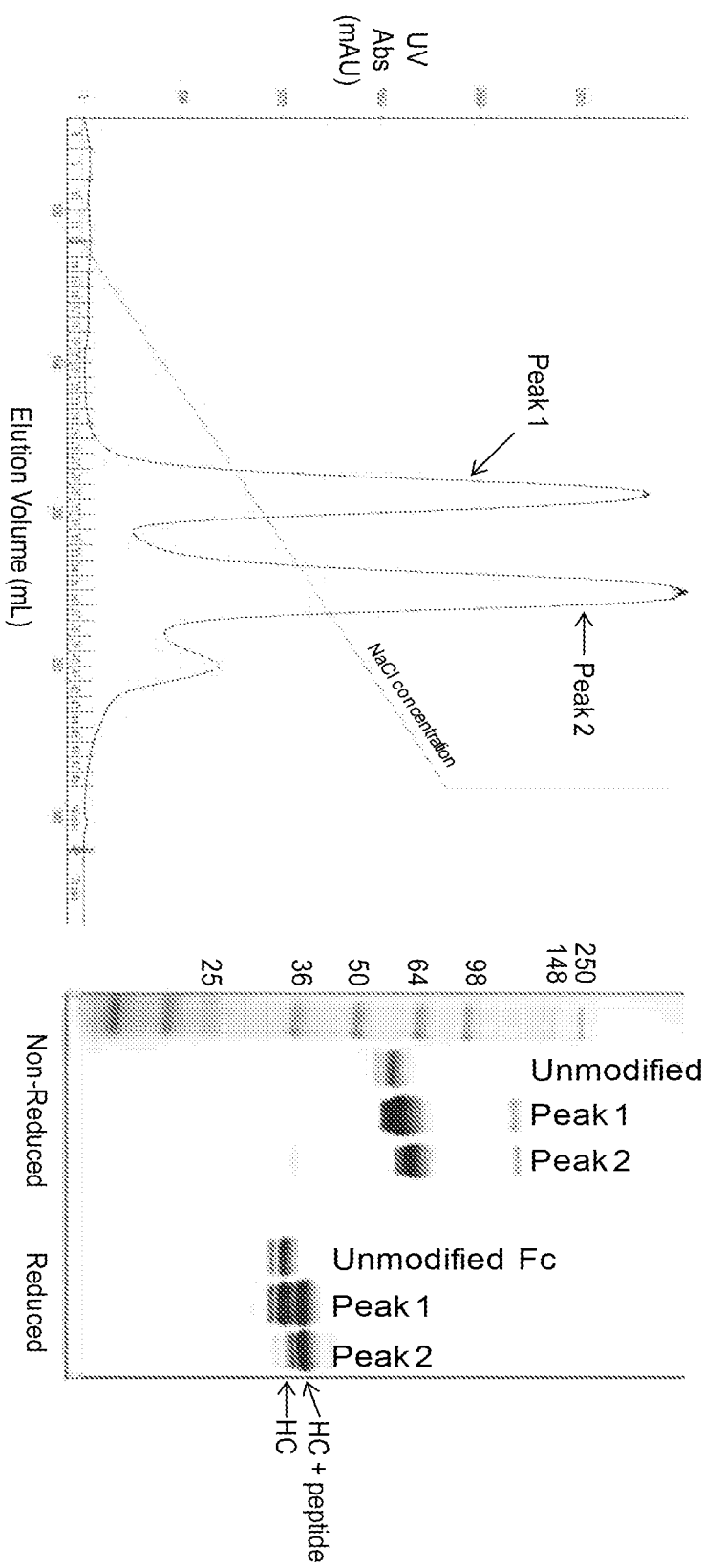

UV Abs (mAU)
Elution Volume (mL)
Peak 1
Peak 2
NaCl concentration
25
36
50
64
98
148
250
Non-Reduced
Unmodified Fc
Peak 1
Peak 2
Reduced
Unmodified Fc
Peak 1
Peak 2
HC
HC + peptide

FIG. 84

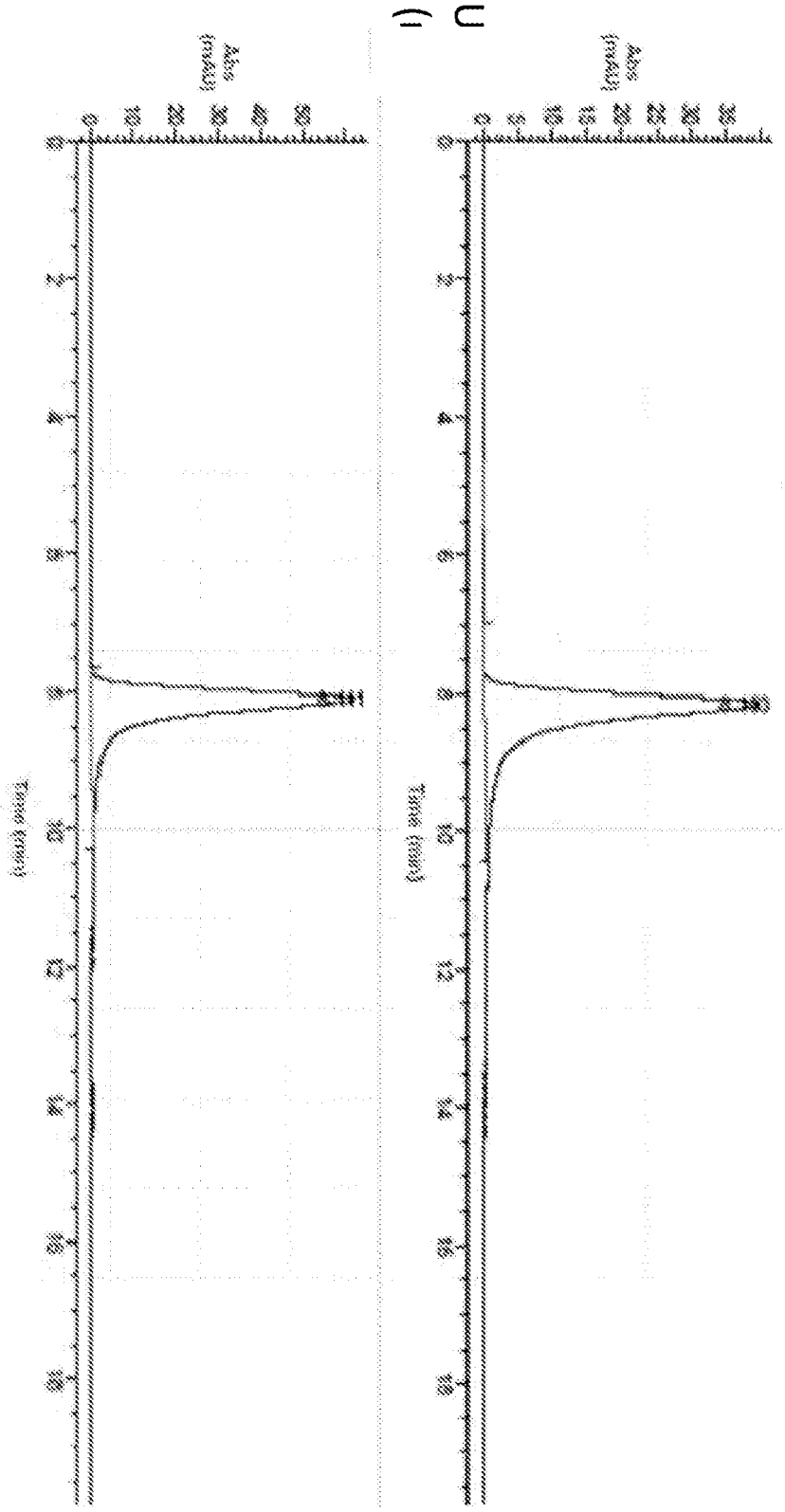


FIG. 85

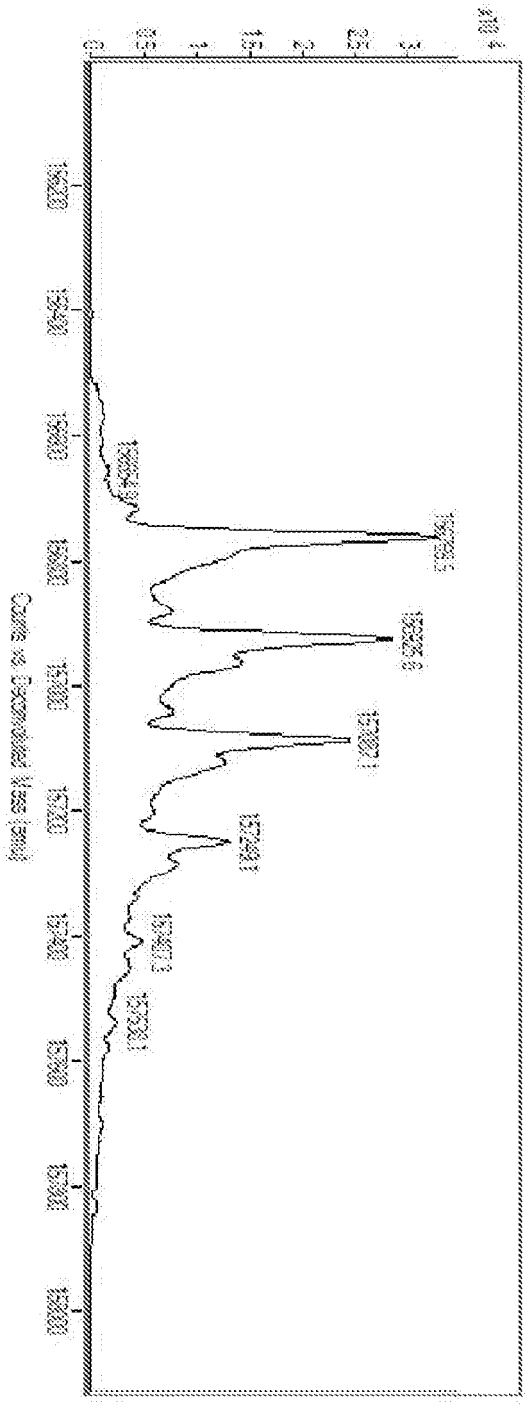

Counts vs. Deconvoluted Mass (Da)
1600
1550
1500
1450
1400
1350
1300
1250
1200
1150
1100
1050
1000
950
900
850
800
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
0.00
0.50
1.00
1.50
2.00
2.50
3.00
x10^4

FIG. 86

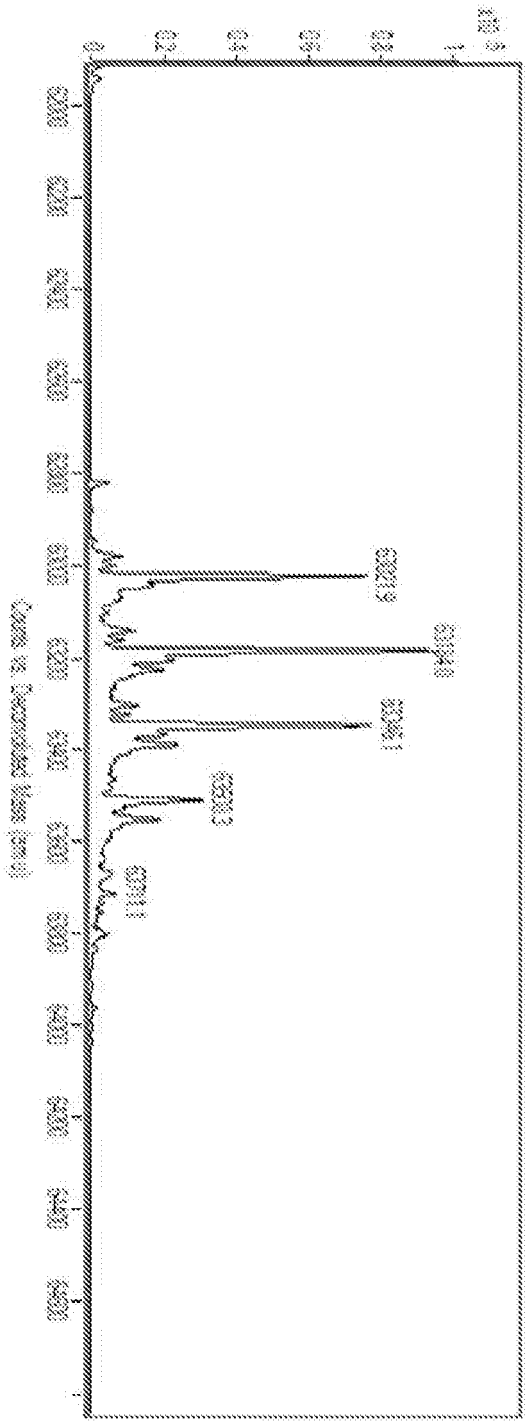


FIG. 87

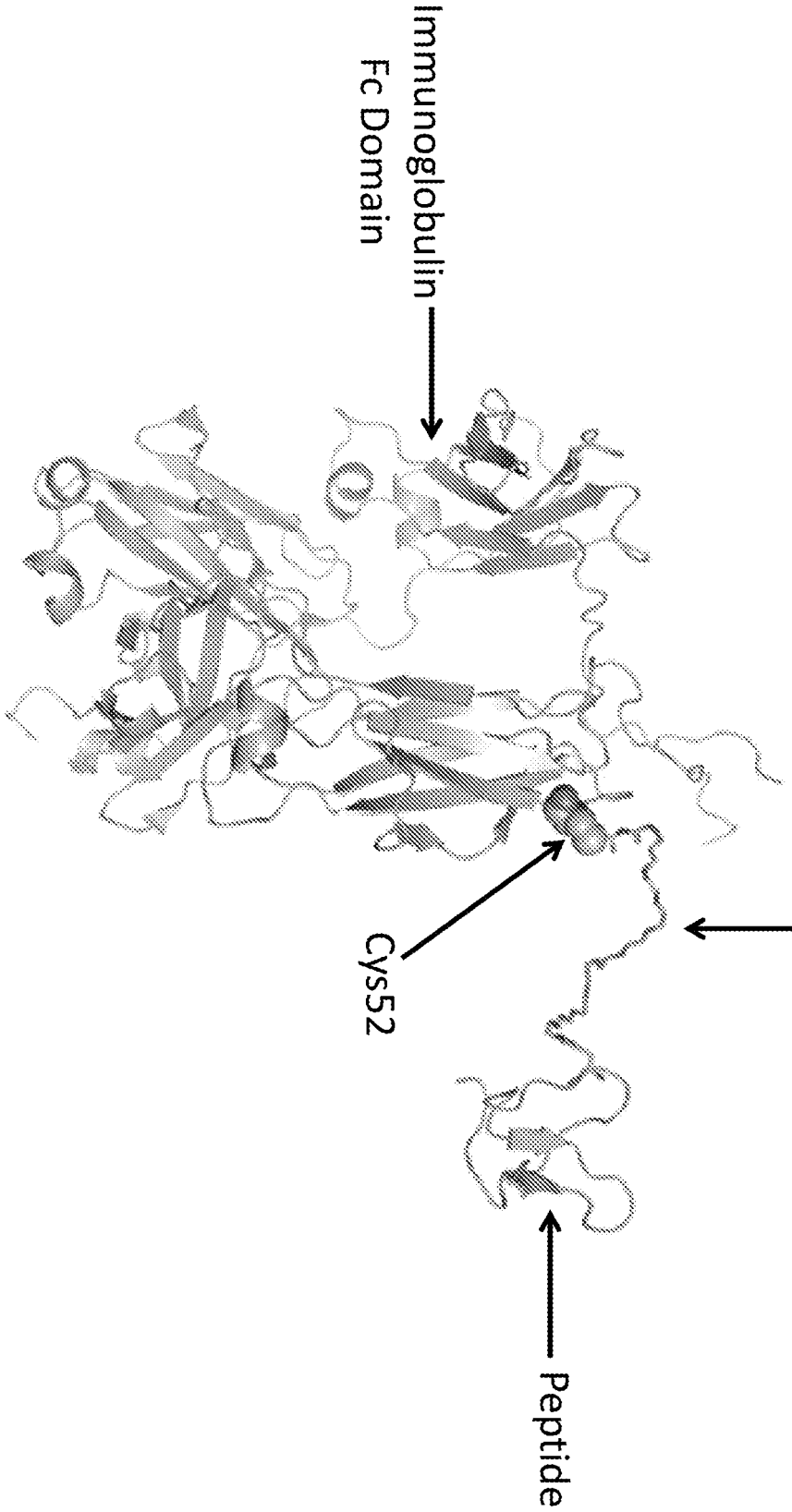


FIG. 88

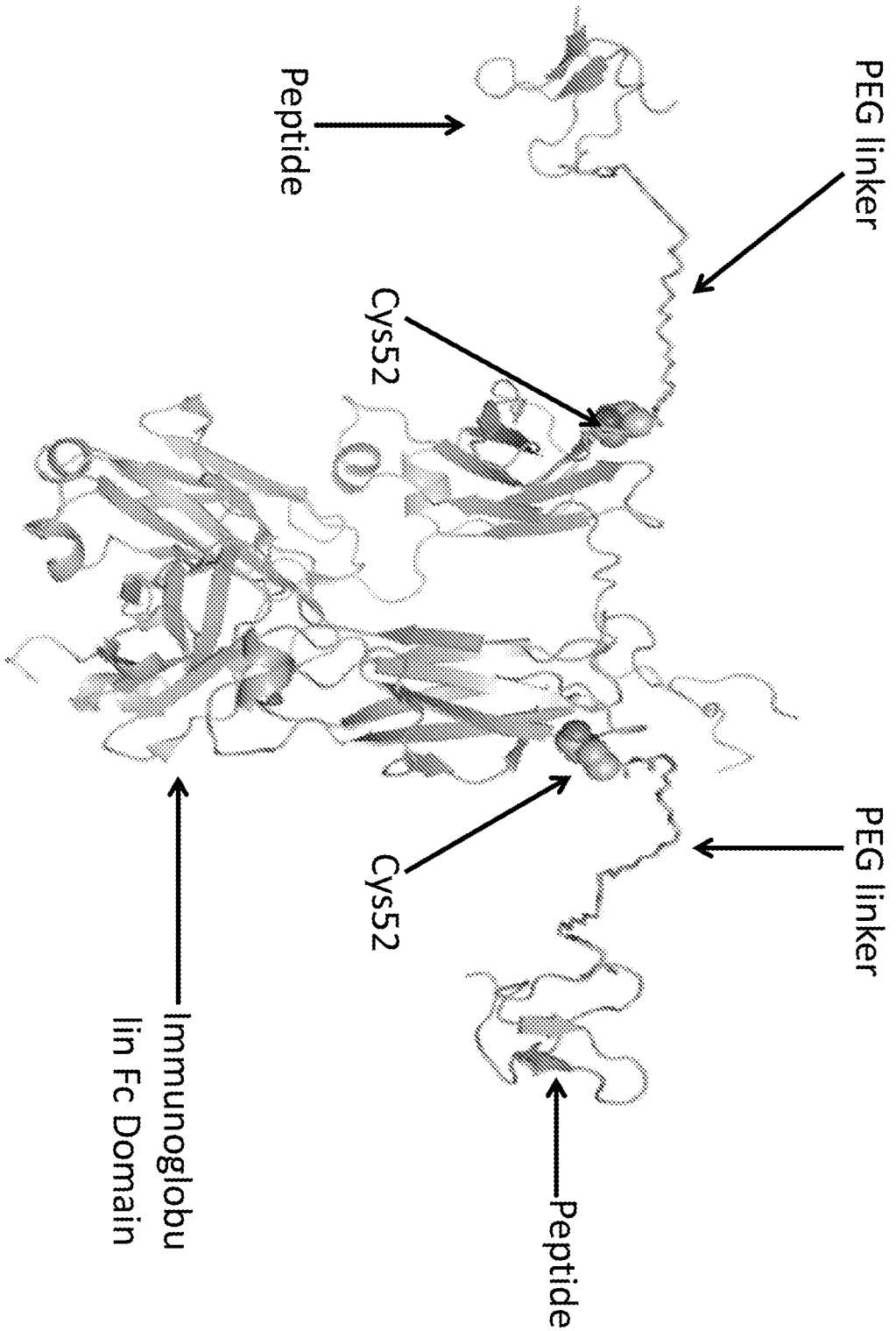

Peptide
PEG linker
Cys52
Cys52
PEG linker
Immunoglobu
lin Fc Domain
Peptide

FIG. 89

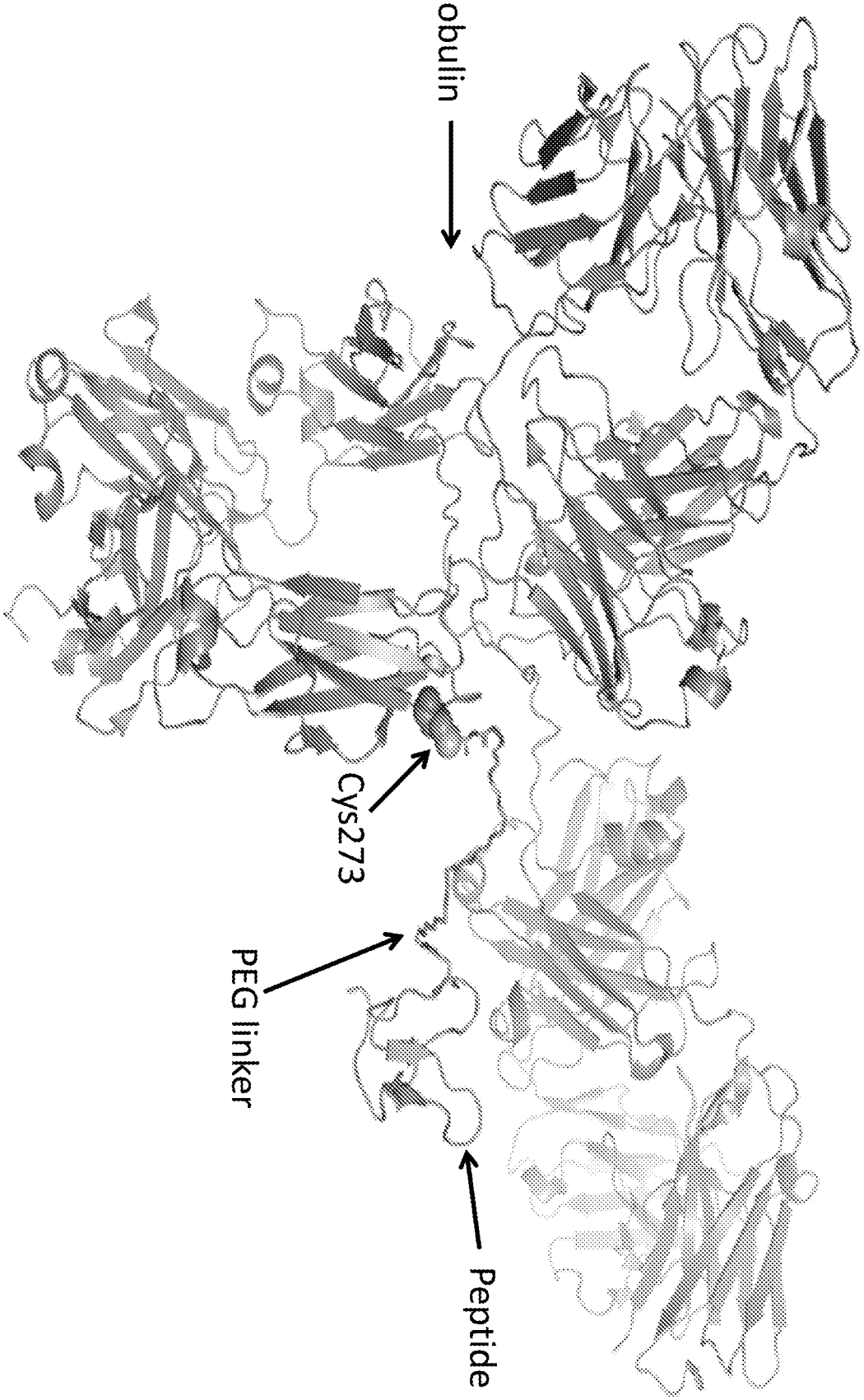


FIG. 90

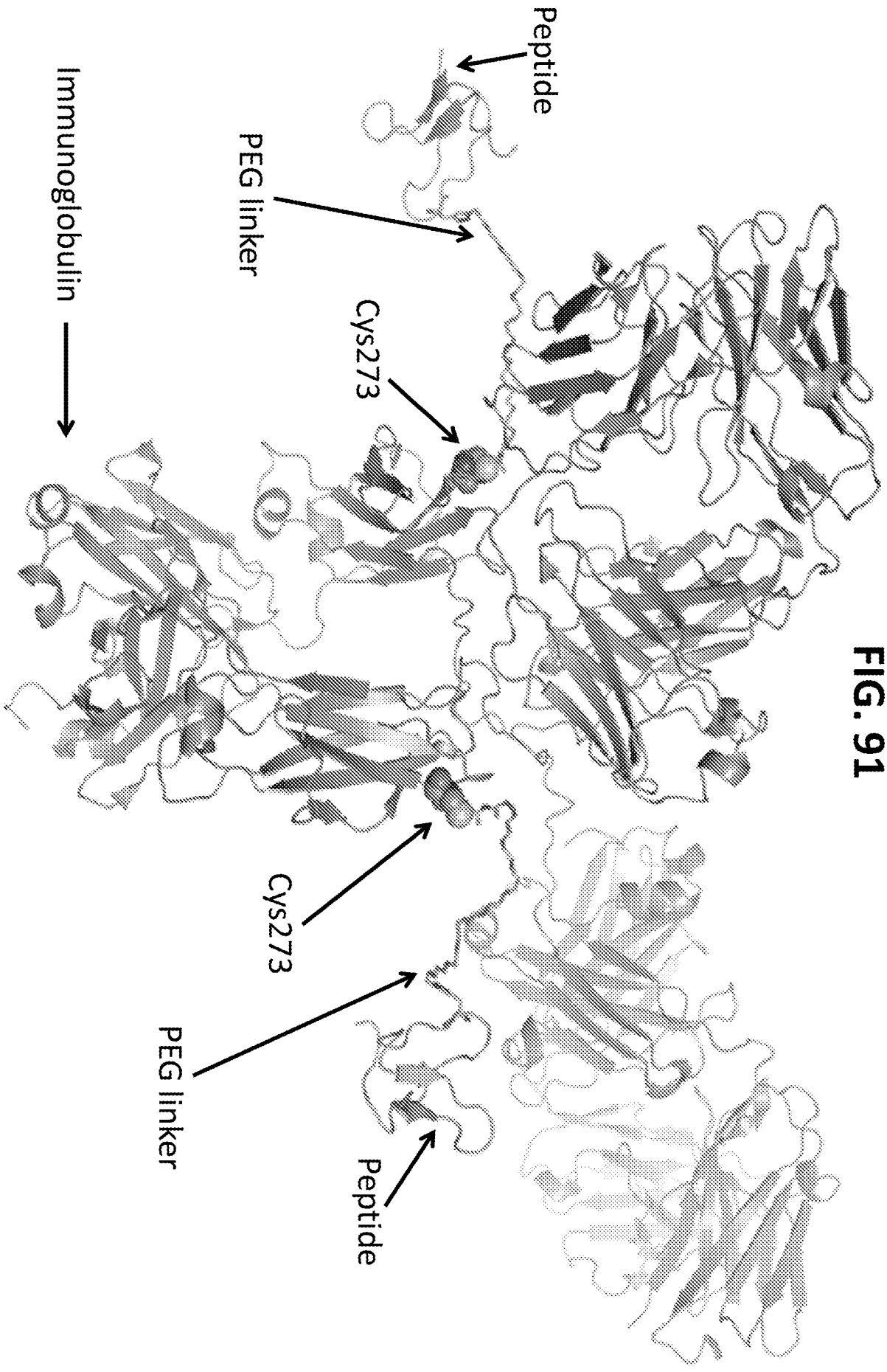

Peptide
PEG linker
Immunoglobulin
Cys273
Cys273
PEG linker
Peptide

FIG. 91

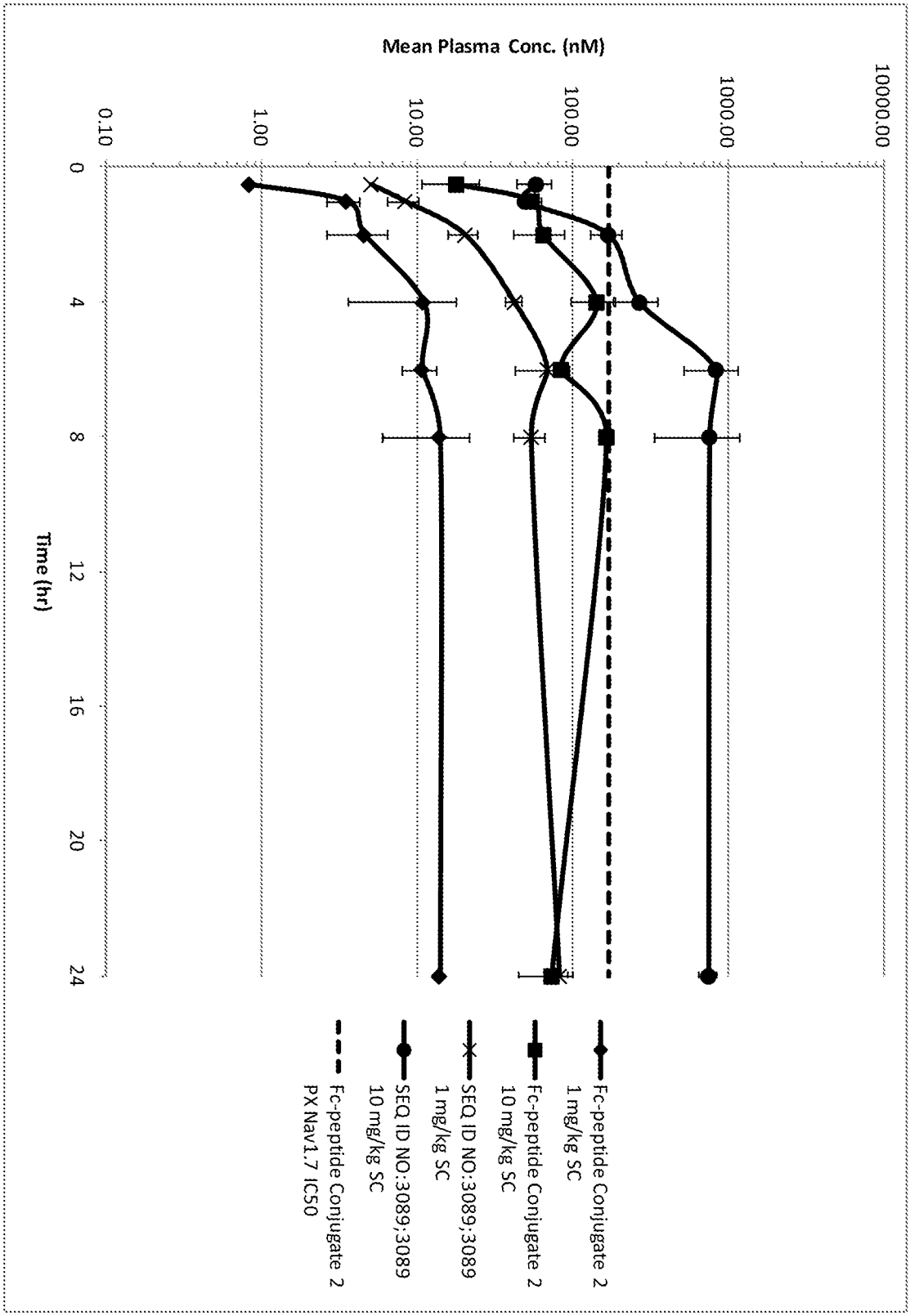

Mean Plasma Conc. (nM)
10000.00
1000.00
100.00
10.00
1.00
0.10
0
4
8
12
16
20
24
Time (hr)
Fc-peptide Conjugate 2 1 mg/kg SC
Fc-peptide Conjugate 2 10 mg/kg SC
SEQ ID NO:3089;3089 1 mg/kg SC
SEQ ID NO:3089;3089 10 mg/kg SC
Fc-peptide Conjugate 2 PX Nav1.7 IC50

FIG. 92

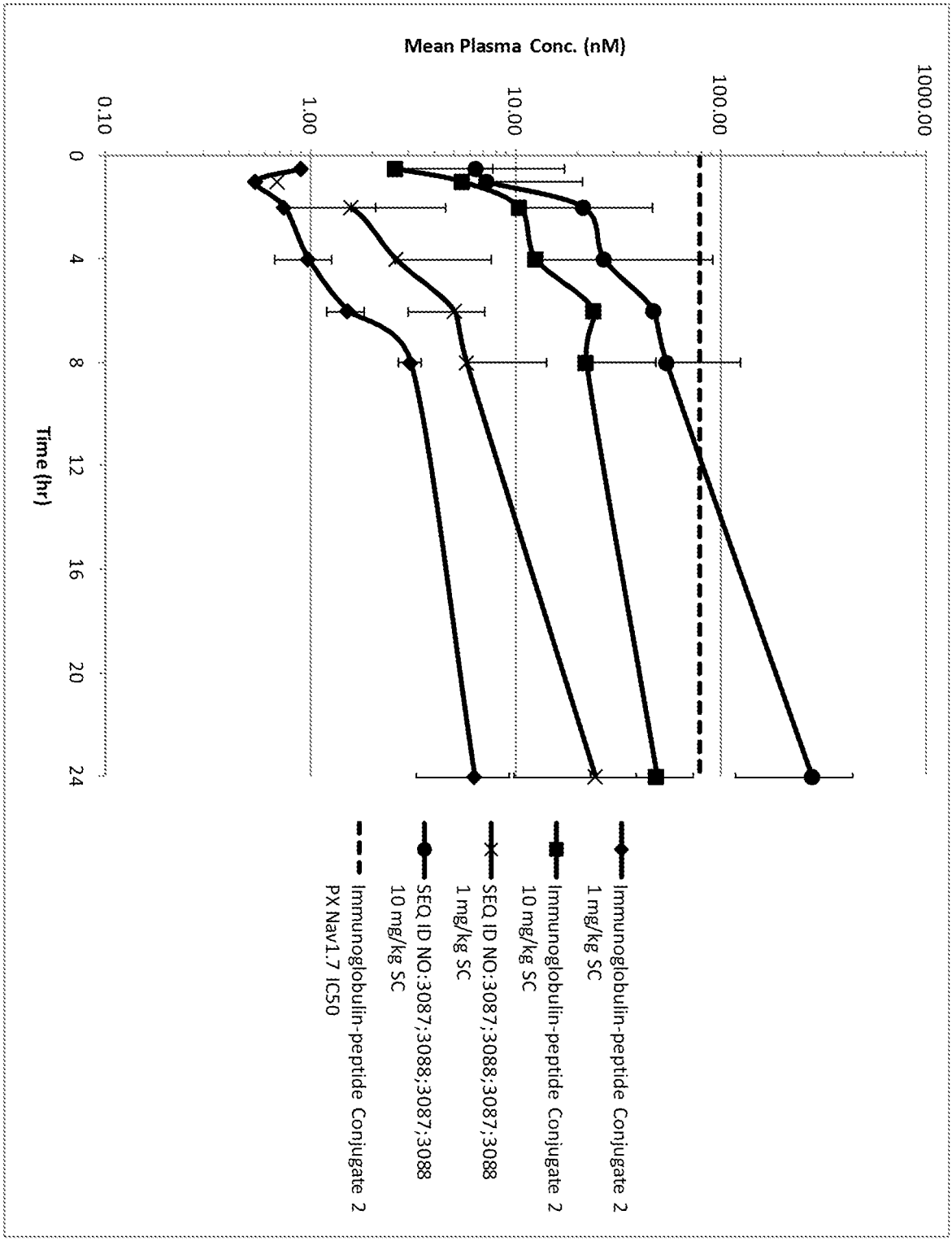

Mean Plasma Conc. (nM)
1000.00
100.00
10.00
1.00
0.10
0
4
8
12
16
20
24
Time (hr)
Immunoglobulin-peptide Conjugate 2 1 mg/kg SC
Immunoglobulin-peptide Conjugate 2 10 mg/kg SC
SEQ ID NO:3087;3088;3087;3088 1 mg/kg SC
SEQ ID NO:3087;3088;3087;3088 10 mg/kg SC
Immunoglobulin-peptide Conjugate 2 PX Nav1.7 IC50

FIG. 93

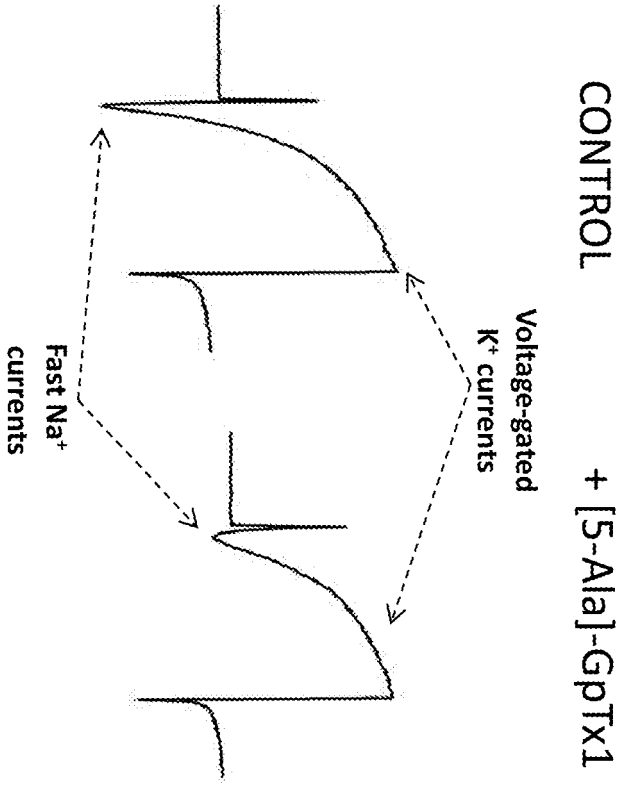
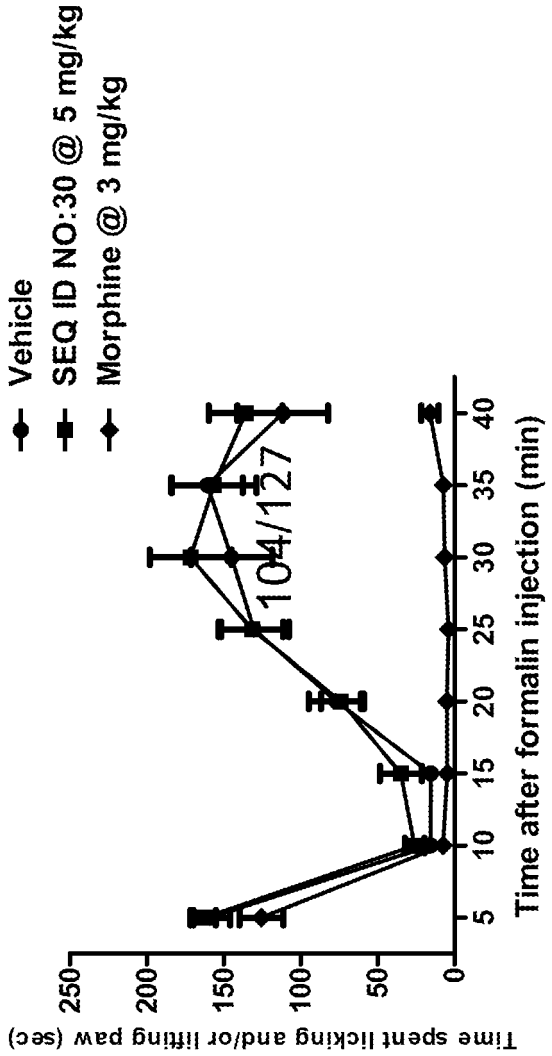

CONTROL
+ [5-Ala]-GpTx1
Voltage-gated
K+ currents
Fast Na+
currents

FIG. 94

FIG. 95



104/127

FIG. 96

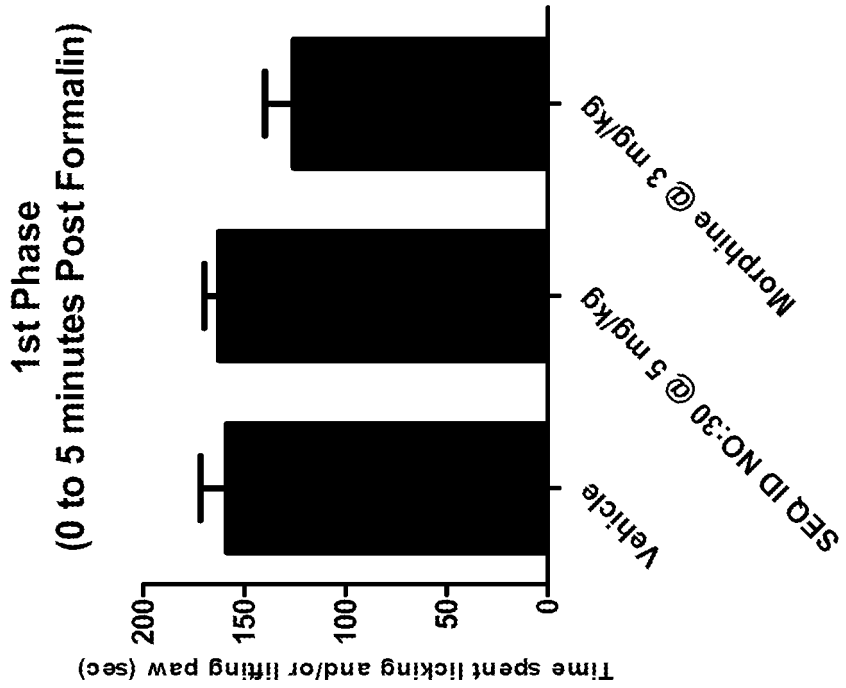

1st Phase
(0 to 5 minutes Post Formalin)
Time spent licking and/or lifting paw (sec)
200
150
100
50
0
Vehicle
SEQ ID NO:30 @ 5 mg/kg
Morphine @ 3 mg/kg

FIG. 97

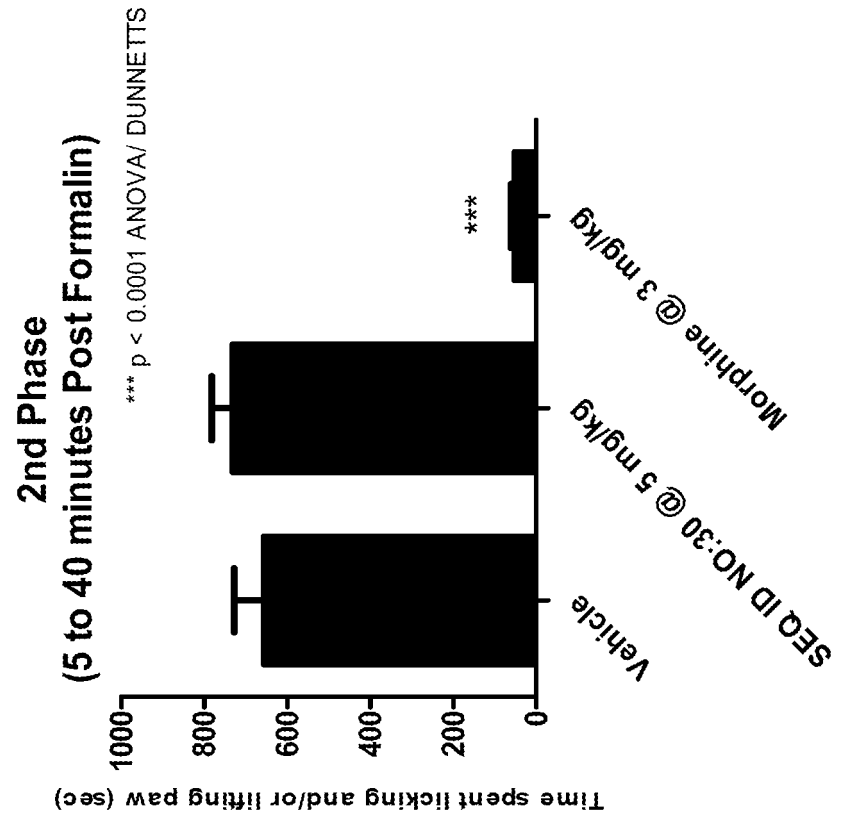

2nd Phase
(5 to 40 minutes Post Formalin)
*** p < 0.0001 ANOVA/ DUNNETTS
Time spent licking and/or lifting paw (sec)
1000
800
600
400
200
0
***
Vehicle
SEQ ID NO:30 @ 5 mg/kg
Morphine @ 3 mg/kg

FIG. 98

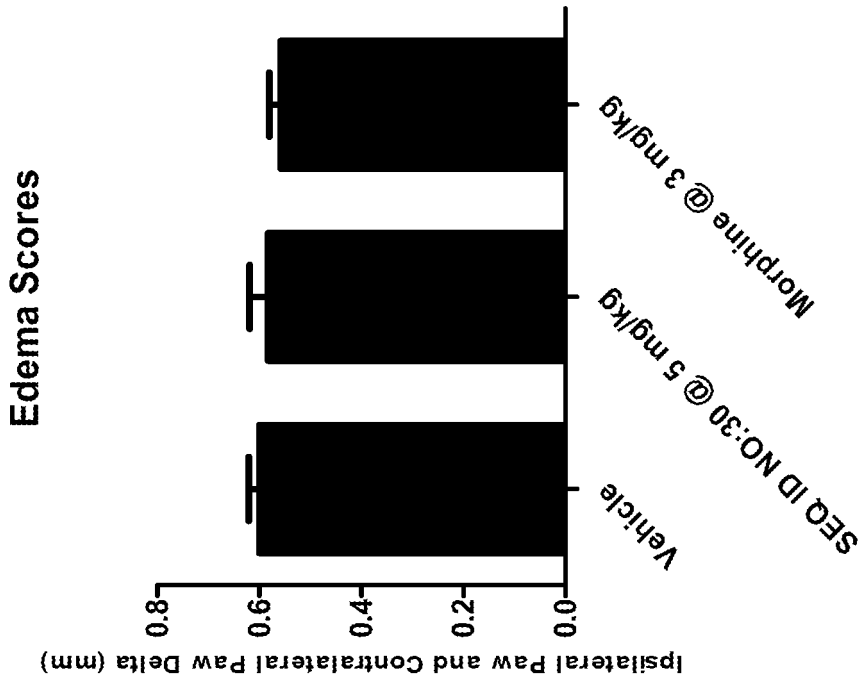

Edema Scores
Ipsilateral Paw and Contralateral Paw Delta (mm)
0.0
0.2
0.4
0.6
0.8
Vehicle
SEQ ID NO:30 @ 5 mg/kg
Morphine @ 3 mg/kg

FIG. 99

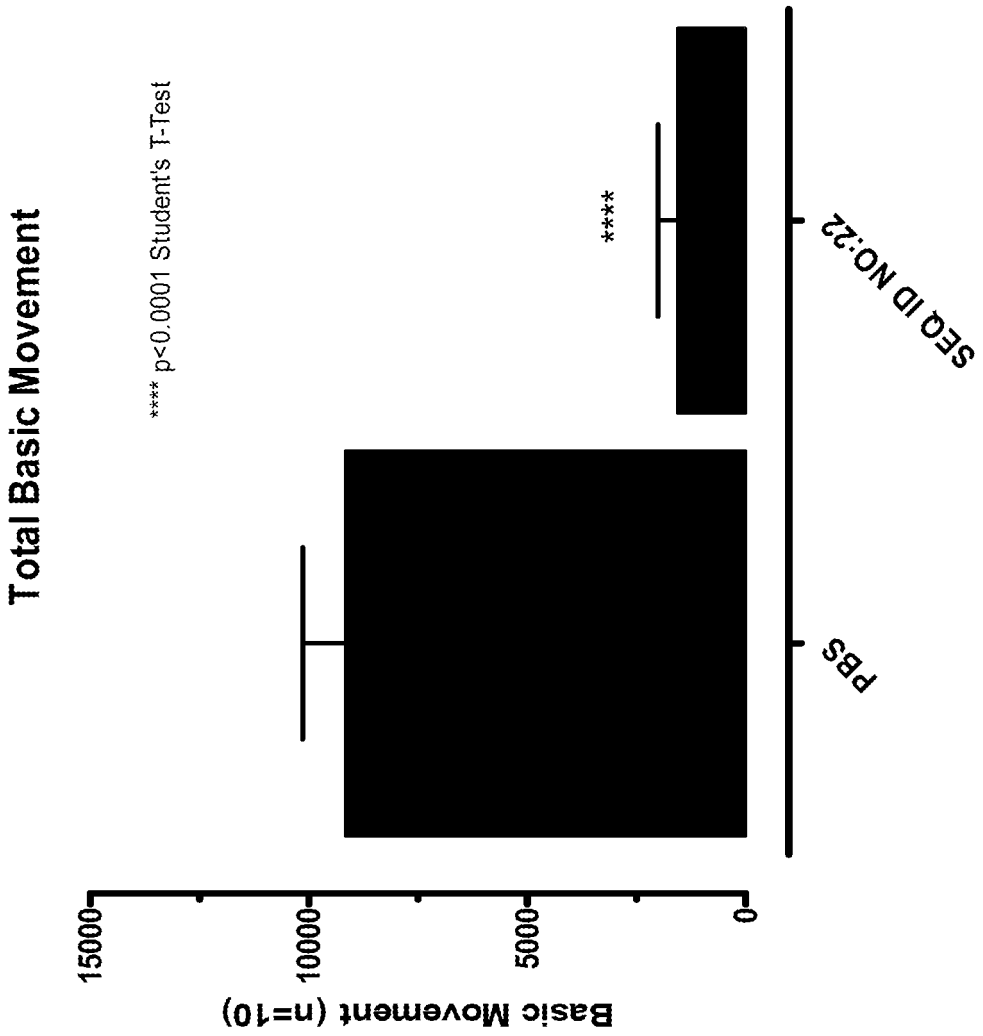
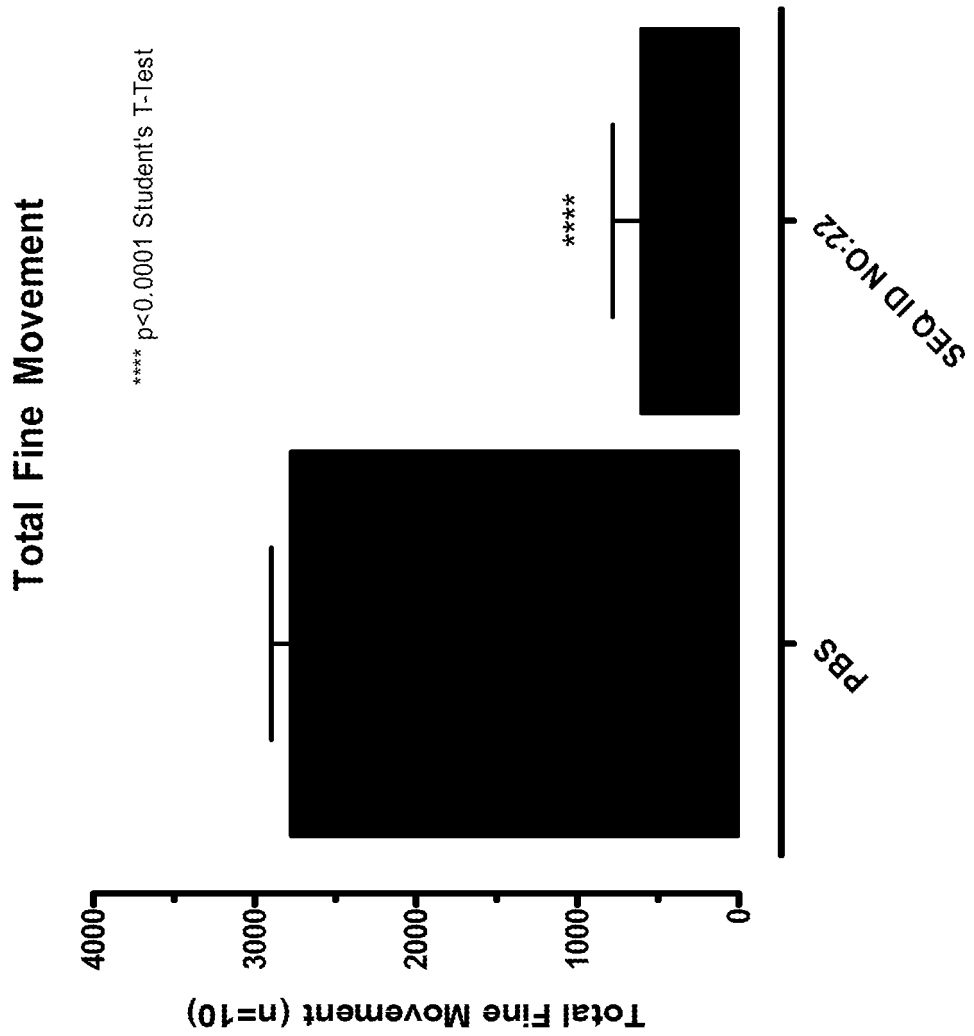

Total Basic Movement
**** p<0.0001 Student's T-Test
Basic Movement (n=10)
15000
10000
5000
0
****
PBS
SEQ ID NO:22

FIG. 100


Total Fine Movement
**** p<0.0001 Student's T-Test
Total Fine Movement (n=10)
4000
3000
2000
1000
0
****
PBS
SEQ ID NO:22



Total Rearing

**** p<0.0001 Student's T-Test

FIG. 101

FIG. 102

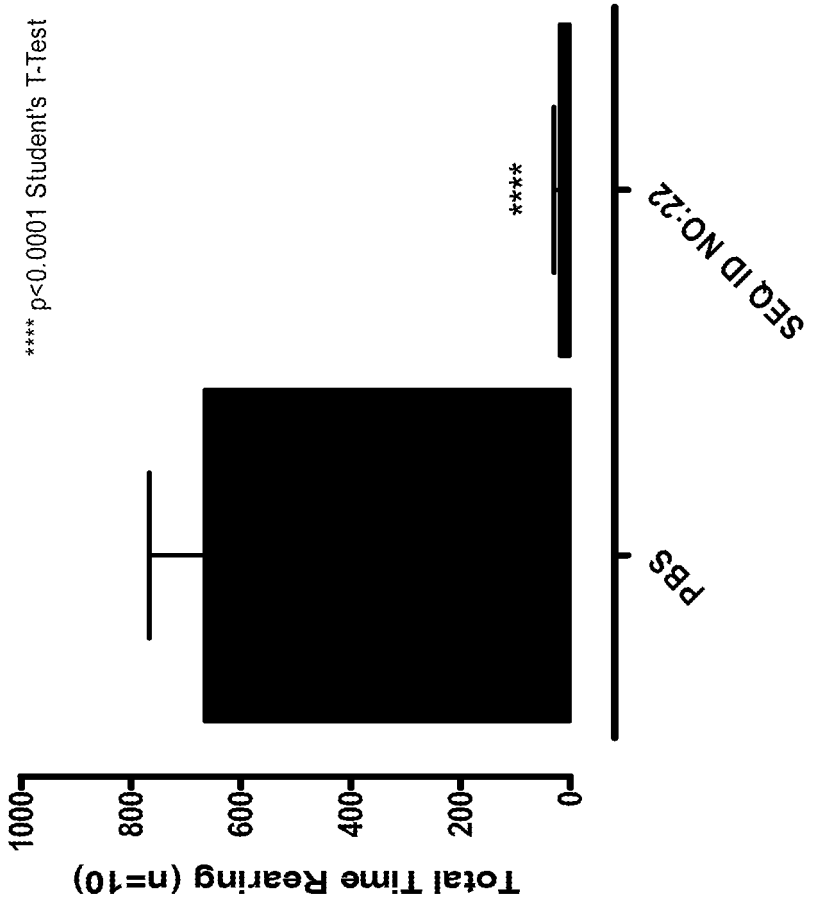

Total Time Rearing
**** p<0.0001 Student's T-Test
****
Total Time Rearing (n=10)
0
200
400
600
800
1000
PBS
SEQ ID NO:22

FIG. 103

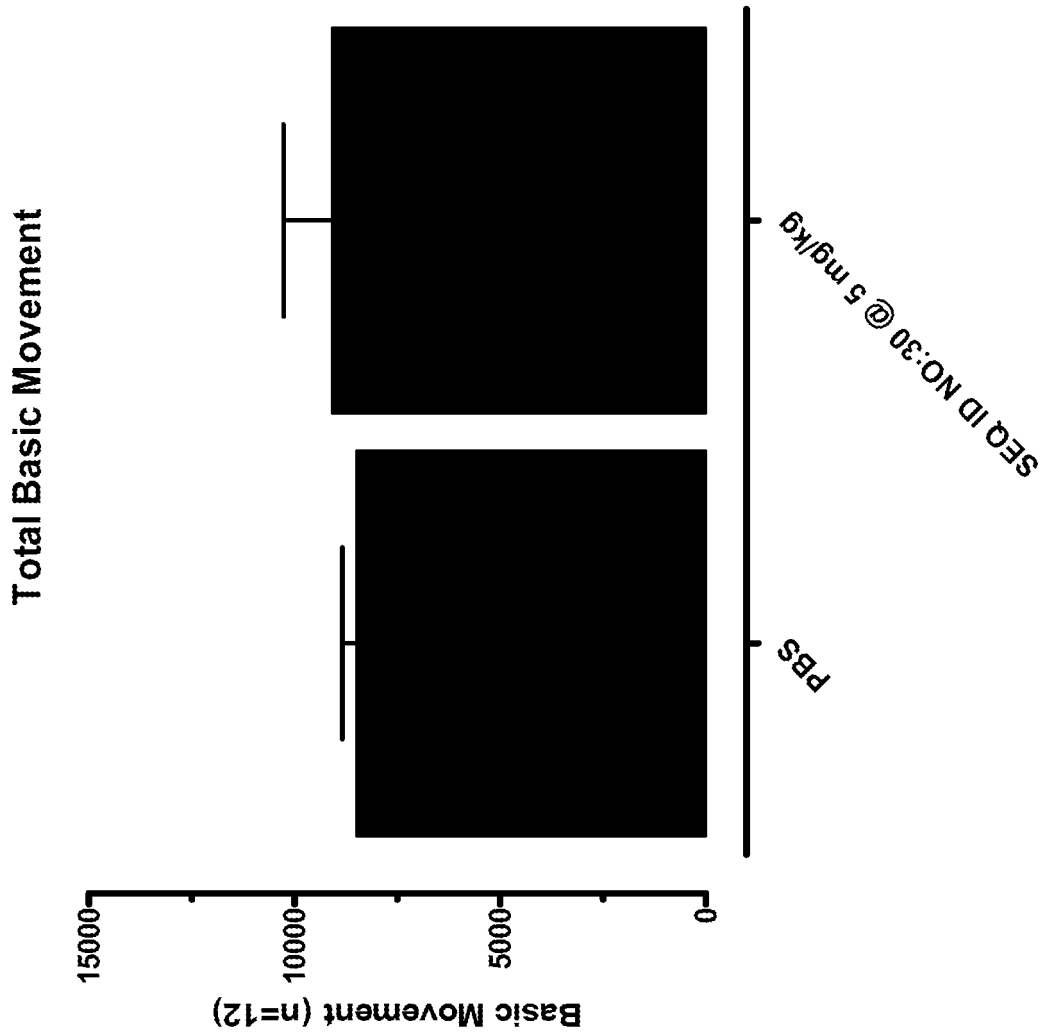

Total Basic Movement
Basic Movement (n=12)
15000
10000
5000
0
PBS
SEQ ID NO:30 @ 5 mg/kg

FIG. 104

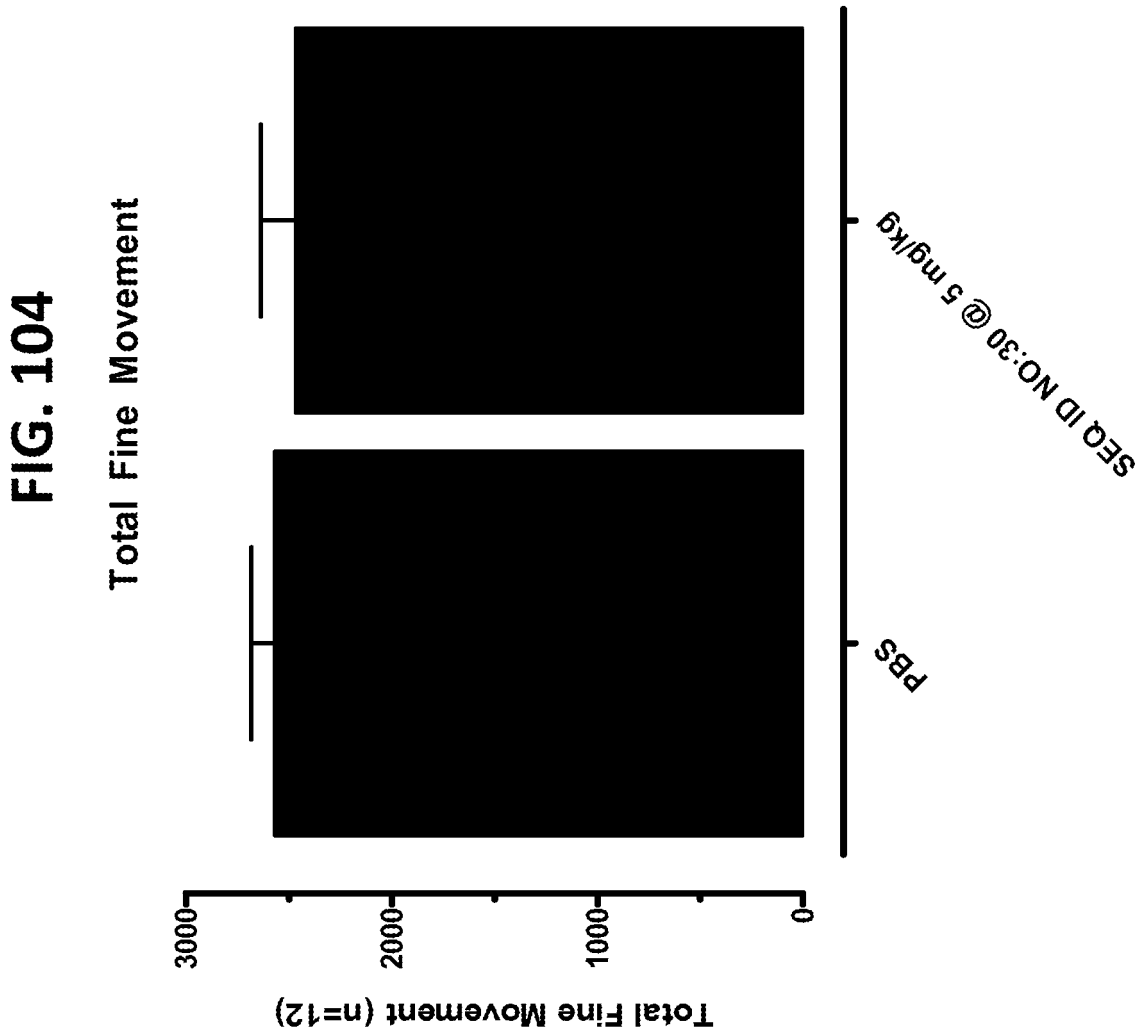

Total Fine Movement
Total Fine Movement (n=12)
3000
2000
1000
0
PBS
SEQ ID NO:30 @ 5 mg/kg

FIG. 105

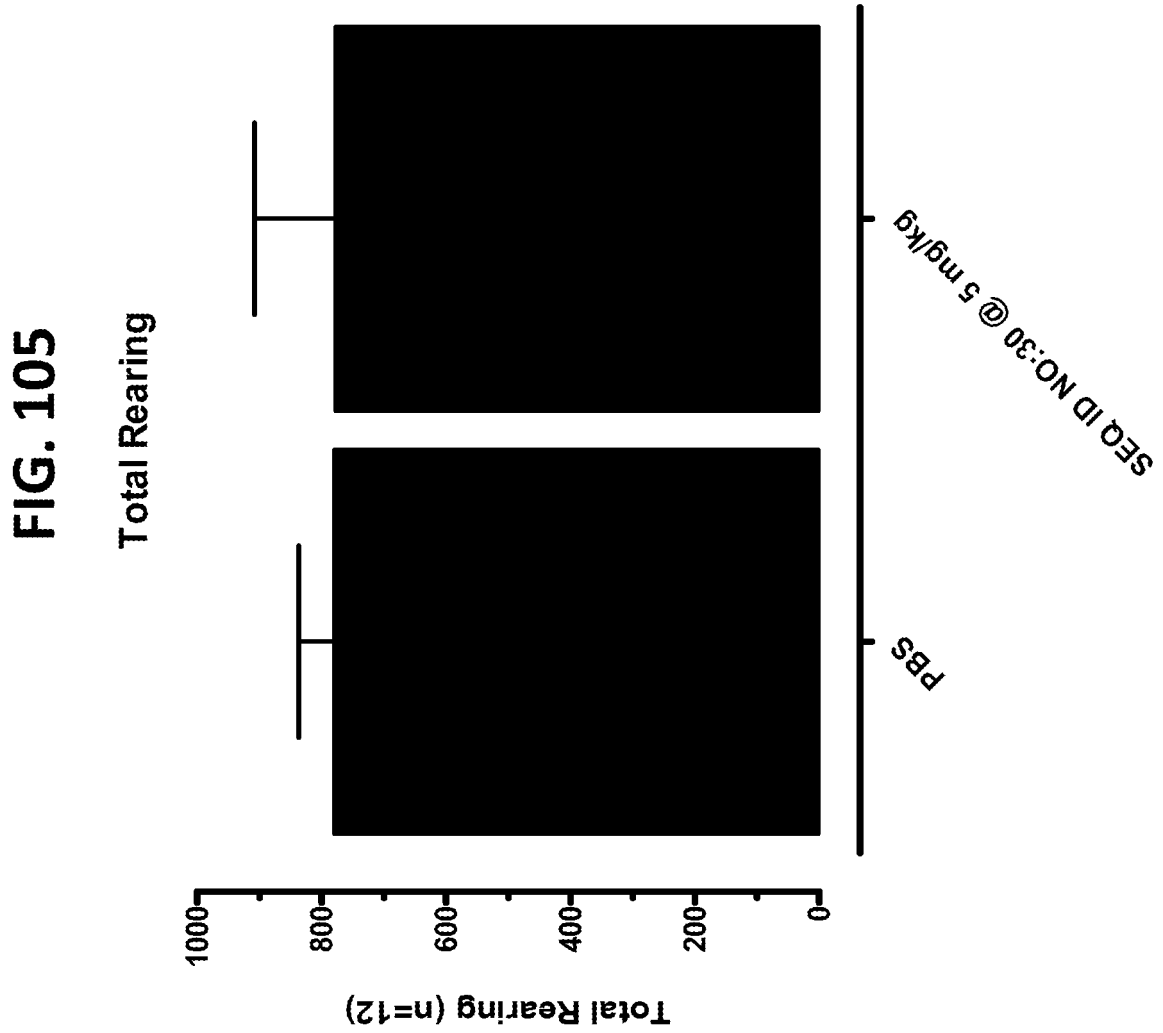

Total Rearing
Total Rearing (n=12)
1000
800
600
400
200
0
PBS
SEQ ID NO:30 @ 5 mg/kg

FIG. 106

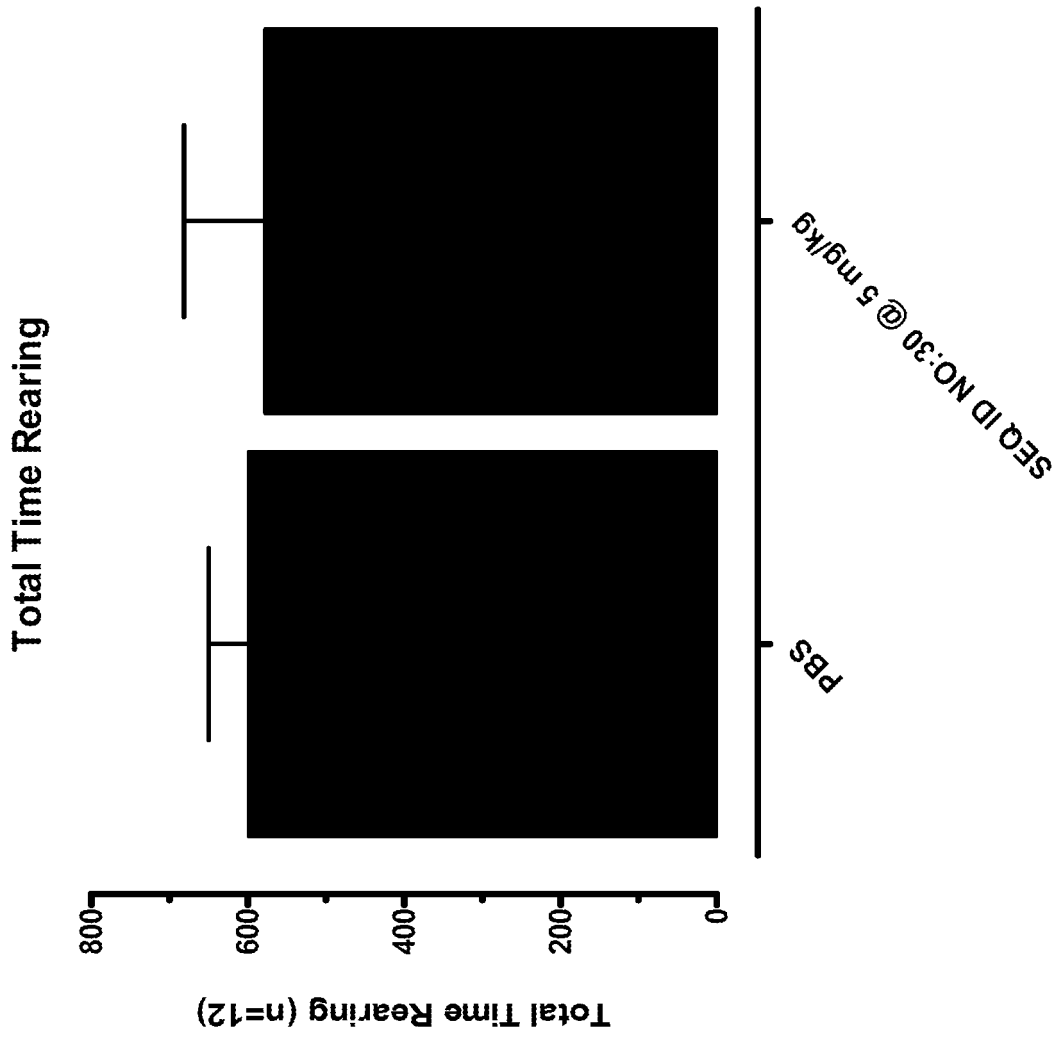

Total Time Rearing
Total Time Rearing (n=12)
800
600
400
200
0
PBS
SEQ ID NO:30 @ 5 mg/kg

FIG. 107

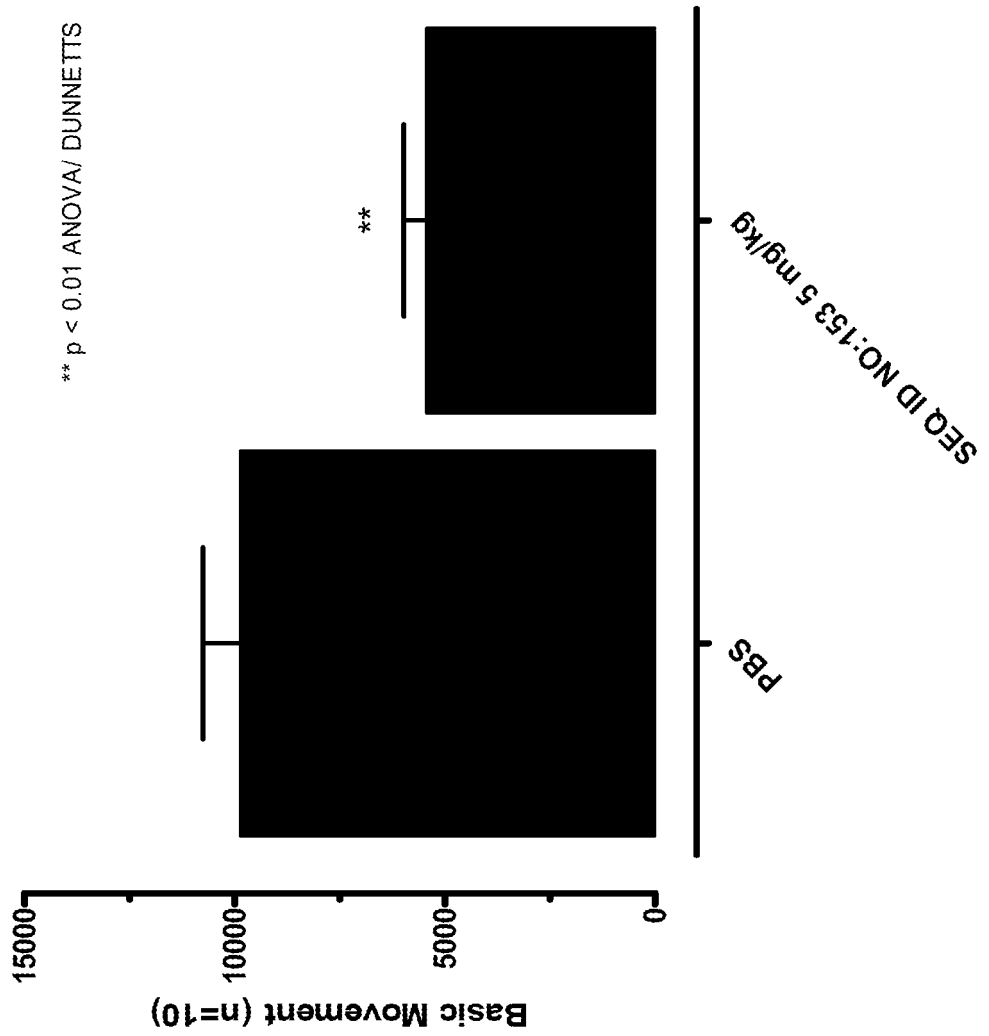

Total Basic Movement
** p < 0.01 ANOVA/ DUNNETTS
**
Basic Movement (n=10)
15000
10000
5000
0
PBS
SEQ ID NO:153 5 mg/kg

FIG. 108

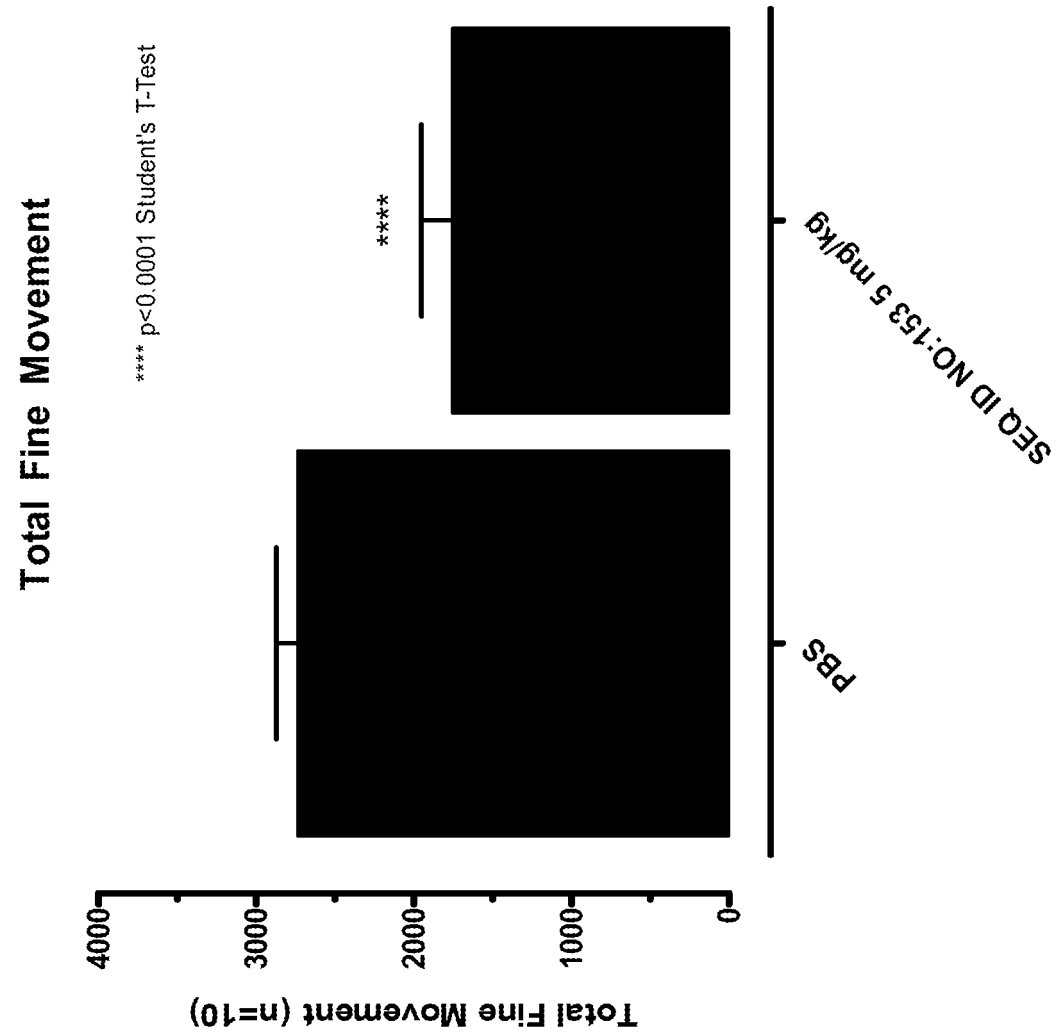

Total Fine Movement
**** p<0.0001 Student's T-Test
****
Total Fine Movement (n=10)
4000
3000
2000
1000
0
PBS
SEQ ID NO:153 5 mg/kg

FIG. 109

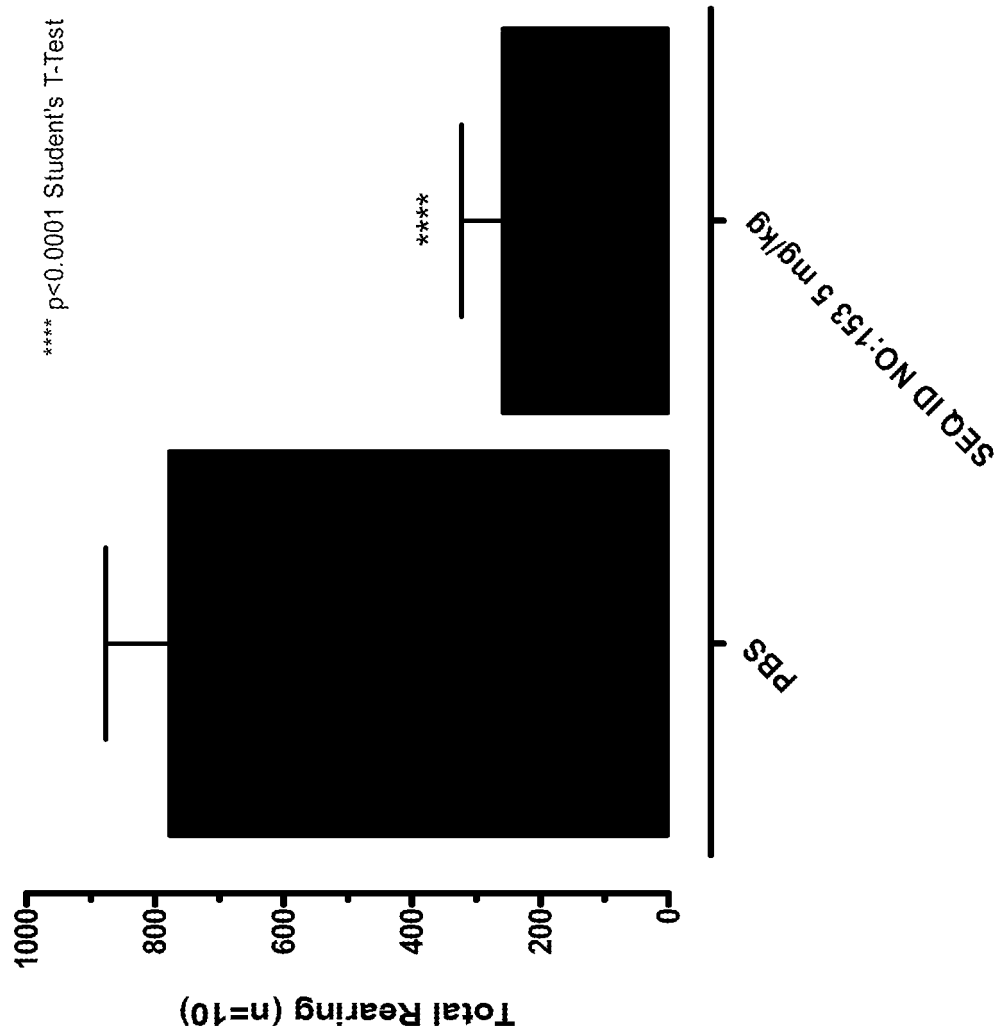

Total Rearing
**** p<0.0001 Student's T-Test
****
Total Rearing (n=10)
1000
800
600
400
200
0
PBS
SEQ ID NO:153 5 mg/kg

FIG. 110

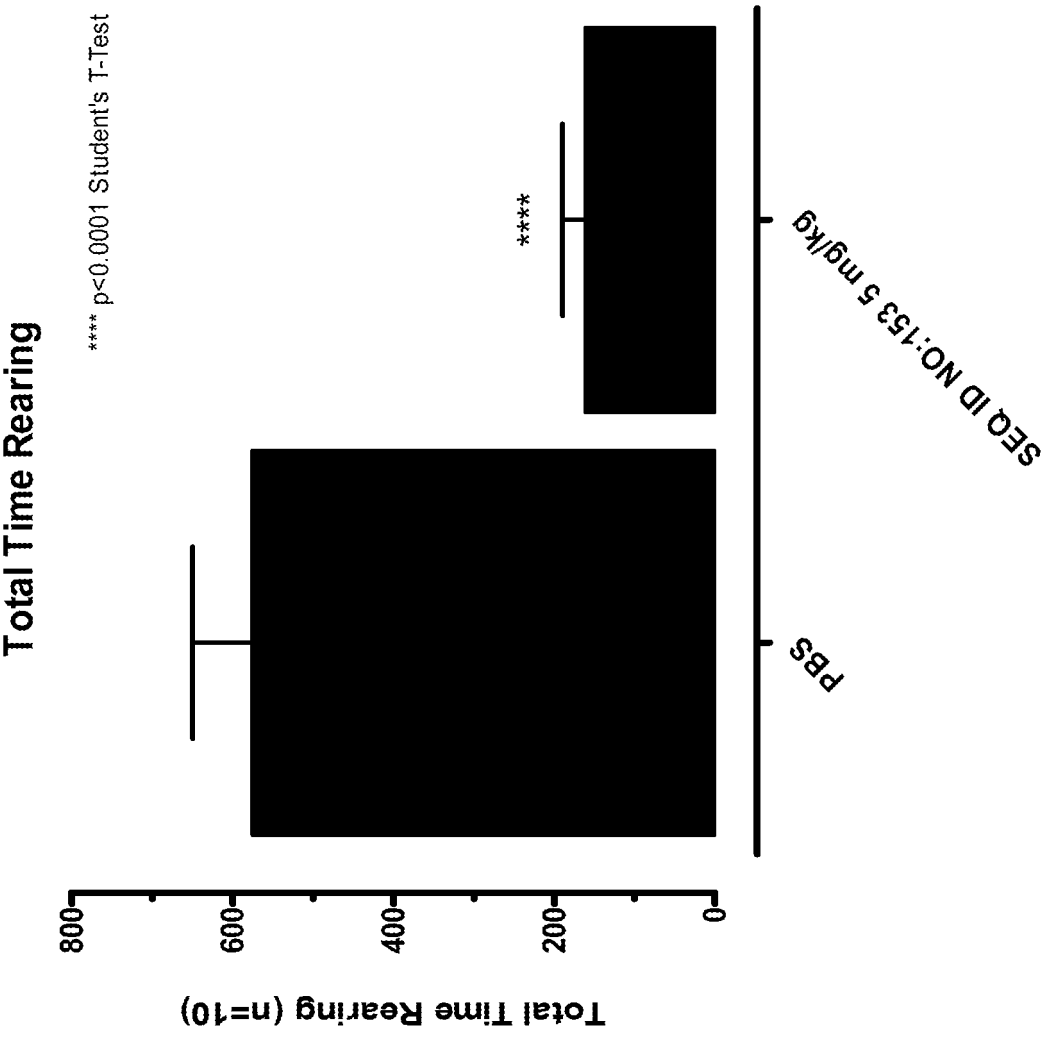

Total Time Rearing
**** p<0.0001 Student's T-Test
****
PBS
SEQ ID NO:153 5 mg/kg
Total Time Rearing (n=10)
800
600
400
200
0

FIG. 111

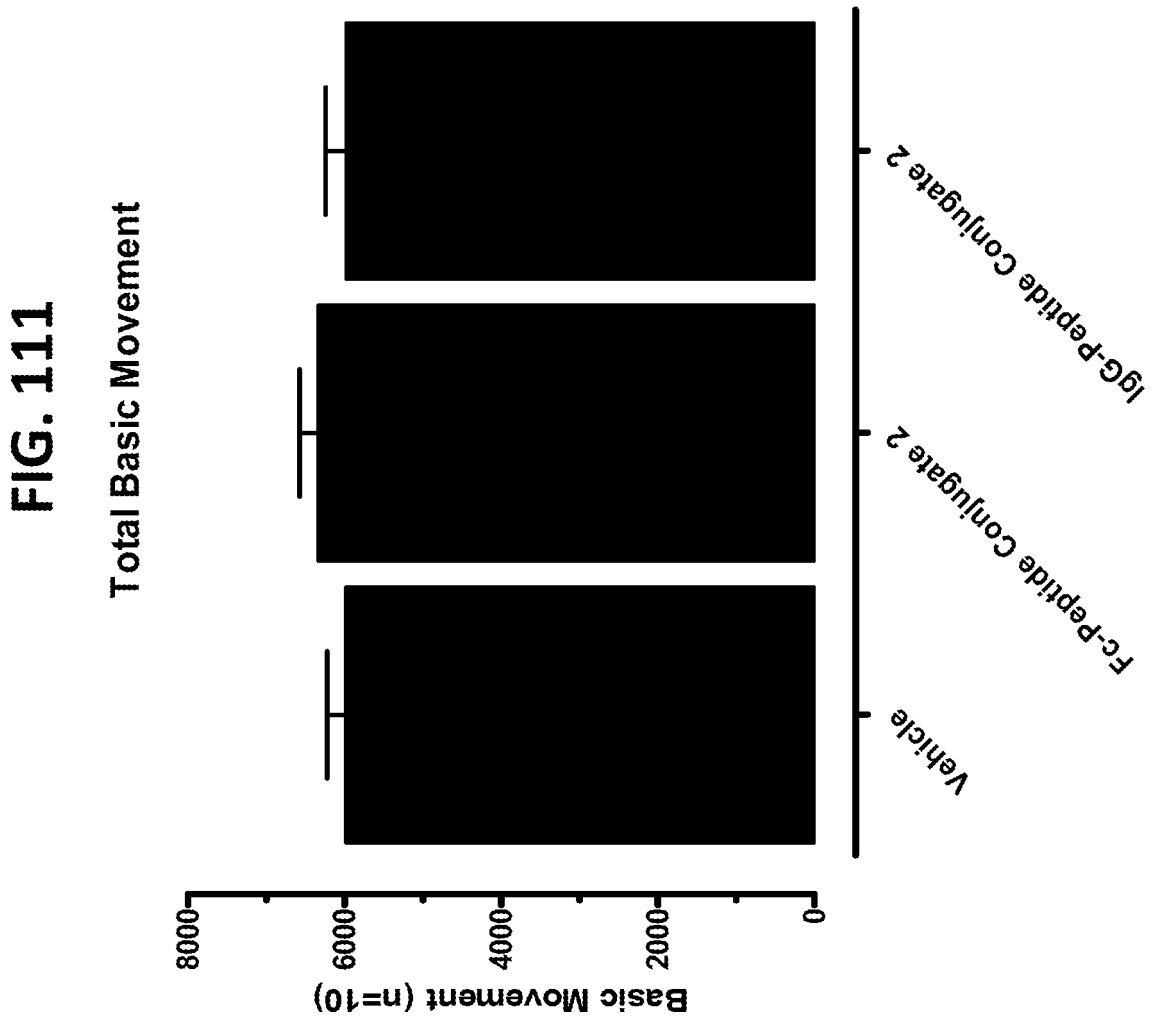

Total Basic Movement
Basic Movement (n=10)
8000
6000
4000
2000
0
Vehicle
Fc-Peptide Conjugate 2
IgG-Peptide Conjugate 2

FIG. 112

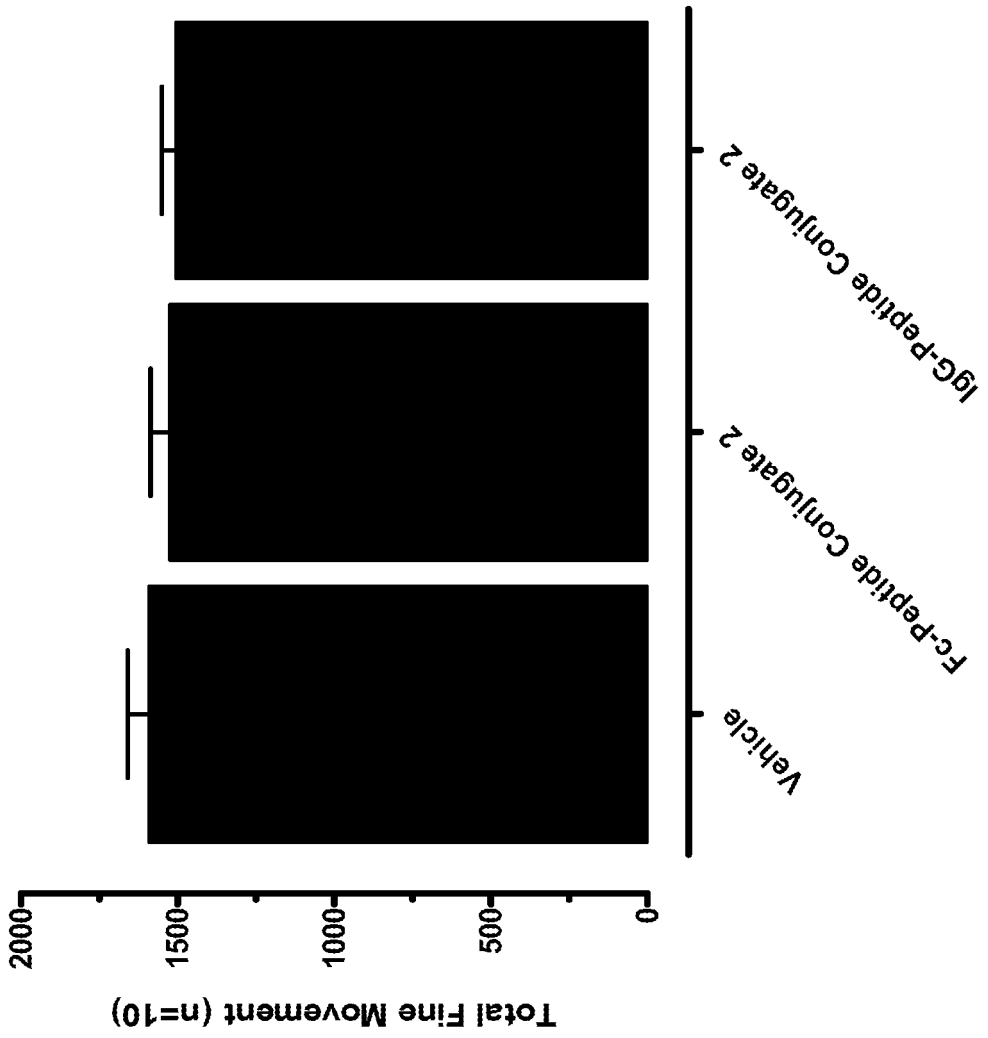

Total Fine Movement
Total Fine Movement (n=10)
2000
1500
1000
500
0
Vehicle
Fc-Peptide Conjugate 2
IgG-Peptide Conjugate 2

FIG. 113

Total Rearing

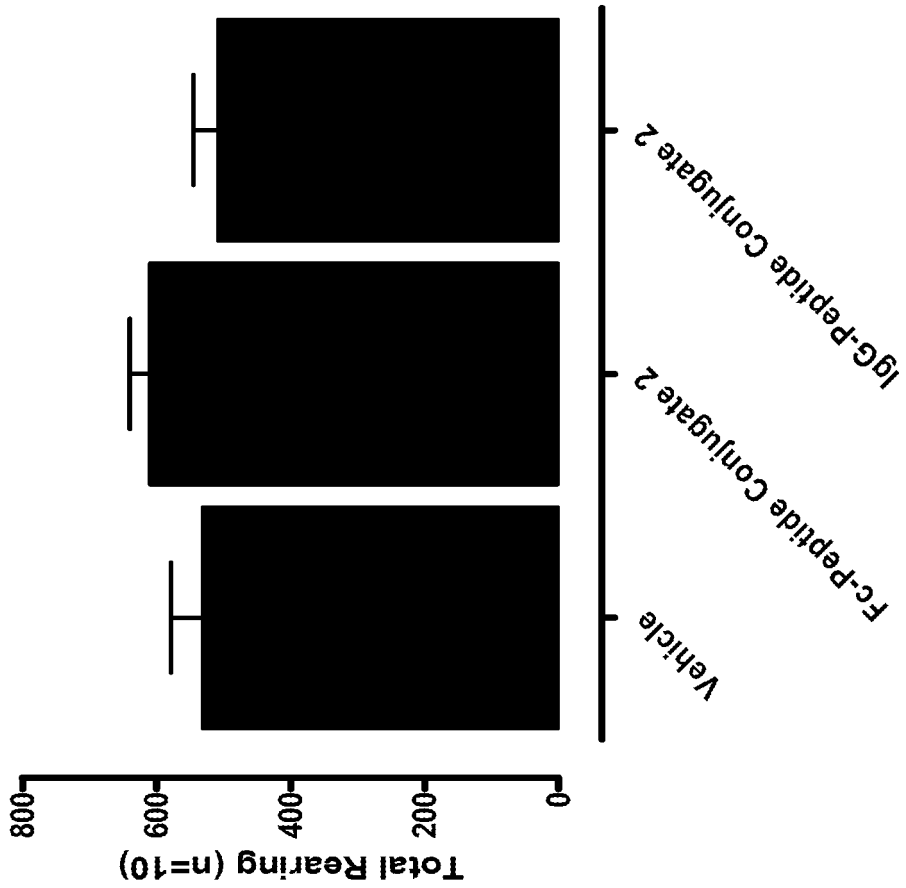


FIG. 114

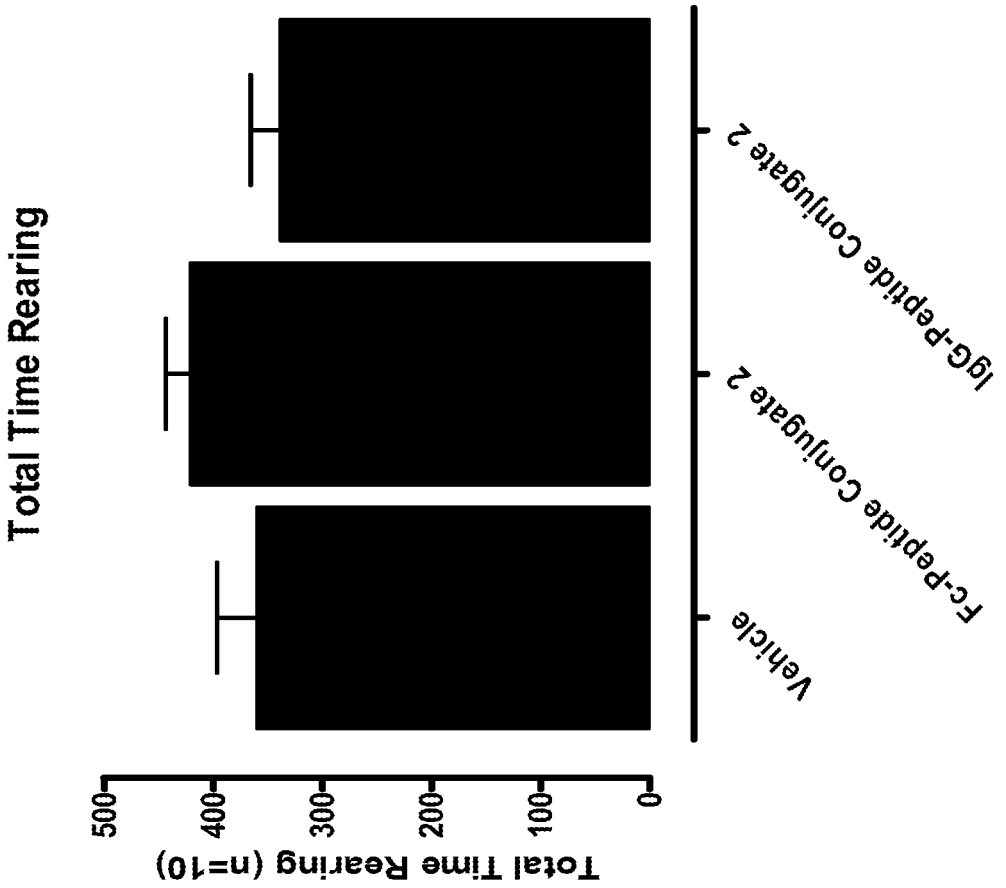

Total Time Rearing
Total Time Rearing (n=10)
0
100
200
300
400
500
Vehicle
Fc-Peptide Conjugate 2
IgG-Peptide Conjugate 2

FIG. 115

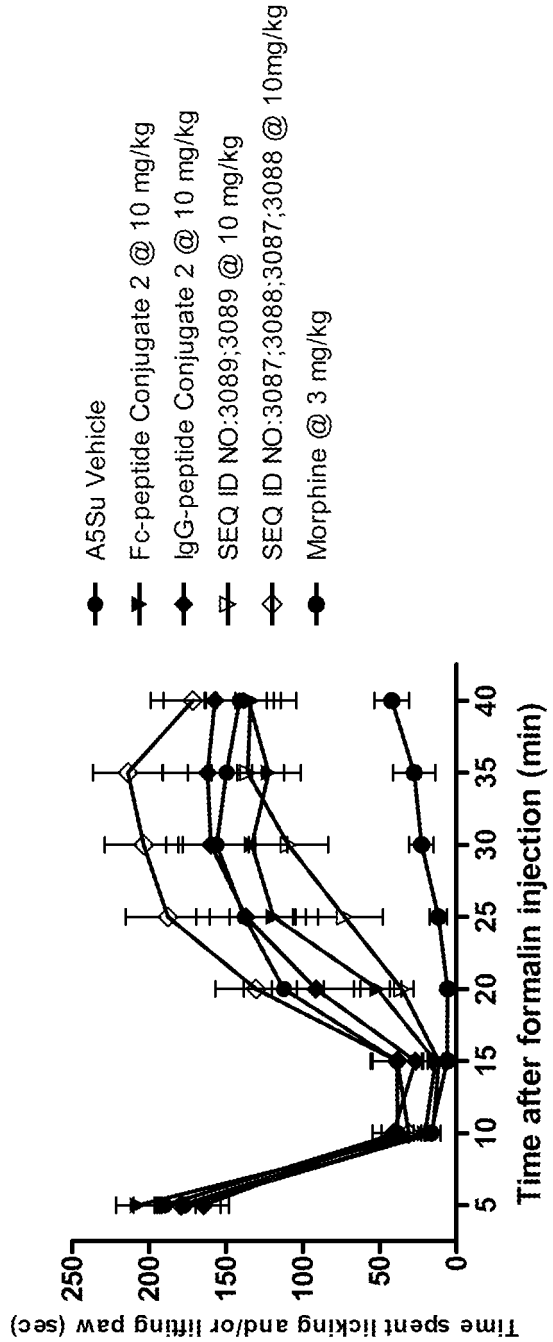

A5Su Vehicle
Fc-peptide Conjugate 2 @ 10 mg/kg
IgG-peptide Conjugate 2 @ 10 mg/kg
SEQ ID NO:3089;3089 @ 10 mg/kg
SEQ ID NO:3087;3088;3087;3088 @ 10mg/kg
Morphine @ 3 mg/kg
Time spent licking and/or lifting paw (sec)
250
200
150
100
50
0
5
10
15
20
25
30
35
40
Time after formalin injection (min)

FIG. 116

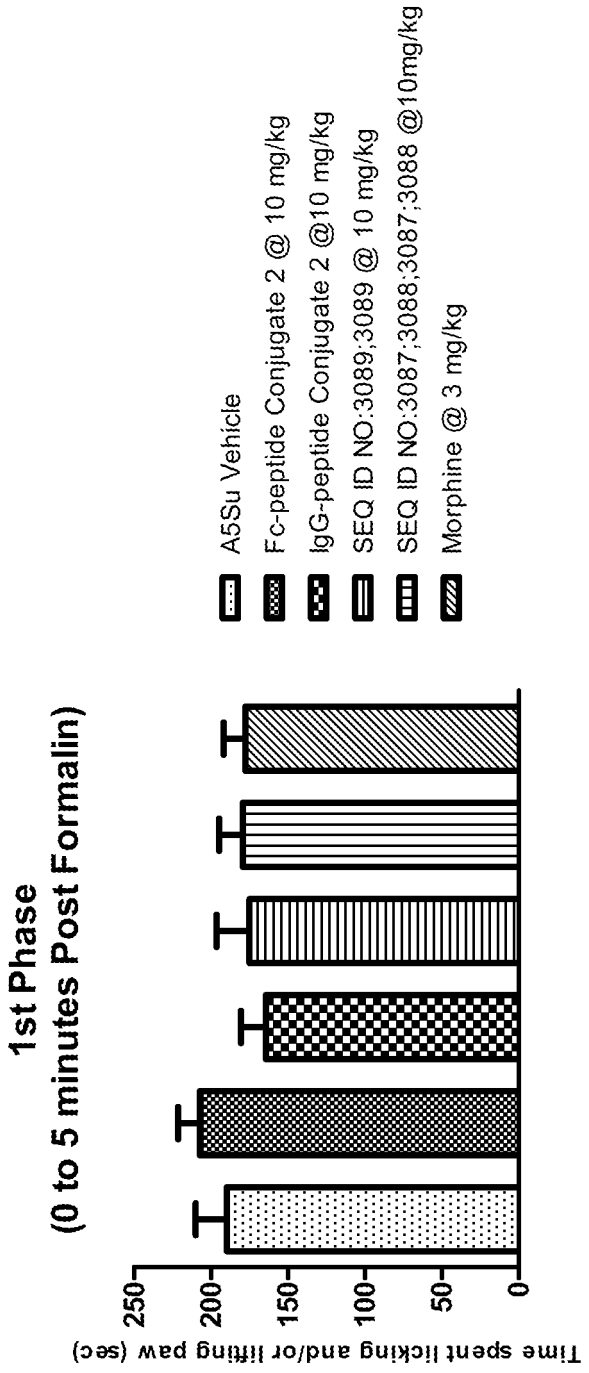
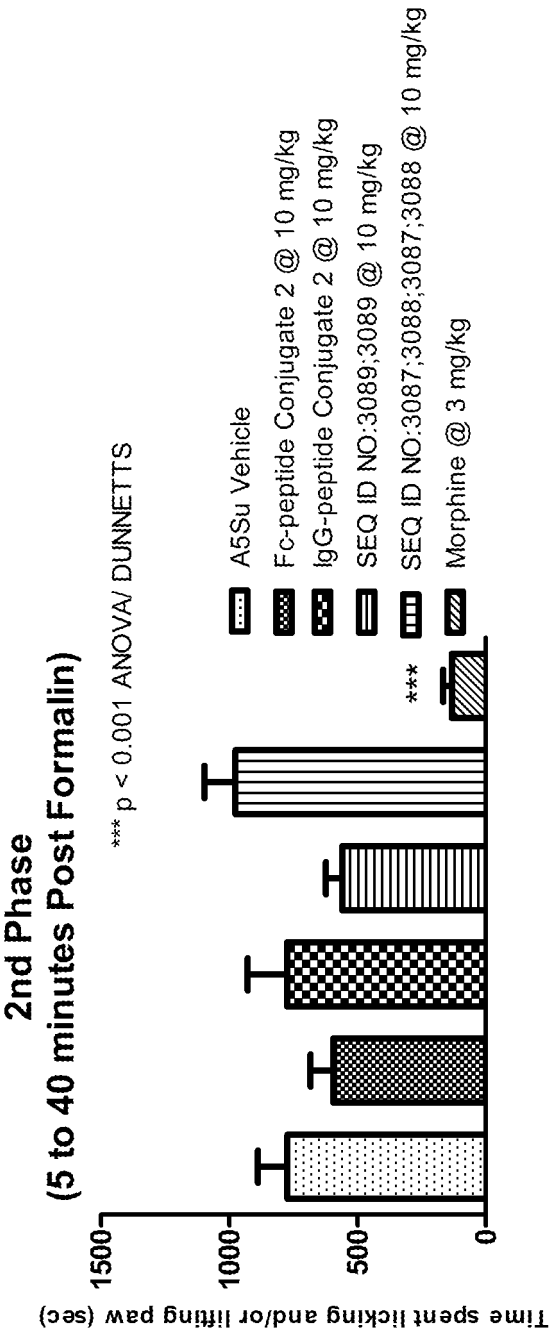

1st Phase
(0 to 5 minutes Post Formalin)
Time spent licking and/or lifting paw (sec)
250
200
150
100
50
0
A5Su Vehicle
Fc-peptide Conjugate 2 @ 10 mg/kg
IgG-peptide Conjugate 2 @10 mg/kg
SEQ ID NO:3089;3089 @ 10 mg/kg
SEQ ID NO:3087;3088;3087;3088 @10mg/kg
Morphine @ 3 mg/kg

FIG. 117


2nd Phase
(5 to 40 minutes Post Formalin)
*** p < 0.001 ANOVA/ DUNNETTS
Time spent licking and/or lifting paw (sec)
1500
1000
500
0
***
A5Su Vehicle
Fc-peptide Conjugate 2 @ 10 mg/kg
IgG-peptide Conjugate 2 @ 10 mg/kg
SEQ ID NO:3089;3089 @ 10 mg/kg
SEQ ID NO:3087;3088;3087;3088 @ 10 mg/kg
Morphine @ 3 mg/kg