FIGURE 1

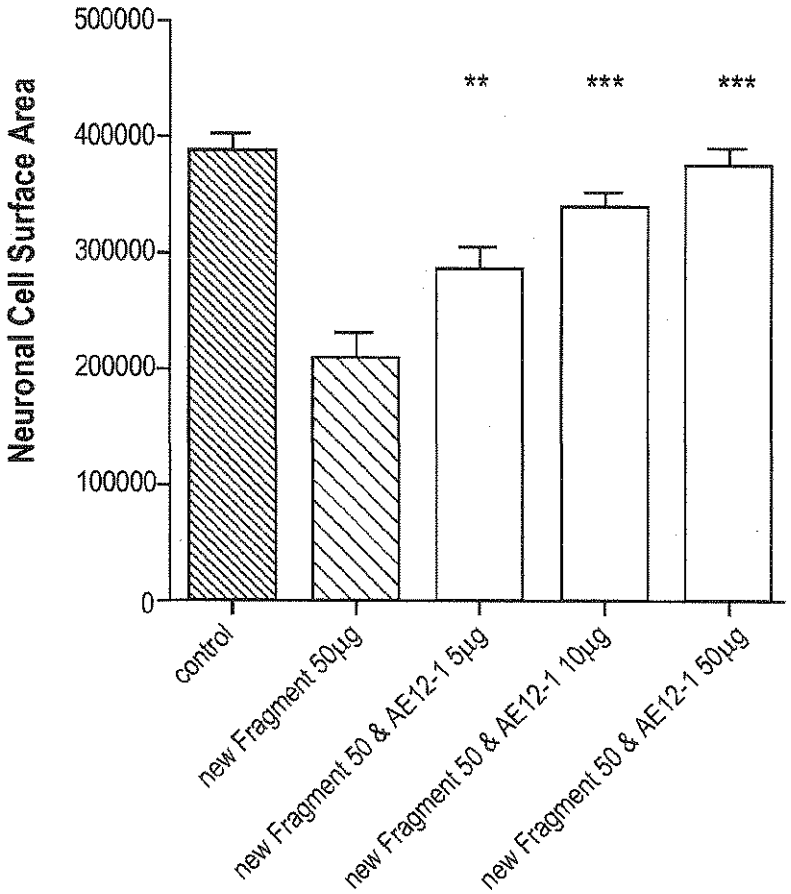

Neuronal Cell Surface Area
500000
400000
300000
200000
100000
0
**
***
***
control
new Fragment 50µg
new Fragment 50 & AE12-1 5µg
new Fragment 50 & AE12-1 10µg
new Fragment 50 & AE12-1 50µg

FIGURE 2

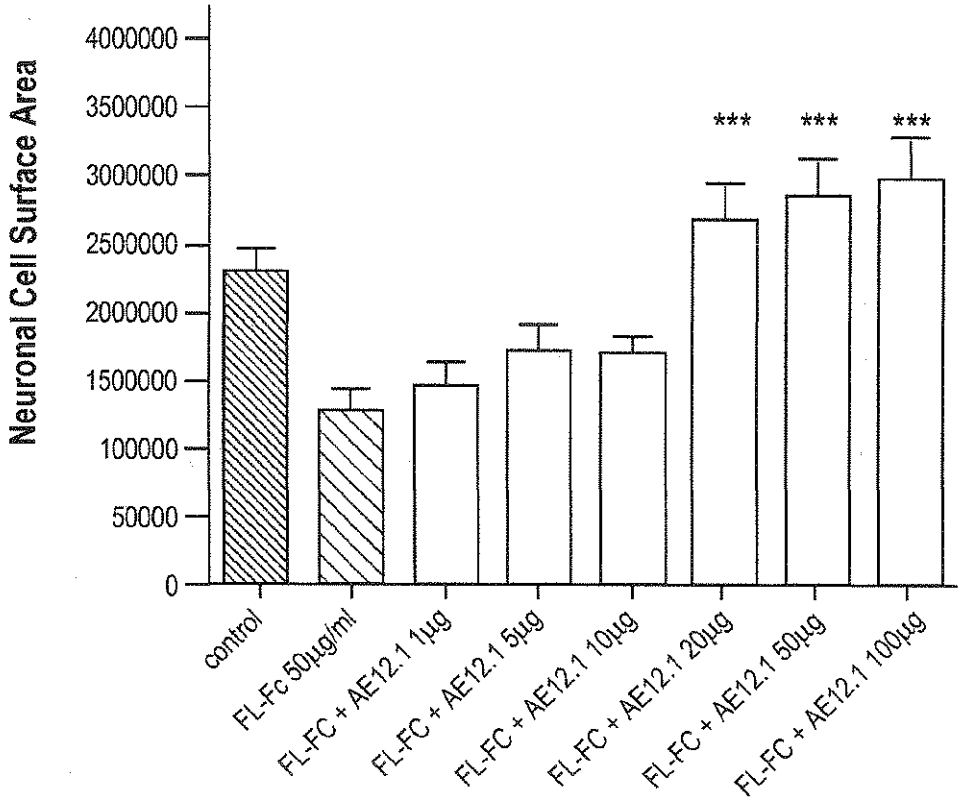

Neuronal Cell Surface Area
4000000
3500000
3000000
2500000
2000000
1500000
100000
50000
0
***
***
***
control
FL-Fc 50µg/ml
FL-FC + AE12.1 1µg
FL-FC + AE12.1 5µg
FL-FC + AE12.1 10µg
FL-FC + AE12.1 20µg
FL-FC + AE12.1 50µg
FL-FC + AE12.1 100µg

FIGURE 3

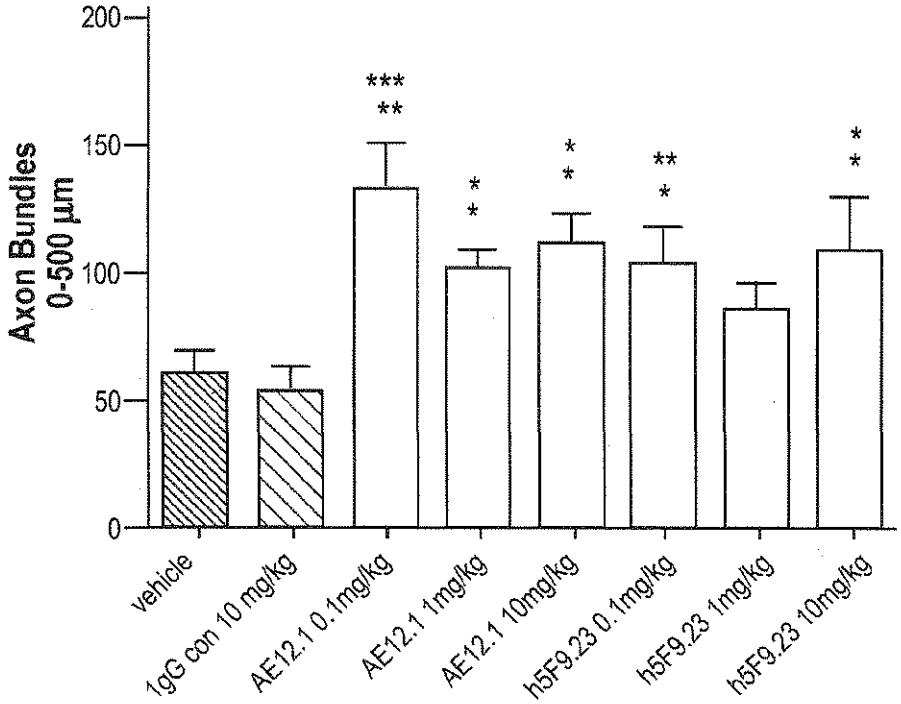

Axon Bundles
0-500 µm
200
150
100
50
0
***
**
*
**
*
**
*
**
*
vehicle
1gG con 10 mg/kg
AE12.1 0.1mg/kg
AE12.1 1mg/kg
AE12.1 10mg/kg
h5F9.23 0.1mg/kg
h5F9.23 1mg/kg
h5F9.23 10mg/kg

FIGURE 4

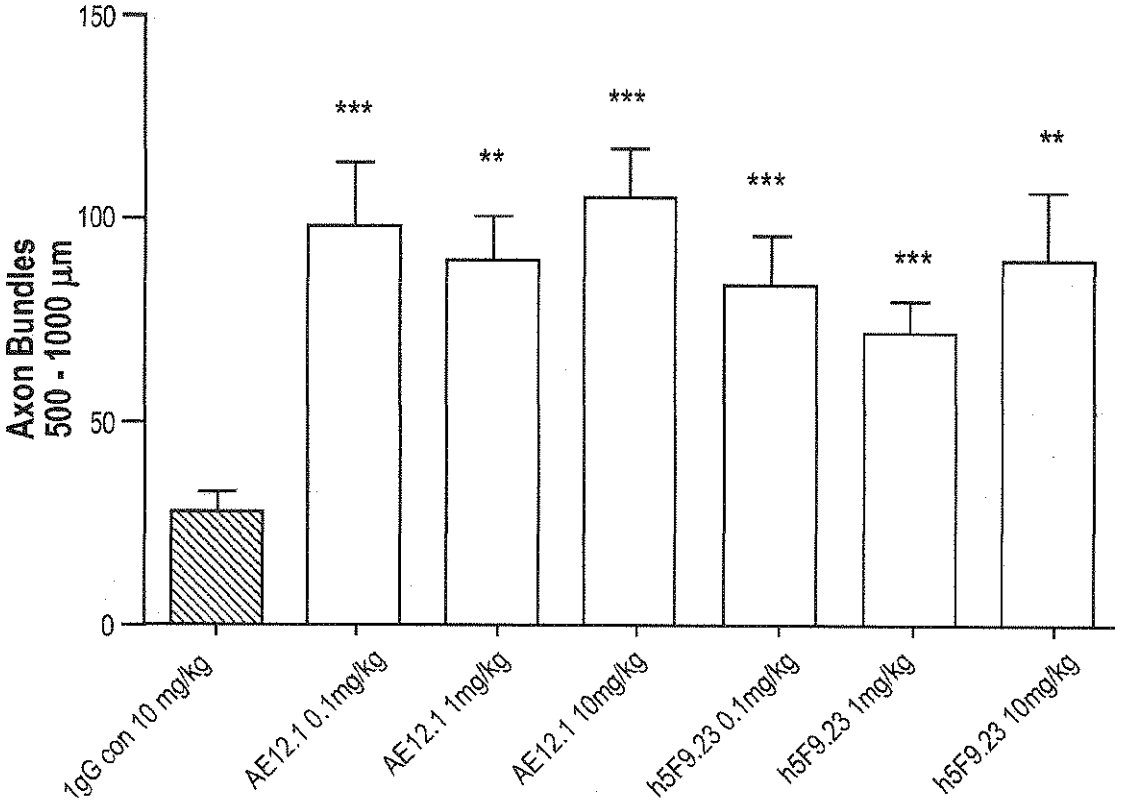

Axon Bundles
500 - 1000 µm
150
100
50
0
***
**
***
***
***
**
1gG con 10 mg/kg
AE12.1 0.1mg/kg
AE12.1 1mg/kg
AE12.1 10mg/kg
h5F9.23 0.1mg/kg
h5F9.23 1mg/kg
h5F9.23 10mg/kg

FIGURE 5

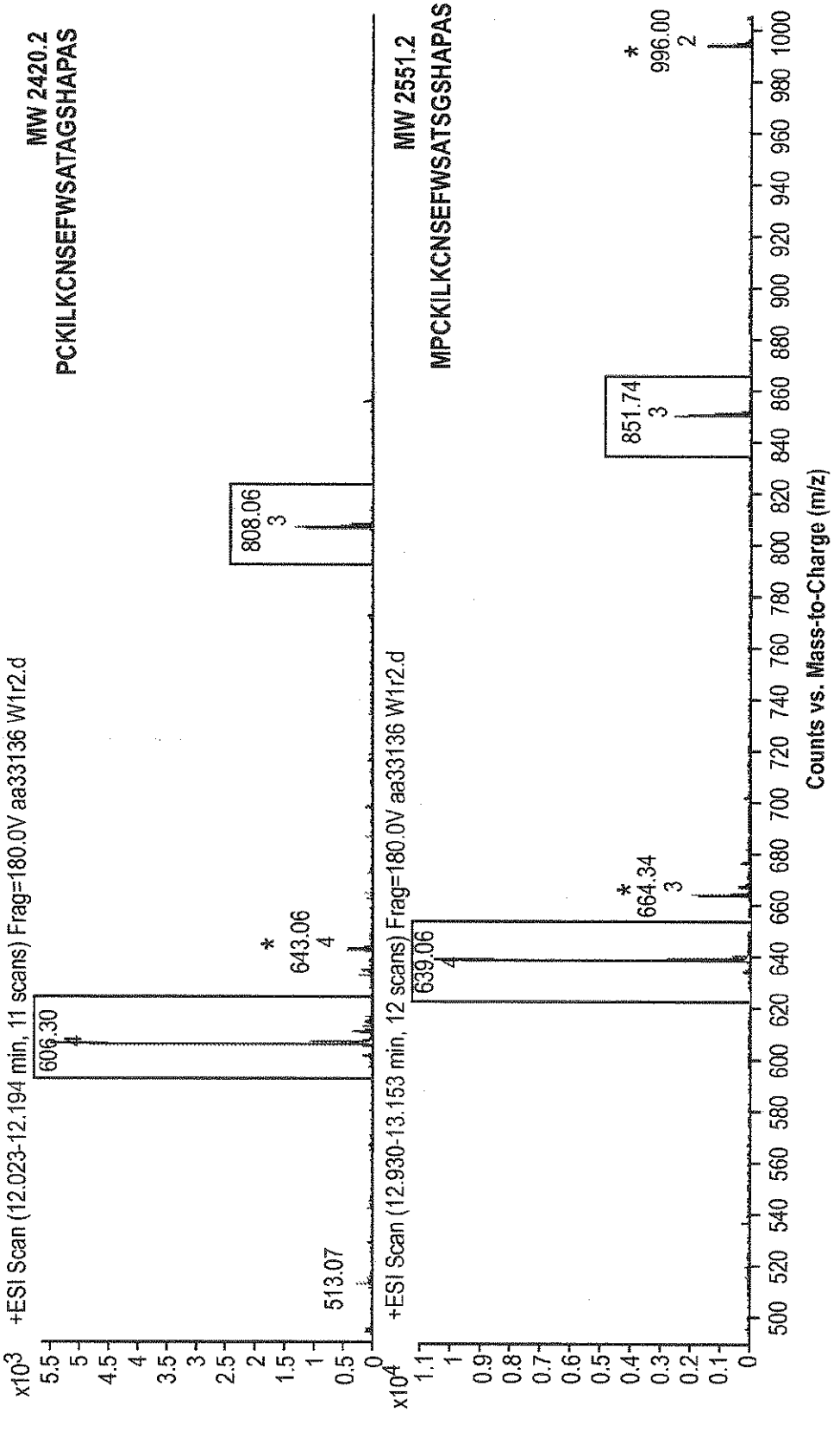

MW 2420.2
PCKILKCNSEFWSATAGSHAPAS
+ESI Scan (12.023-12.194 min, 11 scans) Frag=180.0V aa33136 W1r2.d
x10^3
606.30
4
*
643.06
4
513.07
808.06
3
MW 2551.2
MPCKILKCNSEFWSATSGSHAPAS
+ESI Scan (12.930-13.153 min, 12 scans) Frag=180.0V aa33136 W1r2.d
x10^4
639.06
4
*
664.34
3
851.74
3
*
996.00
2
Counts vs. Mass-to-Charge (m/z)

FIGURE 6

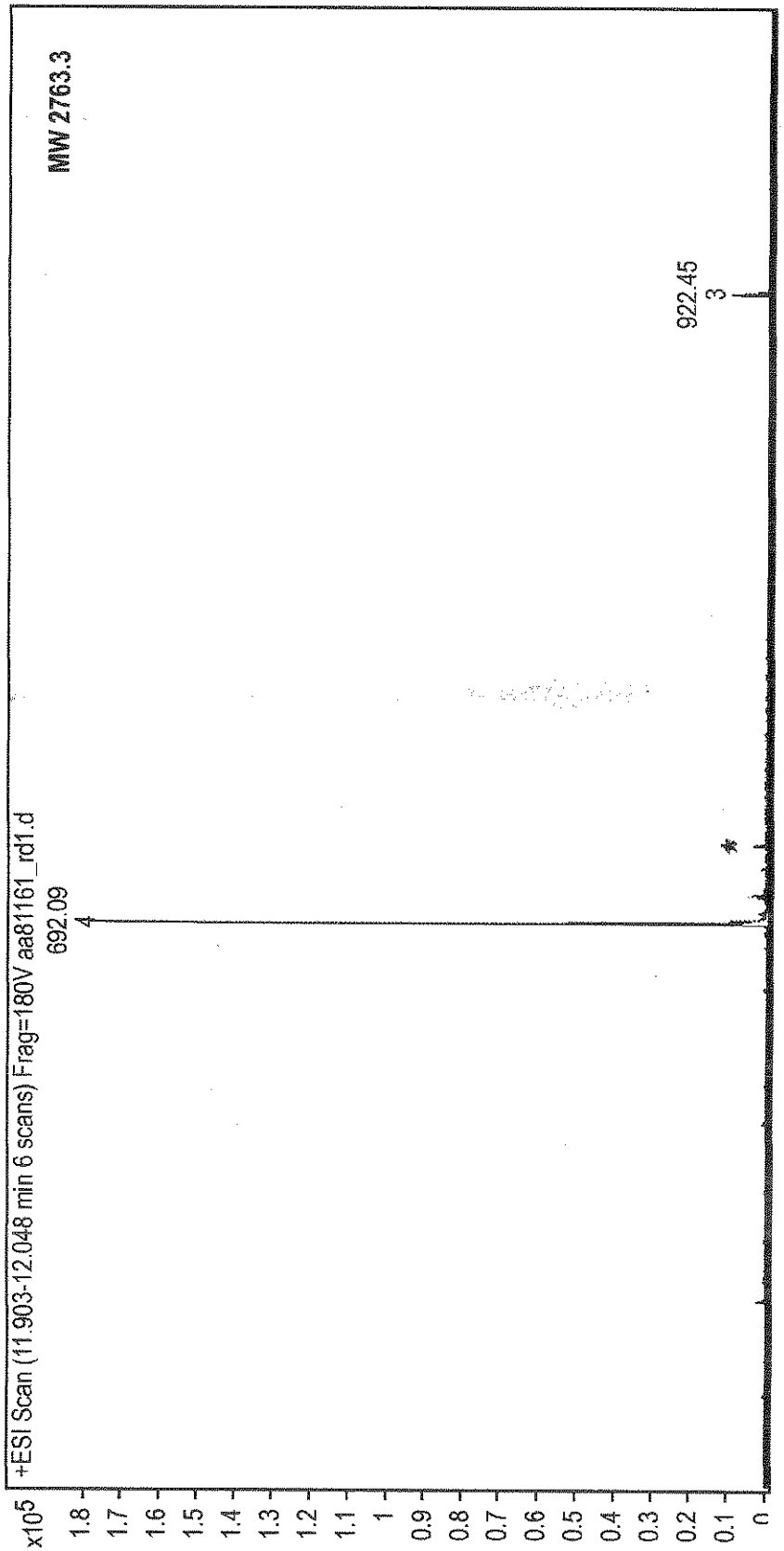

MW 2763.3
+ESI Scan (11.903-12.048 min 6 scans) Frag=180V aa81161_rd1.d
692.09
4
922.45
3
x10^5
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0

FIGURE 6 (continued)

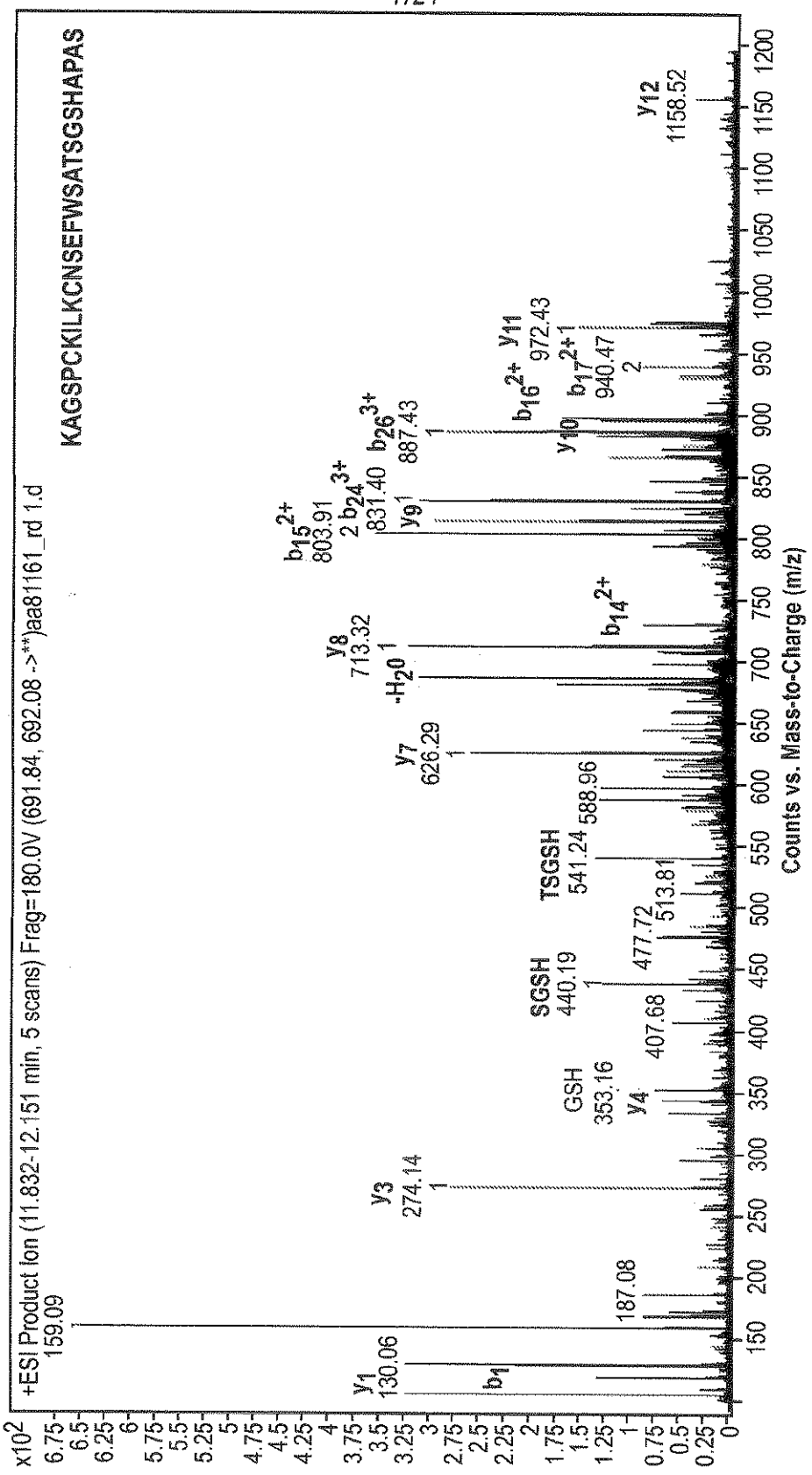


FIGURE 7

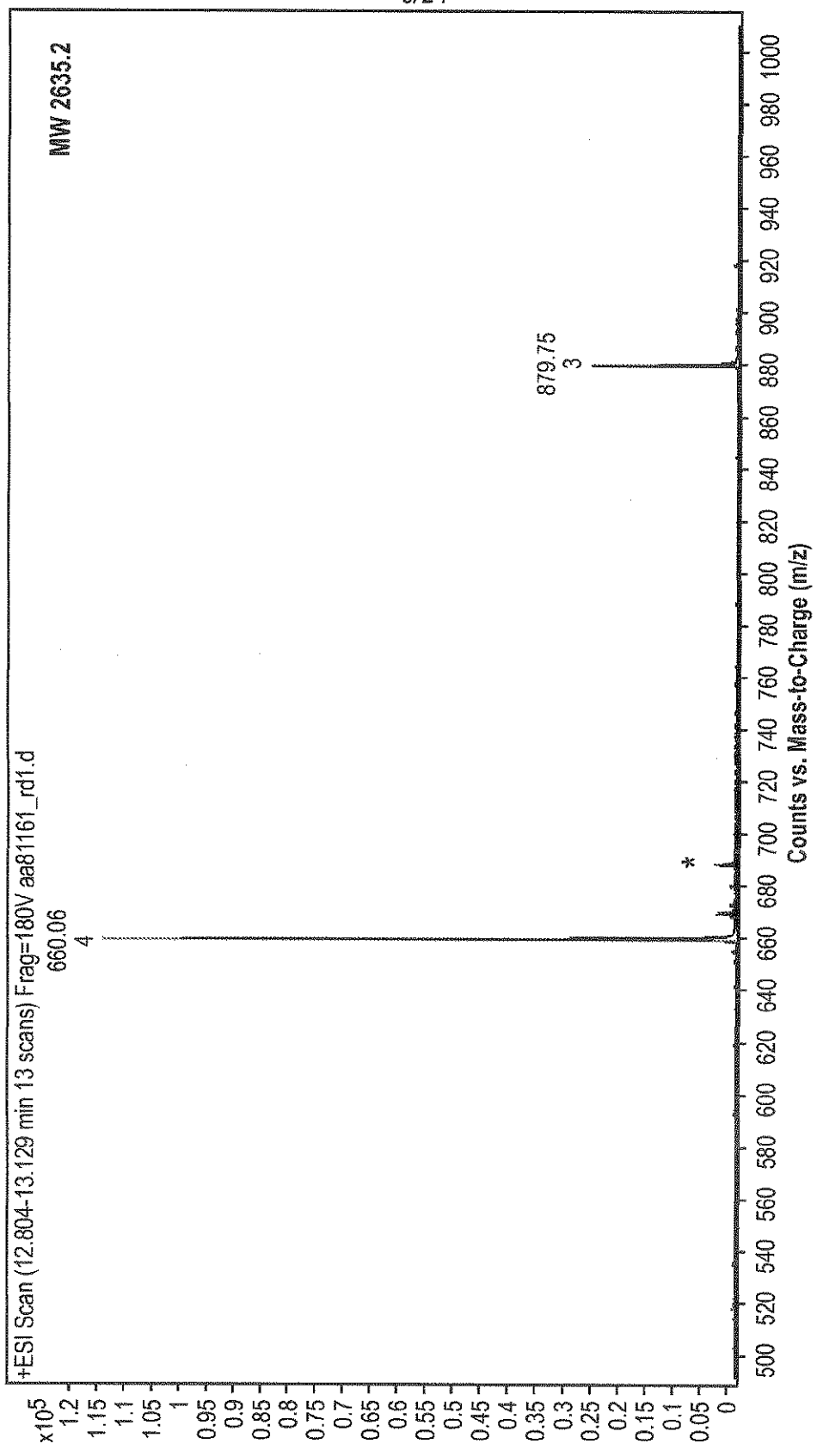

+ESI Scan (12.804-13.129 min 13 scans) Frag=180V aa81161_rd1.d
MW 2635.2
660.06
4
879.75
3
*
x10^5
Counts vs. Mass-to-Charge (m/z)

FIGURE 7 (continued)

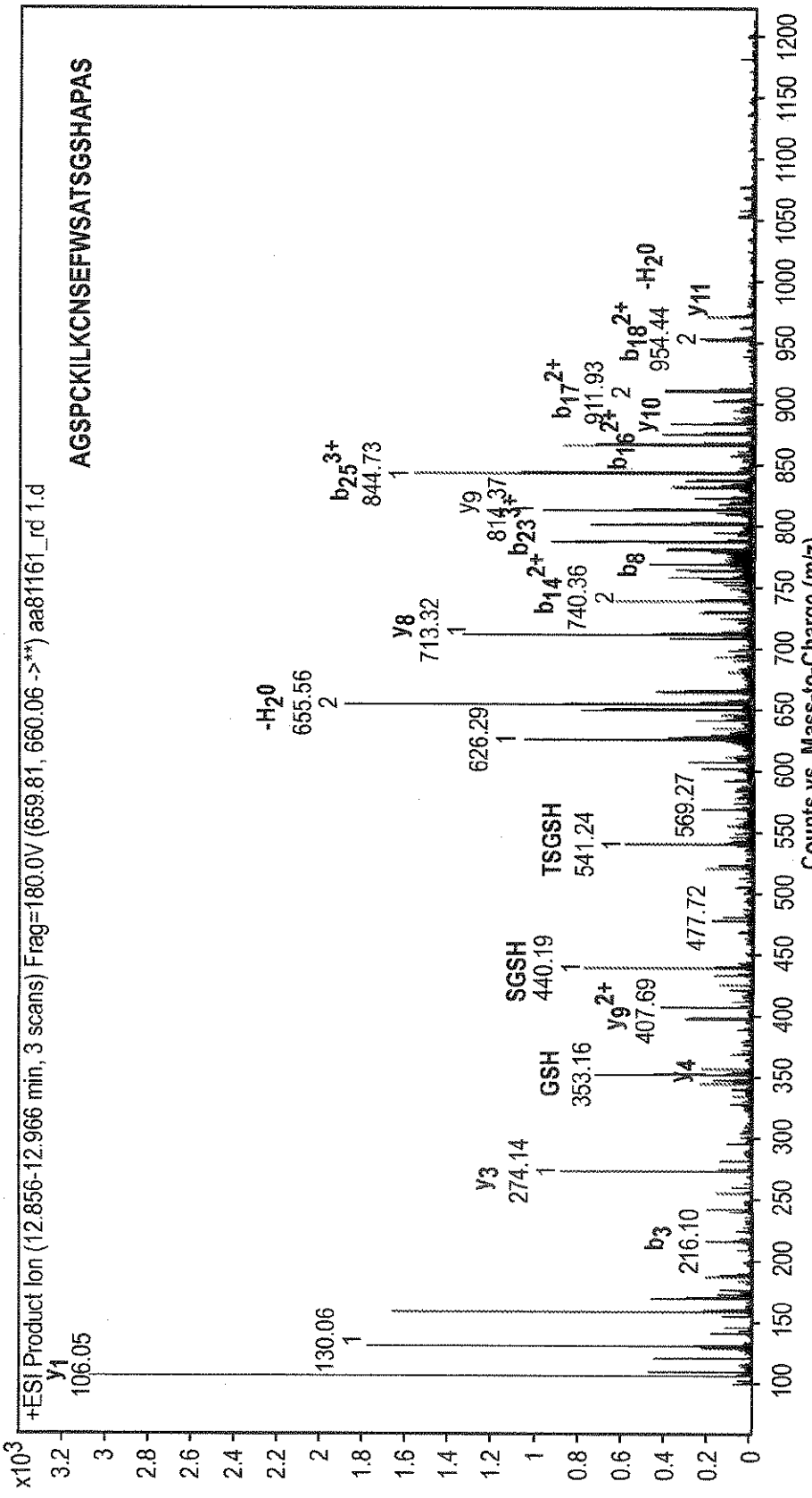
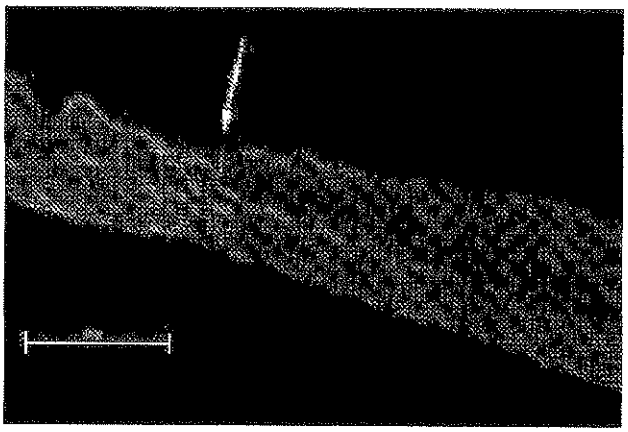
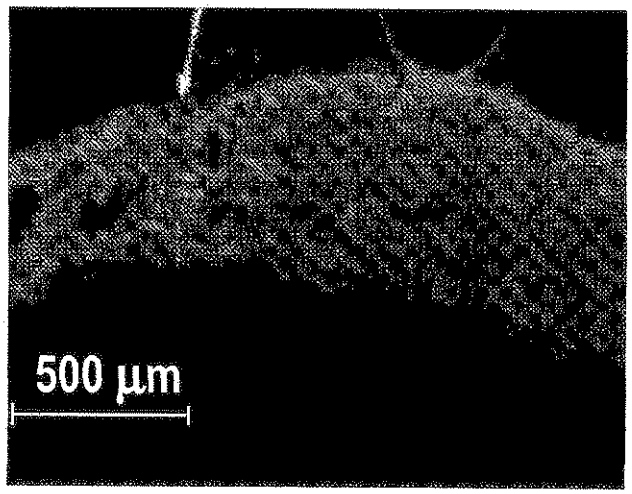


FIGURE 8

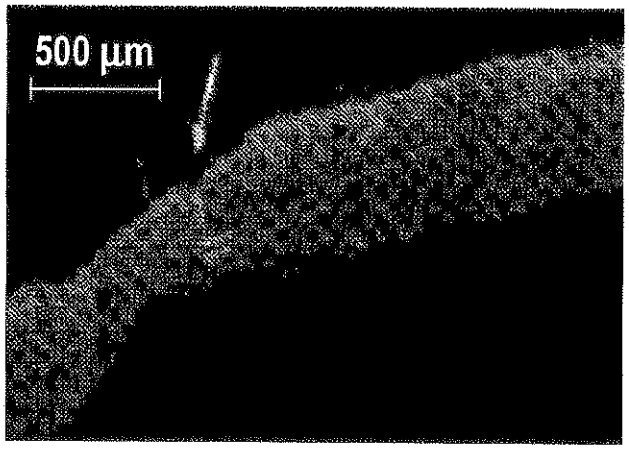
hIgG 10 mg/kg



AE12-11 mg/kg



h5F9.23 1 mg/kg



brain ⟶

FIGURE 9

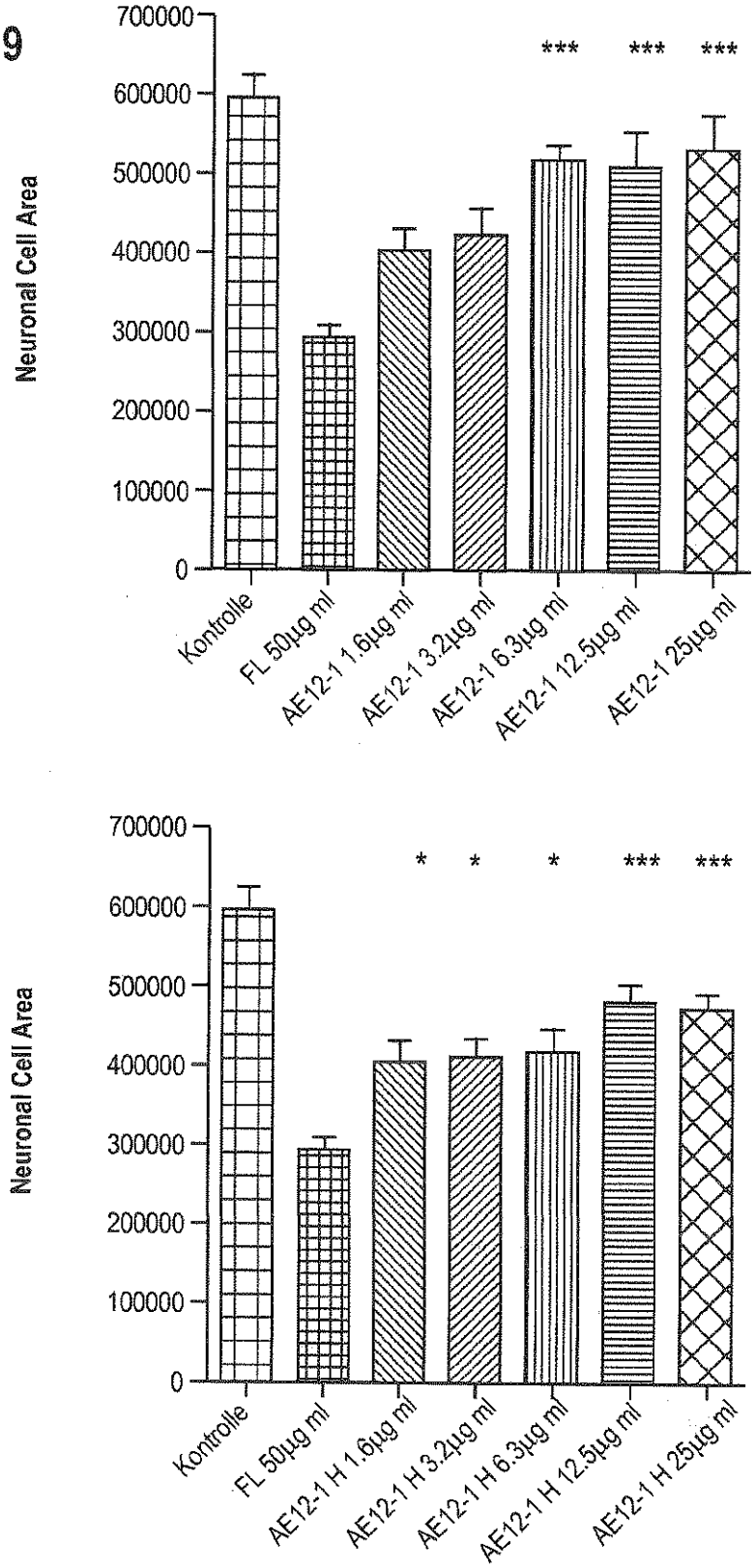

Neuronal Cell Area
700000
600000
500000
400000
300000
200000
100000
0
***
***
***
Kontrolle
FL 50µg ml
AE12-1 1.6µg ml
AE12-1 3.2µg ml
AE12-1 6.3µg ml
AE12-1 12.5µg ml
AE12-1 25µg ml
Neuronal Cell Area
700000
600000
500000
400000
300000
200000
100000
0
*
*
*
***
***
Kontrolle
FL 50µg ml
AE12-1 H 1.6µg ml
AE12-1 H 3.2µg ml
AE12-1 H 6.3µg ml
AE12-1 H 12.5µg ml
AE12-1 H 25µg ml

FIGURE 10

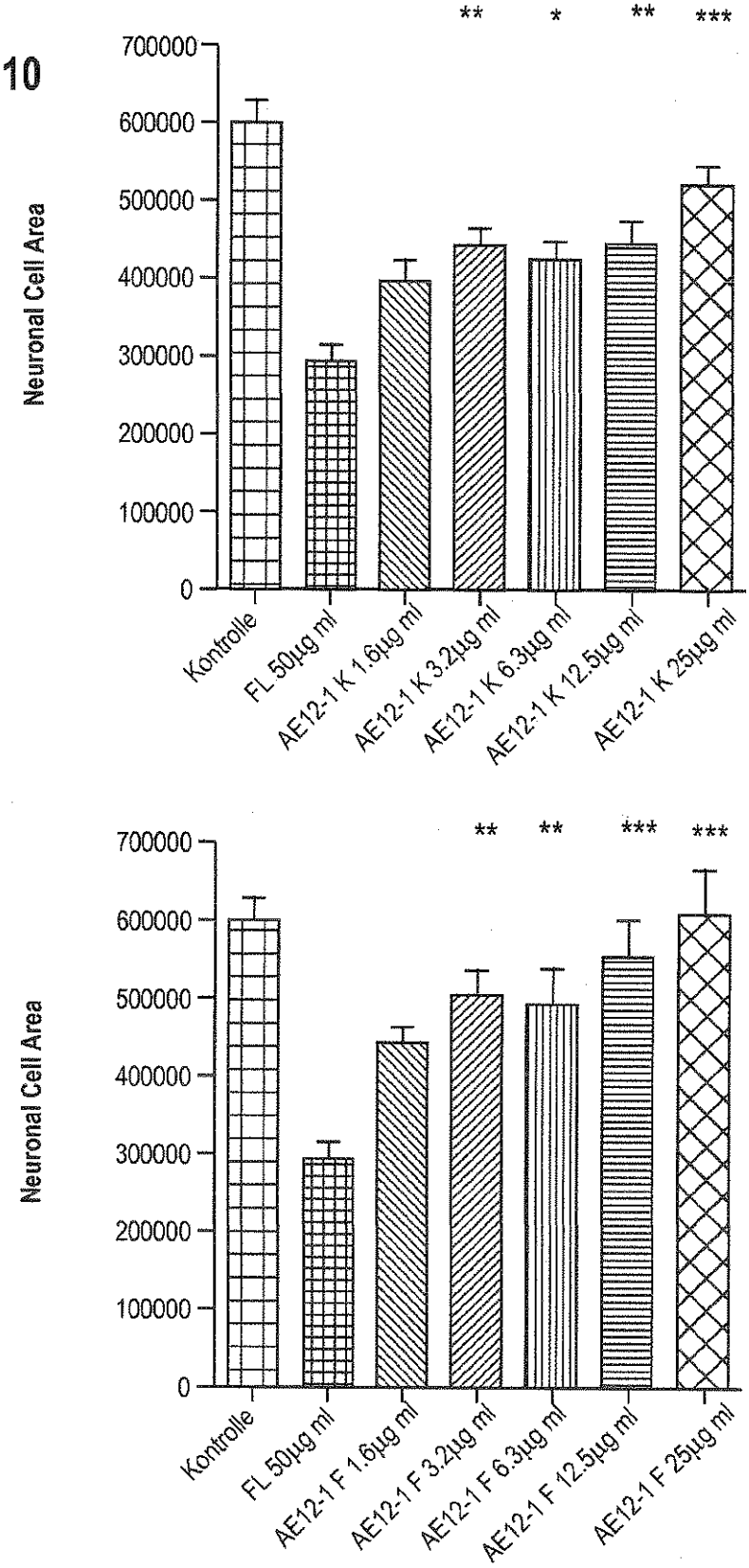

Neuronal Cell Area
700000
600000
500000
400000
300000
200000
100000
0
** * ** ***
Kontrolle
FL 50µg ml
AE12-1 K 1.6µg ml
AE12-1 K 3.2µg ml
AE12-1 K 6.3µg ml
AE12-1 K 12.5µg ml
AE12-1 K 25µg ml
Neuronal Cell Area
700000
600000
500000
400000
300000
200000
100000
0
** ** *** ***
Kontrolle
FL 50µg ml
AE12-1 F 1.6µg ml
AE12-1 F 3.2µg ml
AE12-1 F 6.3µg ml
AE12-1 F 12.5µg ml
AE12-1 F 25µg ml

FIGURE 11

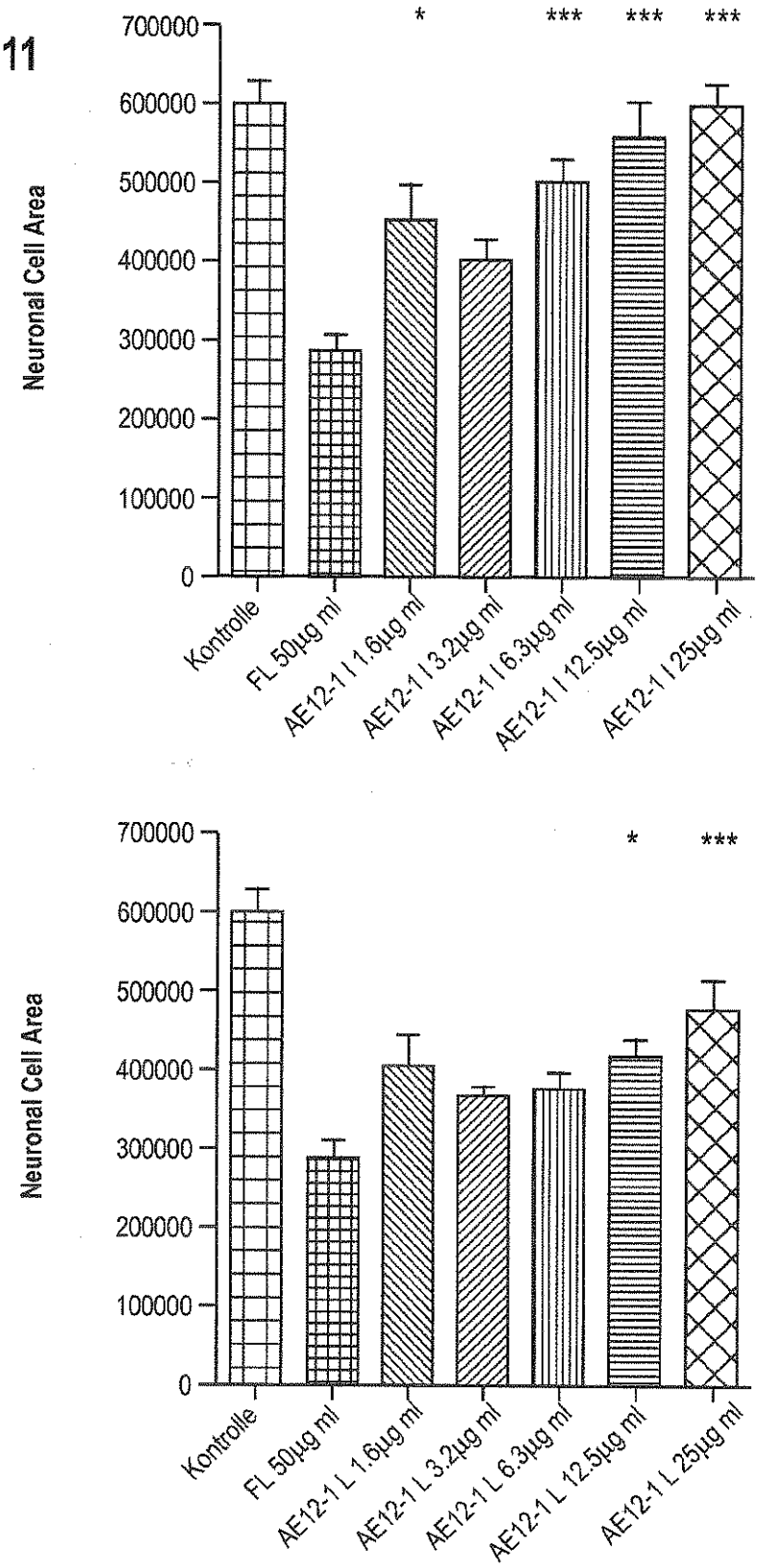

Neuronal Cell Area
700000
600000
500000
400000
300000
200000
100000
0
*
***
***
***
Kontrolle
FL 50µg ml
AE12-1 I 1.6µg ml
AE12-1 I 3.2µg ml
AE12-1 I 6.3µg ml
AE12-1 I 12.5µg ml
AE12-1 I 25µg ml
Neuronal Cell Area
700000
600000
500000
400000
300000
200000
100000
0
*
***
Kontrolle
FL 50µg ml
AE12-1 L 1.6µg ml
AE12-1 L 3.2µg ml
AE12-1 L 6.3µg ml
AE12-1 L 12.5µg ml
AE12-1 L 25µg ml

FIGURE 12

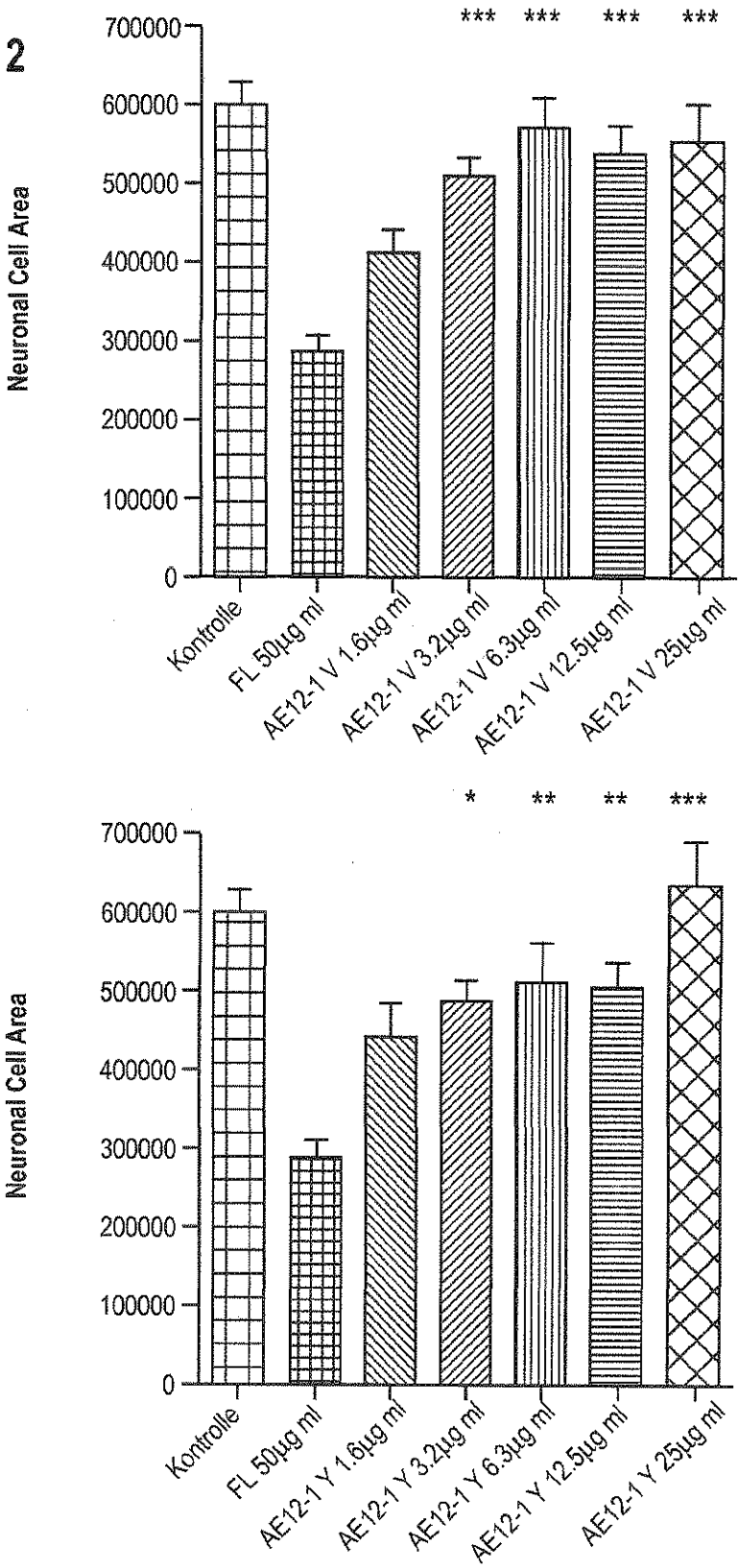

Neuronal Cell Area
700000
600000
500000
400000
300000
200000
100000
0
*** *** *** ***
Kontrolle
FL 50µg ml
AE12-1 V 1.6µg ml
AE12-1 V 3.2µg ml
AE12-1 V 6.3µg ml
AE12-1 V 12.5µg ml
AE12-1 V 25µg ml
Neuronal Cell Area
700000
600000
500000
400000
300000
200000
100000
0
* ** ** ***
Kontrolle
FL 50µg ml
AE12-1 Y 1.6µg ml
AE12-1 Y 3.2µg ml
AE12-1 Y 6.3µg ml
AE12-1 Y 12.5µg ml
AE12-1 Y 25µg ml

FIGURE 13

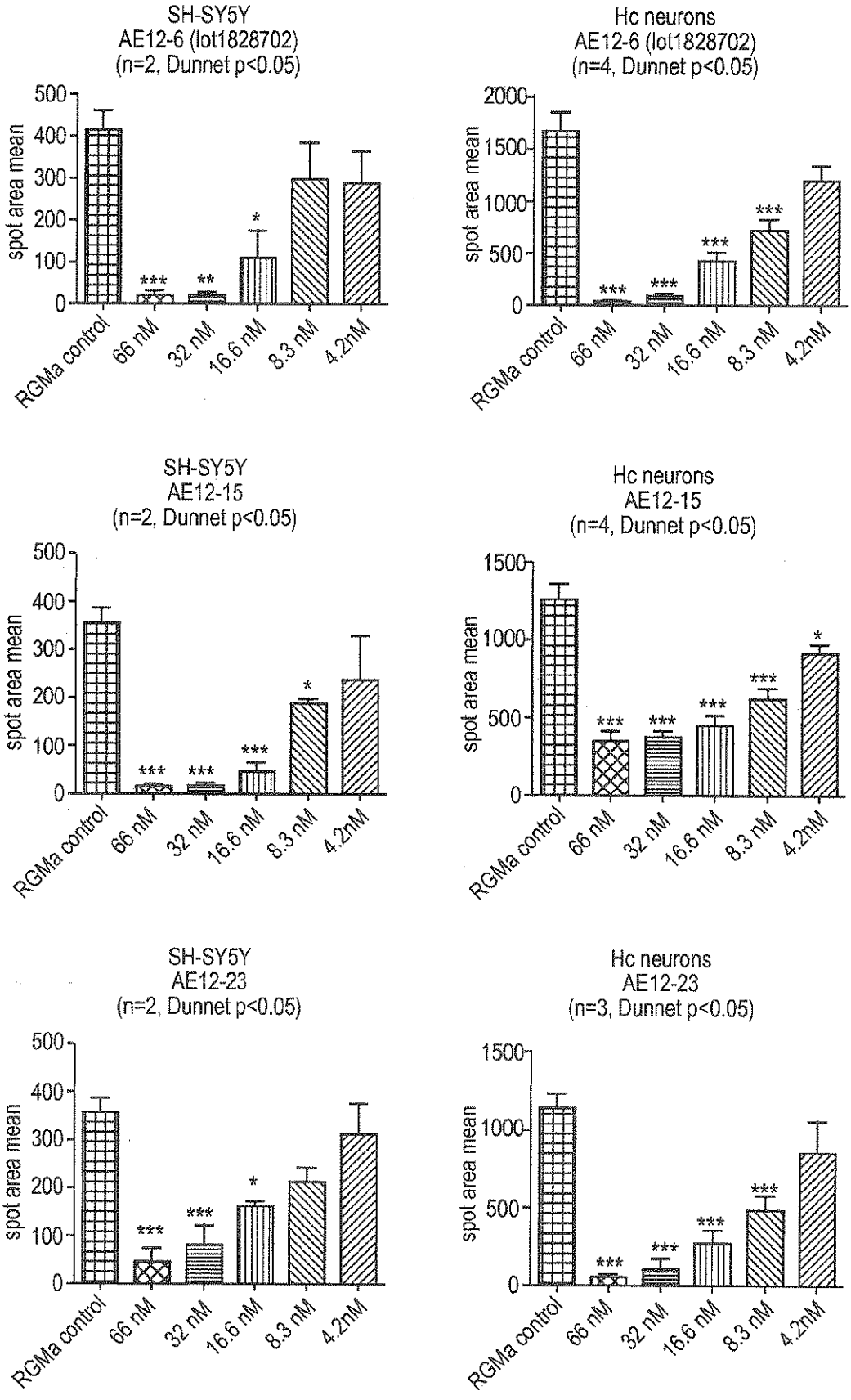

SH-SY5Y
AE12-6 (lot1828702)
(n=2, Dunnet p<0.05)
Hc neurons
AE12-6 (lot1828702)
(n=4, Dunnet p<0.05)
SH-SY5Y
AE12-15
(n=2, Dunnet p<0.05)
Hc neurons
AE12-15
(n=4, Dunnet p<0.05)
SH-SY5Y
AE12-23
(n=2, Dunnet p<0.05)
Hc neurons
AE12-23
(n=3, Dunnet p<0.05)
spot area mean
RGMa control
66 nM
32 nM
16.6 nM
8.3 nM
4.2nM

FIGURE 14

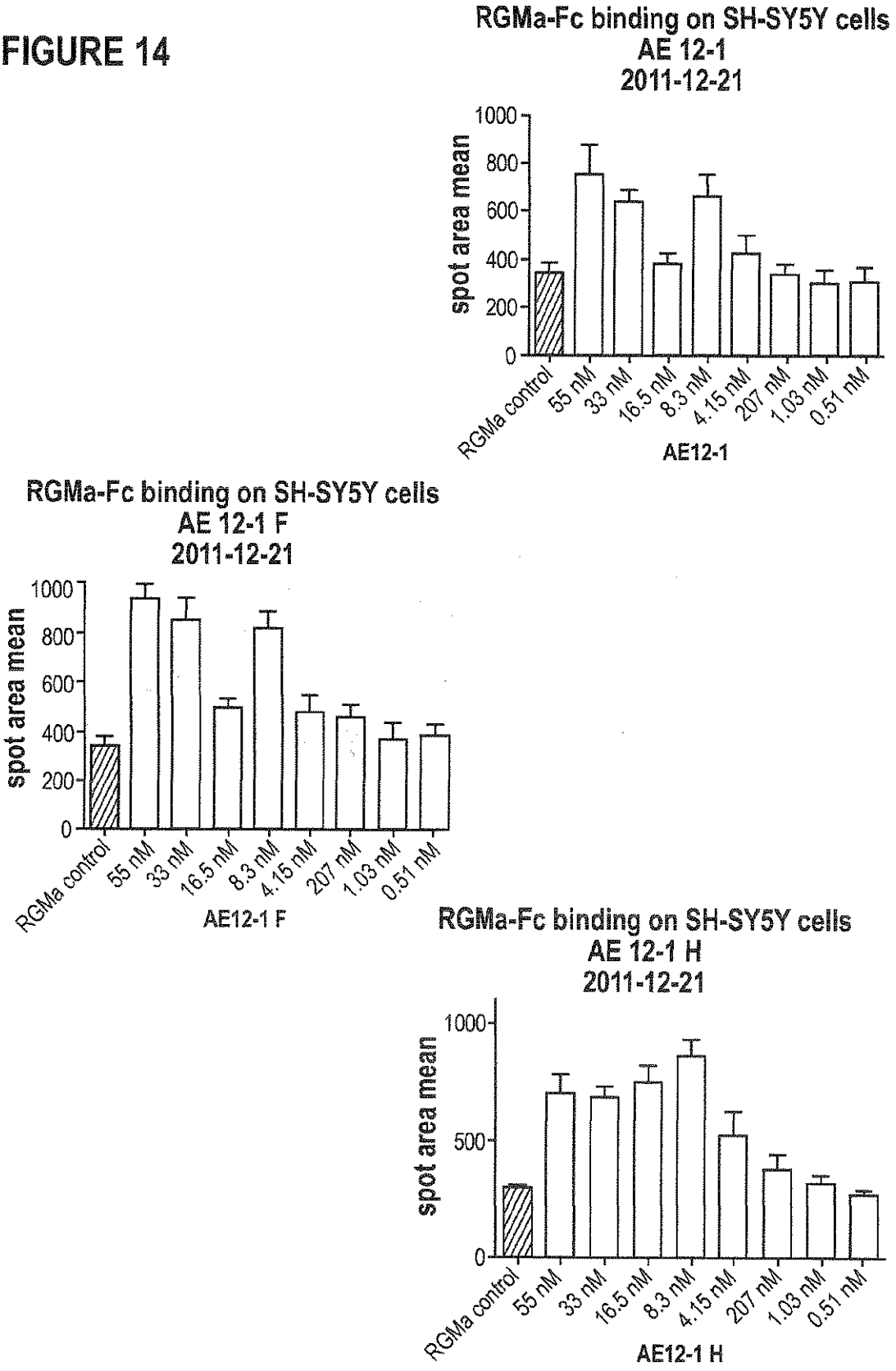
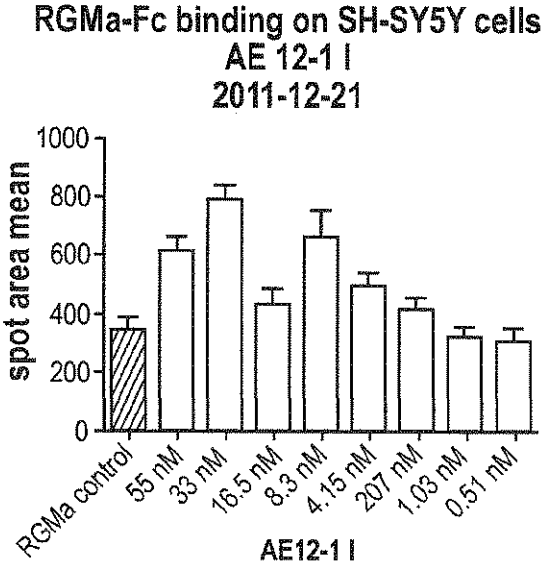
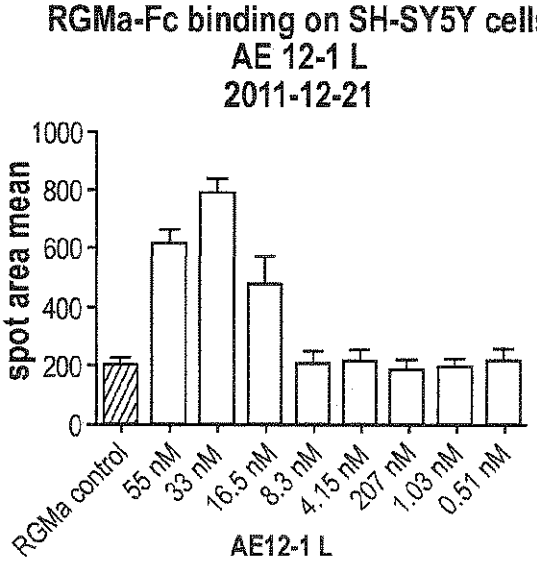

RGMa-Fc binding on SH-SY5Y cells
AE 12-1
2011-12-21
spot area mean
1000
800
600
400
200
0
RGMa control
55 nM
33 nM
16.5 nM
8.3 nM
4.15 nM
207 nM
1.03 nM
0.51 nM
AE12-1
RGMa-Fc binding on SH-SY5Y cells
AE 12-1 F
2011-12-21
spot area mean
1000
800
600
400
200
0
RGMa control
55 nM
33 nM
16.5 nM
8.3 nM
4.15 nM
207 nM
1.03 nM
0.51 nM
AE12-1 F
RGMa-Fc binding on SH-SY5Y cells
AE 12-1 H
2011-12-21
spot area mean
1000
500
0
RGMa control
55 nM
33 nM
16.5 nM
8.3 nM
4.15 nM
207 nM
1.03 nM
0.51 nM
AE12-1 H

FIGURE 14 (continued)





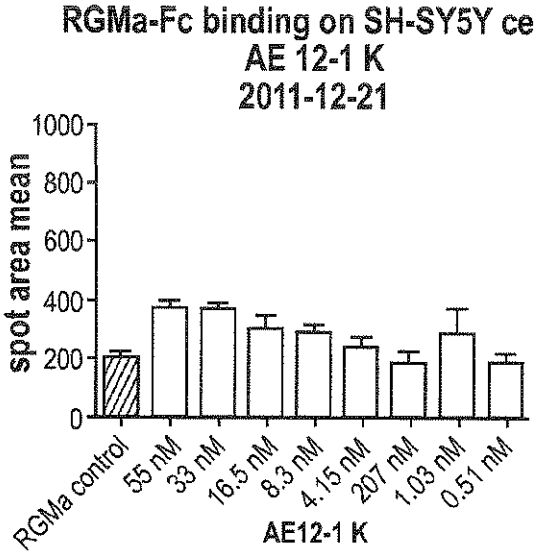
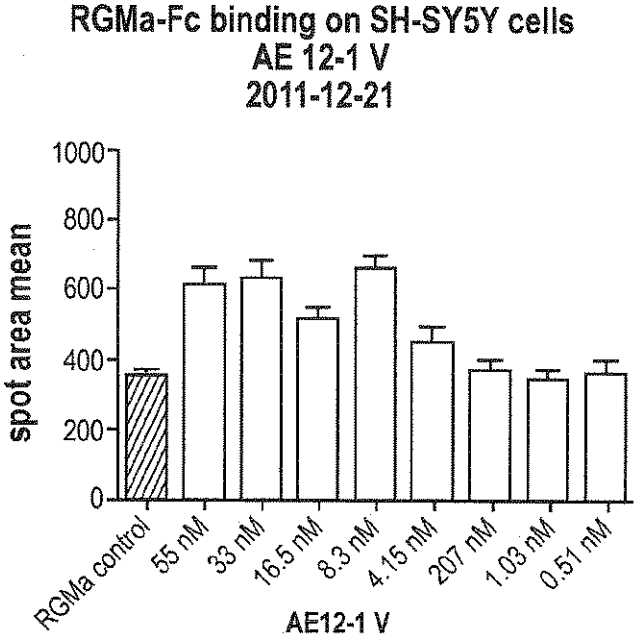


FIGURE 14 (continued)



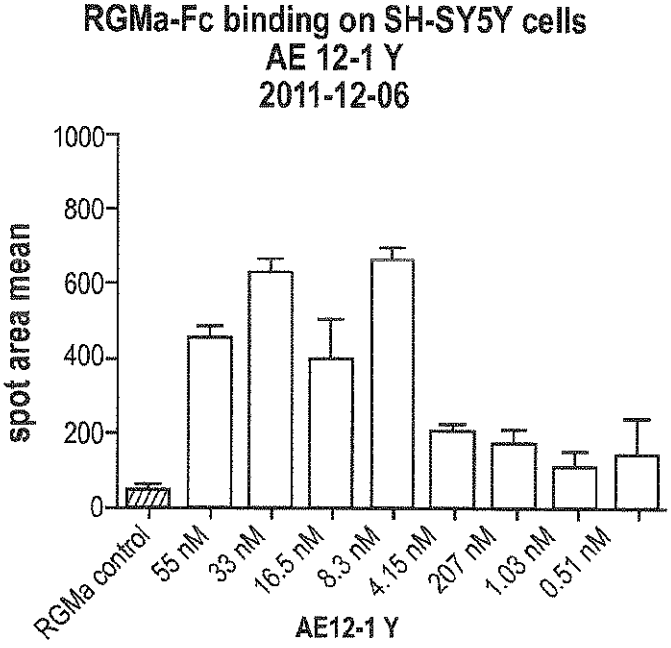


FIGURE 15

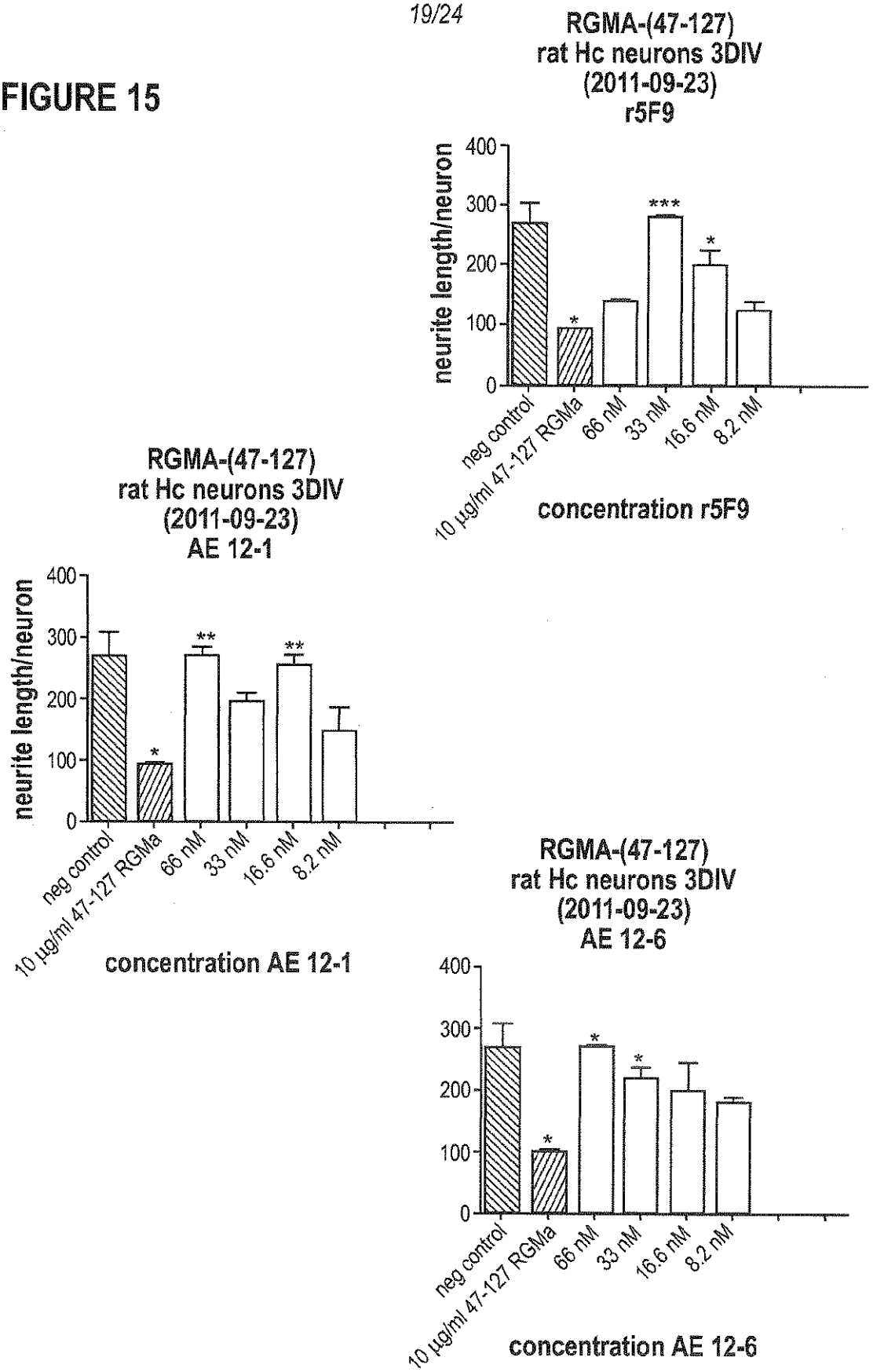

RGMA-(47-127)
rat Hc neurons 3DIV
(2011-09-23)
r5F9
neurite length/neuron
400
300
200
100
0
***
*
*
neg control
10 µg/ml 47-127 RGMa
66 nM
33 nM
16.6 nM
8.2 nM
concentration r5F9
RGMA-(47-127)
rat Hc neurons 3DIV
(2011-09-23)
AE 12-1
neurite length/neuron
400
300
200
100
0
**
**
*
neg control
10 µg/ml 47-127 RGMa
66 nM
33 nM
16.6 nM
8.2 nM
concentration AE 12-1
RGMA-(47-127)
rat Hc neurons 3DIV
(2011-09-23)
AE 12-6
400
300
200
100
0
*
*
*
neg control
10 µg/ml 47-127 RGMa
66 nM
33 nM
16.6 nM
8.2 nM
concentration AE 12-6

FIGURE 16

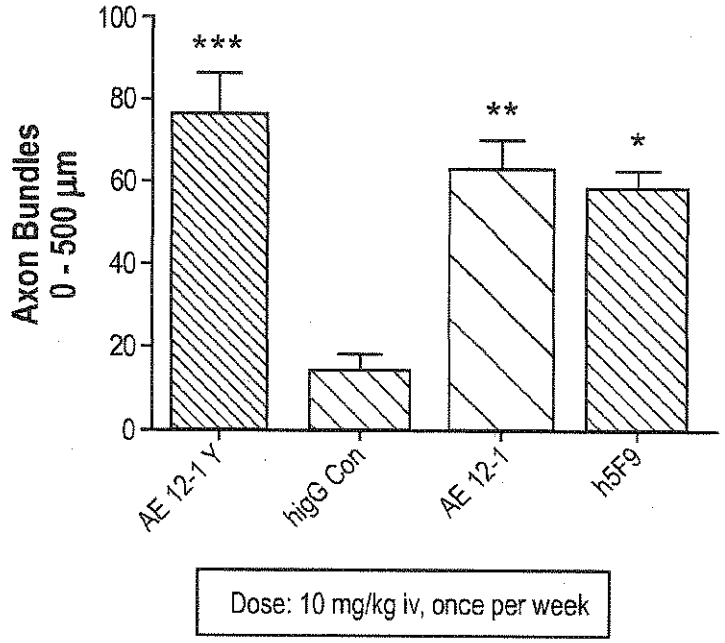
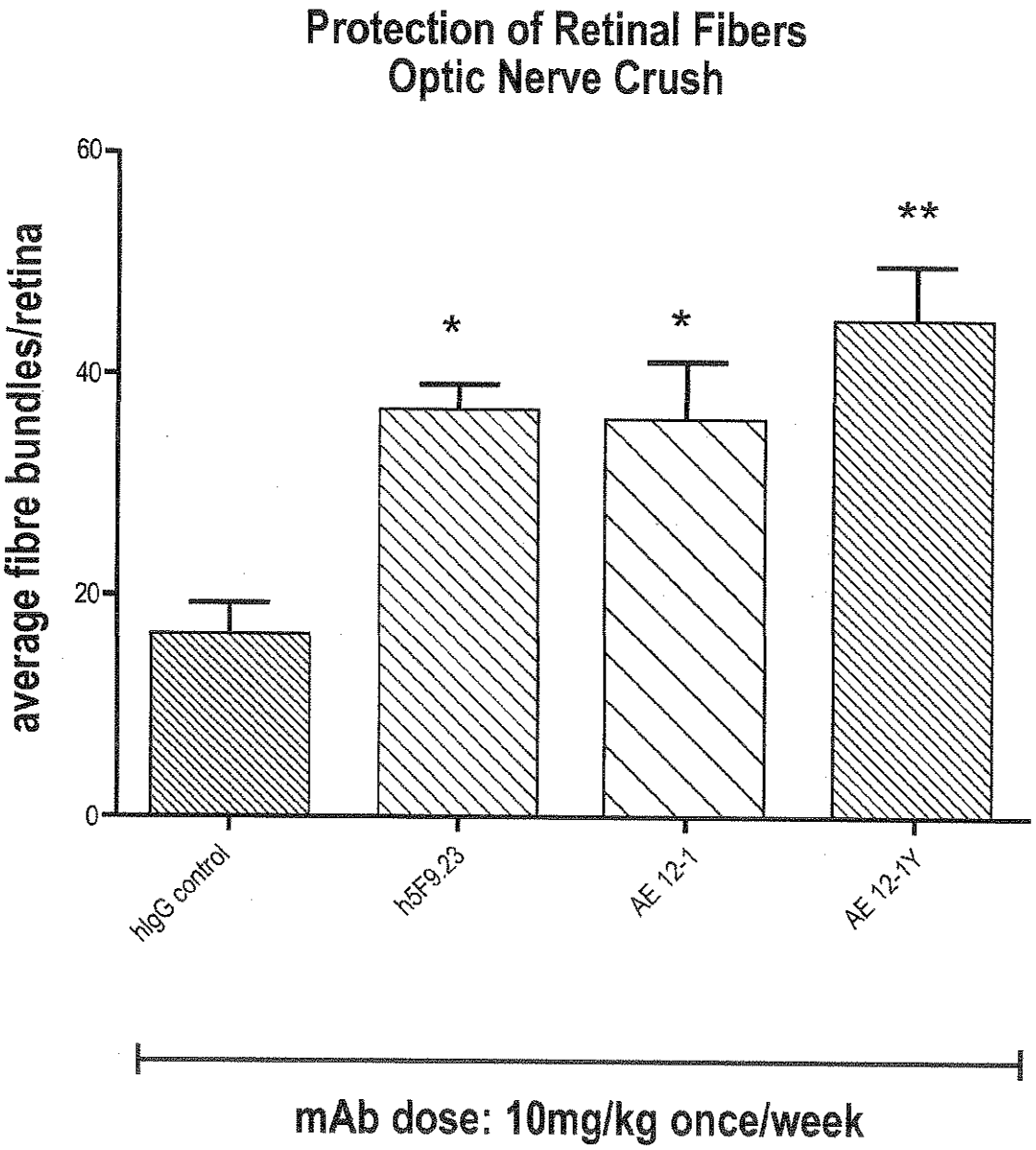

Axon Bundles
0 - 500 µm
100
80
60
40
20
0
***
**
*
AE 12-1 Y
higG Con
AE 12-1
h5Fg
Dose: 10 mg/kg iv, once per week

FIGURE 17


Protection of Retinal Fibers
Optic Nerve Crush
average fibre bundles/retina
60
40
20
0
*
*
**
hIgG control
h5F9.23
AE 12-1
AE 12-1Y
mAb dose: 10mg/kg once/week

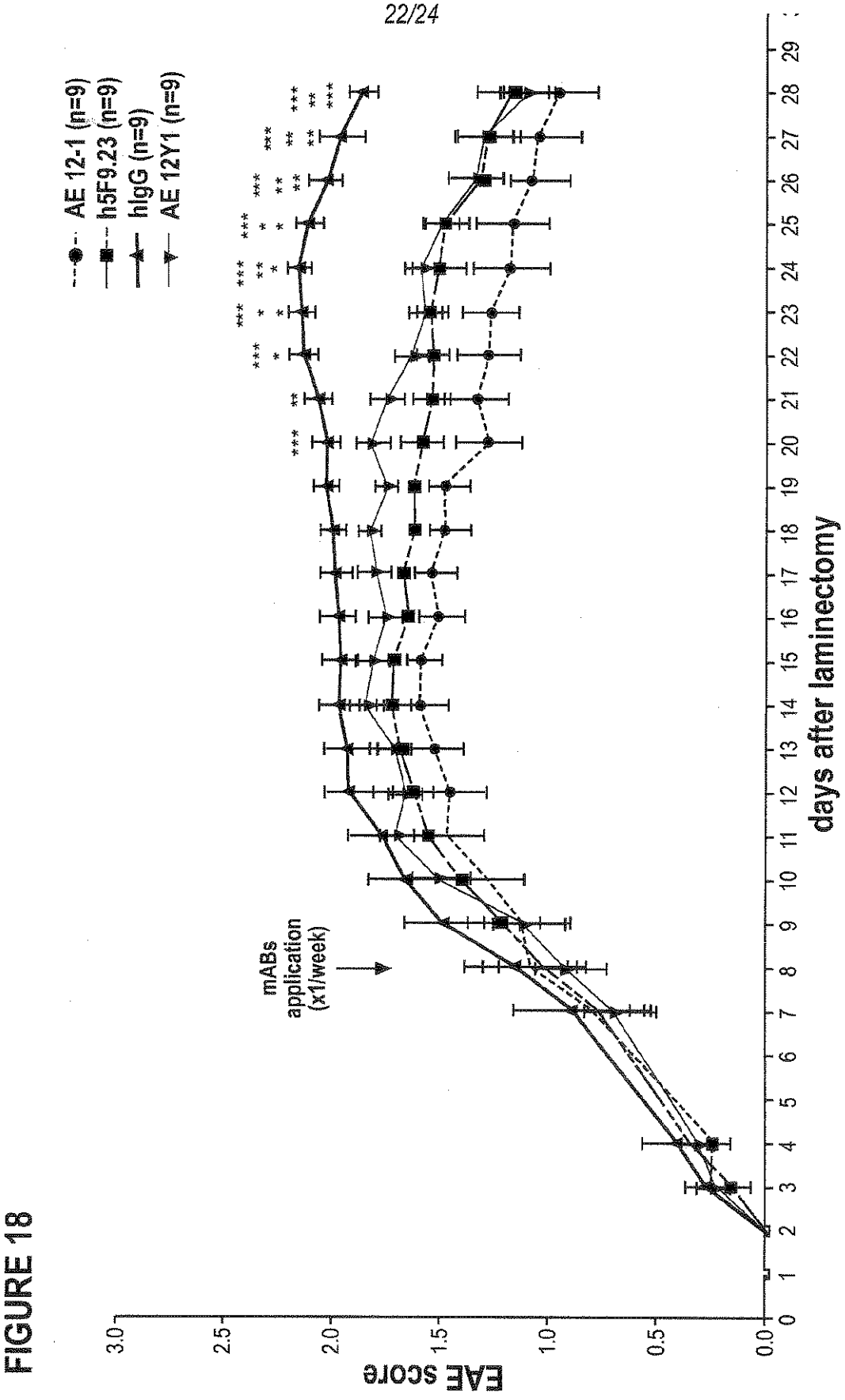

AE 12-1 (n=9)
h5F9.23 (n=9)
hIgG (n=9)
AE 12Y1 (n=9)
mABs application (x1/week)
EAE score
days after laminectomy
0.0
0.5
1.0
1.5
2.0
2.5
3.0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29

FIGURE 18

FIGURE 19

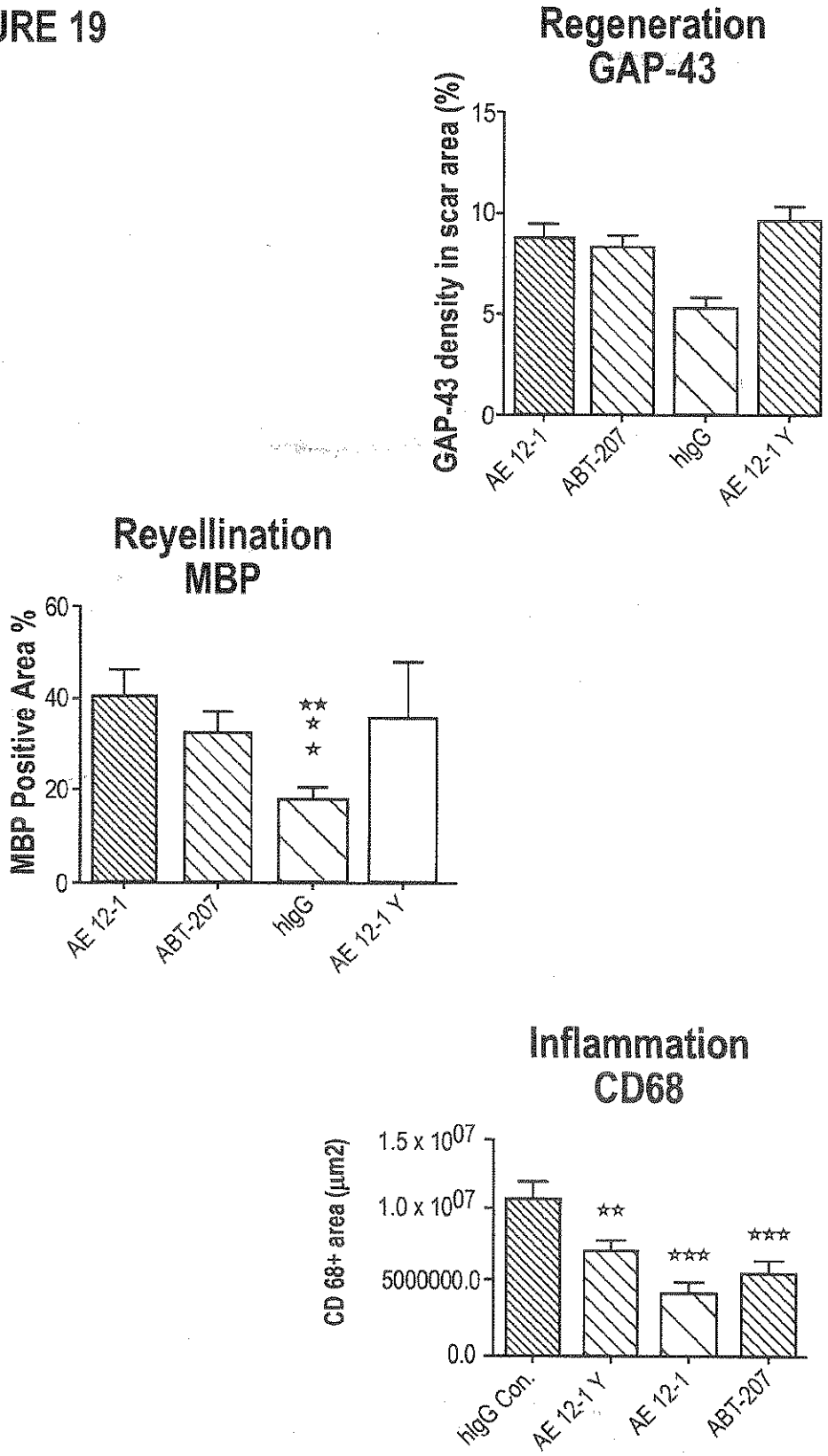
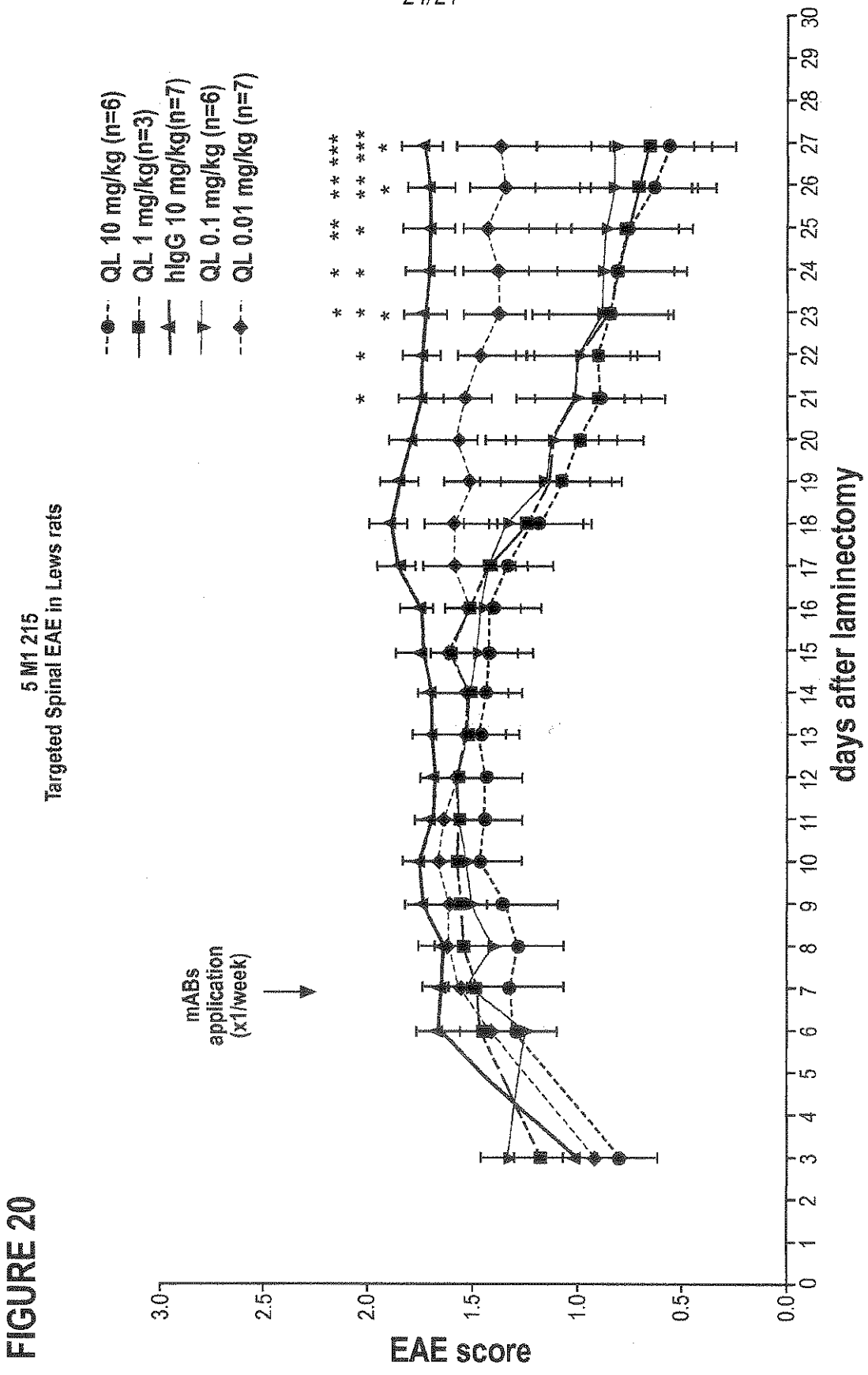

Regeneration
GAP-43
GAP-43 density in scar area (%)
15
10
5
0
AE 12-1
ABT-207
hIgG
AE 12-1 Y
Reyellination
MBP
MBP Positive Area %
60
40
20
0
AE 12-1
ABT-207
hIgG
AE 12-1 Y
Inflammation
CD68
CD 68+ area (µm2)
1.5 x 10^07
1.0 x 10^07
5000000.0
0.0
hIgG Con.
AE 12-1 Y
AE 12-1
ABT-207

FIGURE 20


5 M1 215
Targeted Spinal EAE in Lews rats
QL 10 mg/kg (n=6)
QL 1 mg/kg(n=3)
hIgG 10 mg/kg(n=7)
QL 0.1 mg/kg (n=6)
QL 0.01 mg/kg (n=7)
mABs application (x1/week)
EAE score
days after laminectomy
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0 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