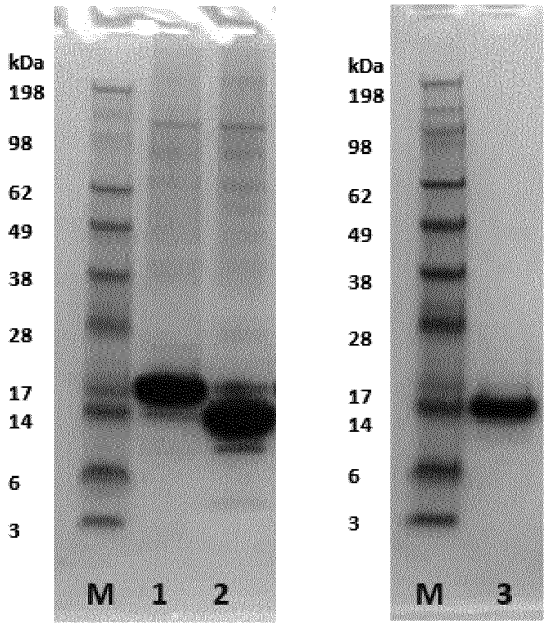
Fig. 1

A


kDa
198
98
62
49
38
28
17
14
6
3
M
1
2
kDa
198
98
62
49
38
28
17
14
6
3
M
3

B

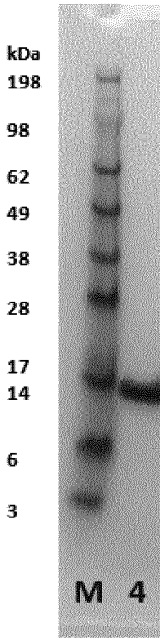

kDa
198
98
62
49
38
28
17
14
6
3
M
4

Fig. 2

A

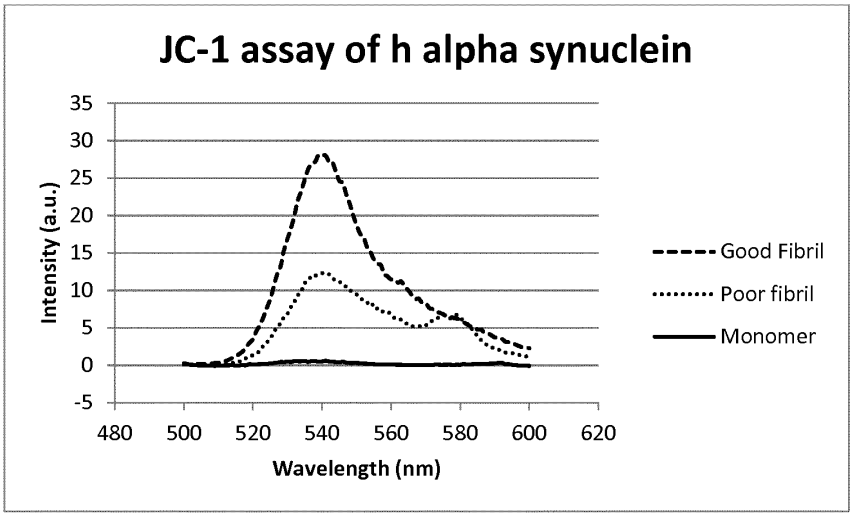

JC-1 assay of h alpha synuclein
Intensity (a.u.)
35
30
25
20
15
10
5
0
-5
480
500
520
540
560
580
600
620
Wavelength (nm)
Good Fibril
Poor fibril
Monomer

Fig. 2 (cont.)

B

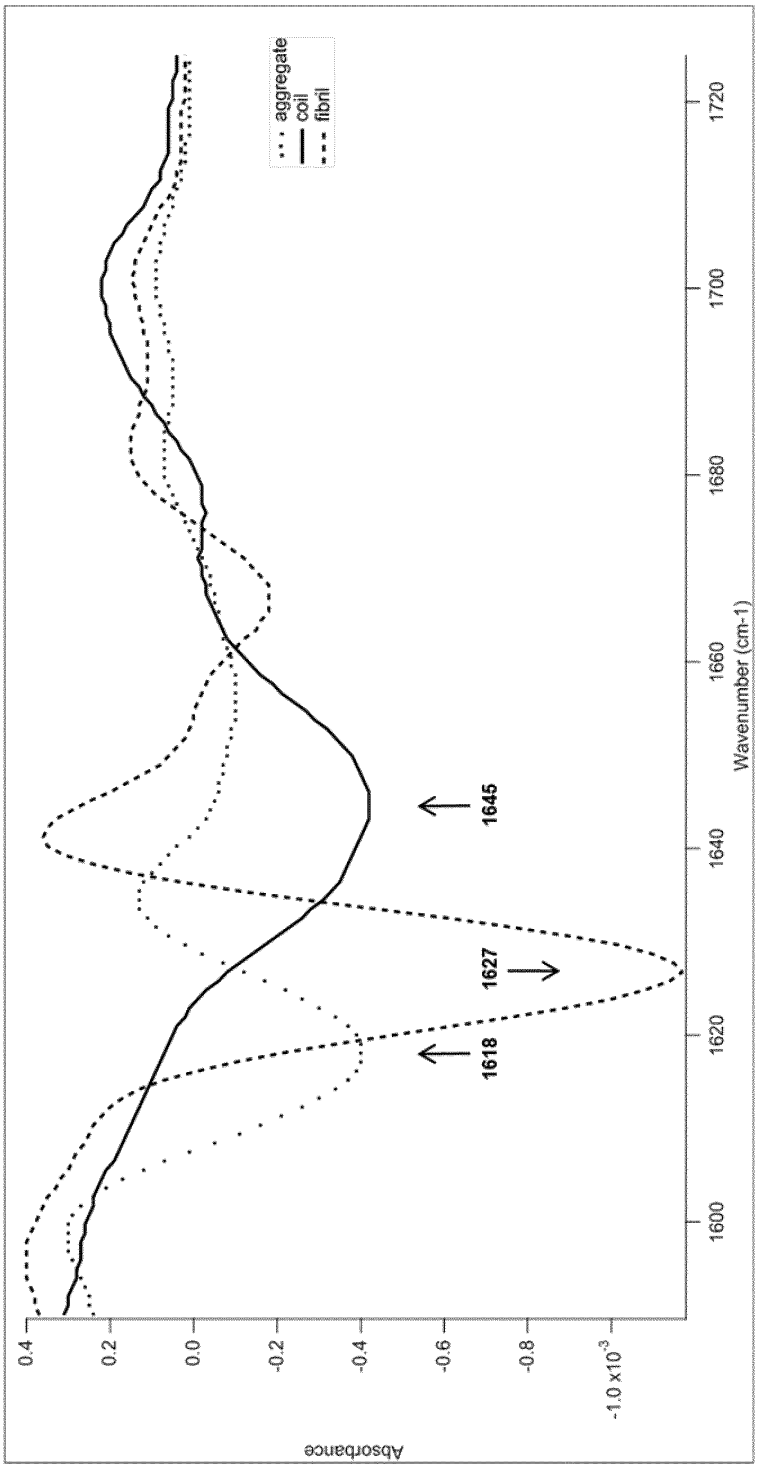

aggregate
coil
fibril
1645
1627
1618
Wavenumber (cm-1)
1600
1620
1640
1660
1680
1700
1720
Absorbance
0.4
0.2
0.0
-0.2
-0.4
-0.6
-0.8
-1.0 x10-3

Fig. 3

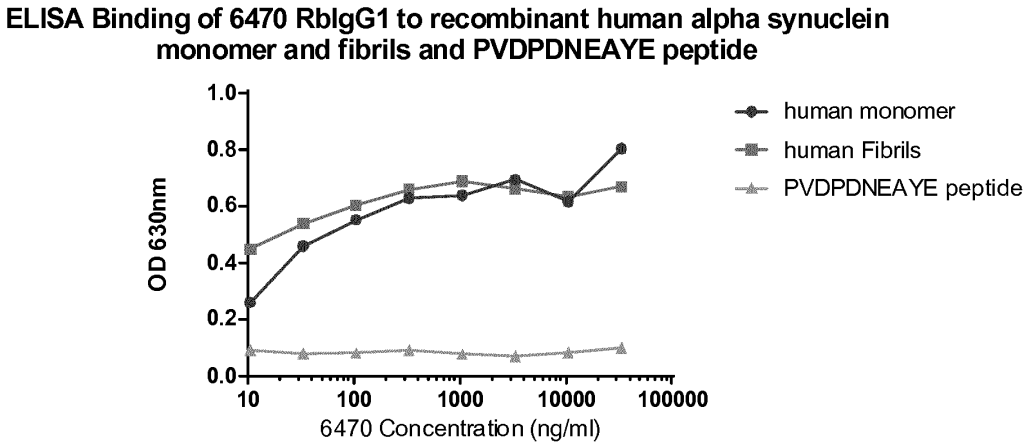
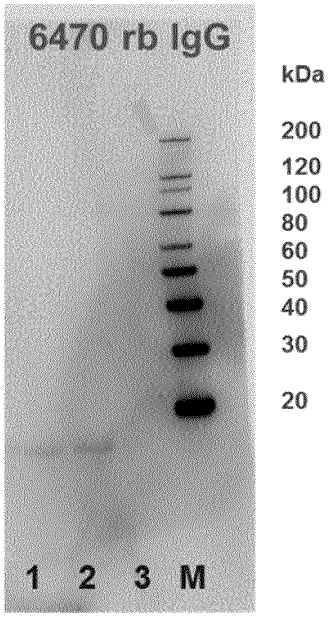

ELISA Binding of 6470 RbIgG1 to recombinant human alpha synuclein monomer and fibrils and PVDPDNEAYE peptide
OD 630nm
1.0
0.8
0.6
0.4
0.2
0.0
10
100
1000
10000
100000
6470 Concentration (ng/ml)
human monomer
human Fibrils
PVDPDNEAYE peptide

Fig. 4

A


6470 rb IgG
kDa
200
120
100
80
60
50
40
30
20
1 2 3 M

B

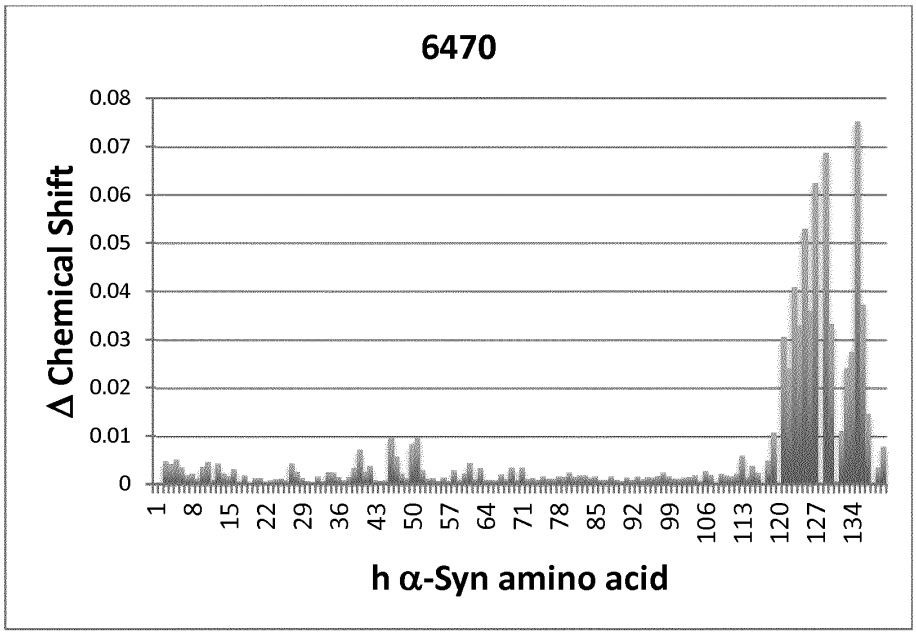

6470
Δ Chemical Shift
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
1 8 15 22 29 36 43 50 57 64 71 78 85 92 99 106 113 120 127 134
h α-Syn amino acid

Fig. 5

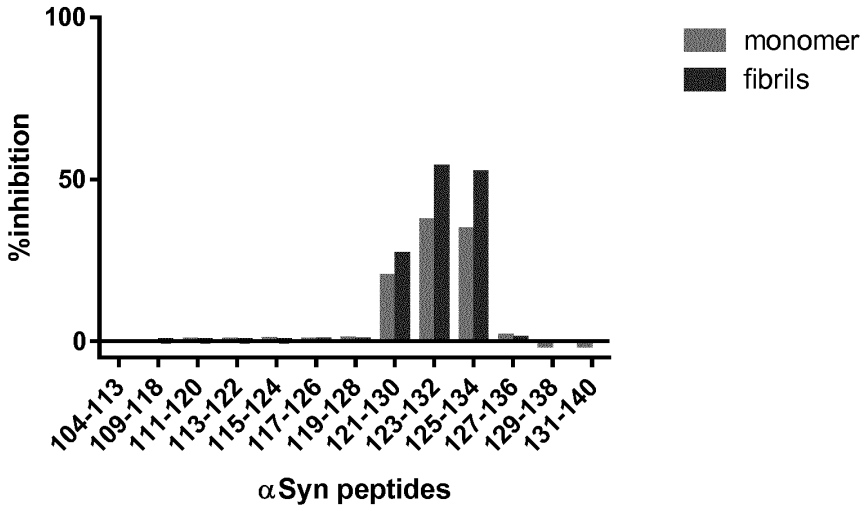

100
50
0
%inhibition
monomer
fibrils
104-113
109-118
111-120
113-122
115-124
117-126
119-128
121-130
123-132
125-134
127-136
129-138
131-140
αSyn peptides

Fig. 6

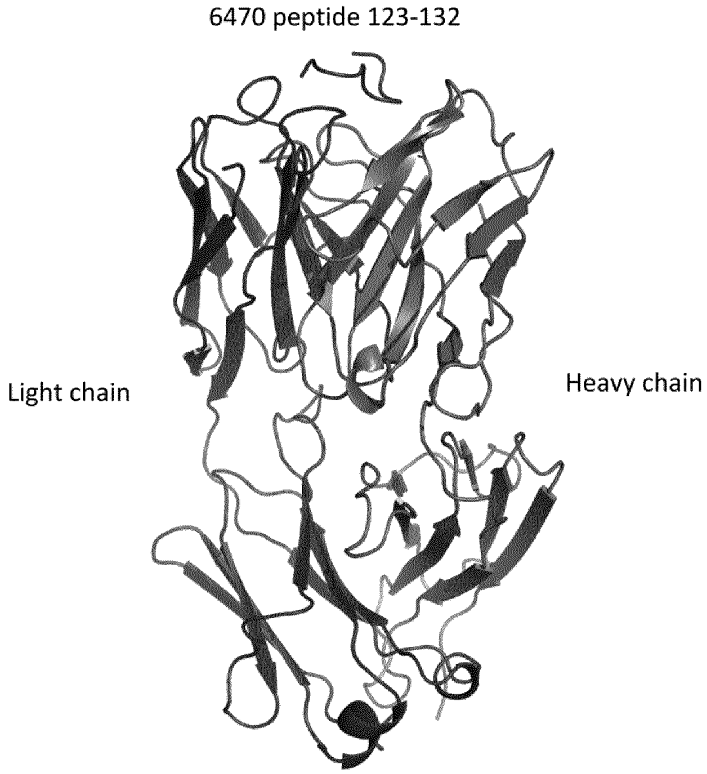


Fig. 7

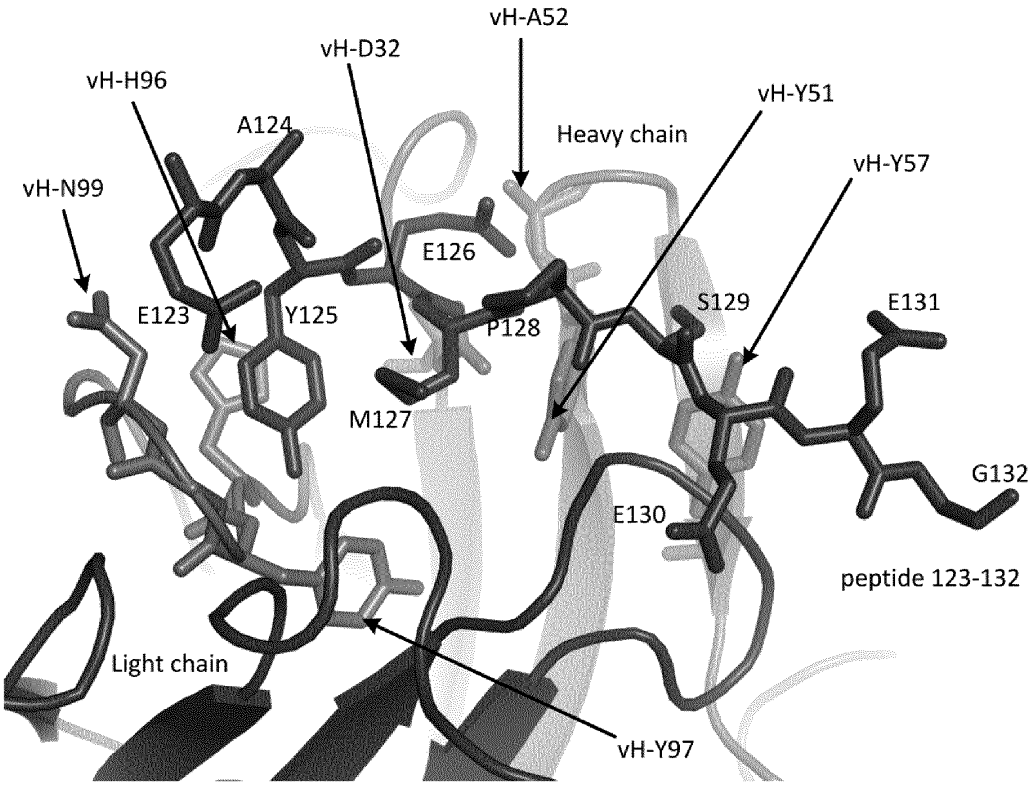

vH-A52
vH-D32
vH-H96
vH-Y51
A124
Heavy chain
vH-Y57
vH-N99
E126
E123
Y125
P128
S129
E131
M127
G132
E130
peptide 123-132
Light chain
vH-Y97

Fig. 8

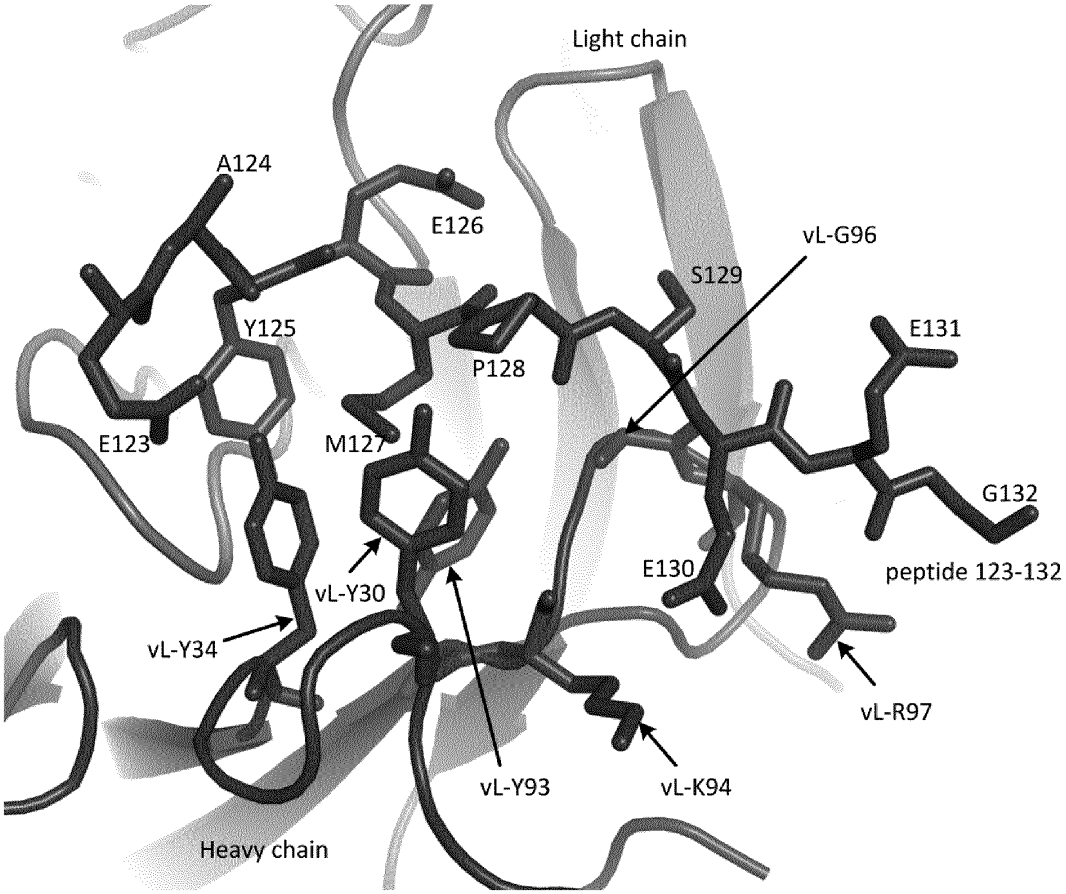

Light chain
A124
E126
vL-G96
S129
Y125
E131
P128
E123
M127
G132
E130
peptide 123-132
vL-Y30
vL-Y34
vL-R97
vL-Y93
vL-K94
Heavy chain

Fig. 9

```
                    1   5   10  15  20  25  30  35  40  45  50  55  60  65  70  75  80  85  90  95 | 100 105
Light 6470          AIVMTQTPSSKSVAVGDTVTINCQASQSVYKNNYLAWFQQKPGQPPKQLIYGASTLASGVPSRFKGSGSGTQFTLTISDVVCDDAATYYCAGYKGGRNDGFAFGGGTEVVVK
                    | |   |   | ||  |   |  |||||||                 |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
IGKV1-16            DIQMTQSPSSLSASVGDRVTITCRASQGISN--YLAWFQQKPGKAPKSLIYAAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYNSYP---LTFGGGTKVEIK
                                                                                                                                  |
6470gL3             DIQMTQSPSSLSASVGDRVTITCQASQSVYKNNYLAWFQQKPGKAPKQLIYGASTLASGVPSRFSGSGSGTQFTLTISSLQPEDFATYYCAGYKGGRNDGFAFGGGTKVEIK
6470gL3 N33R        DIQMTQSPSSLSASVGDRVTITCQASQSVYKNRYLAWFQQKPGKAPKQLIYGASTLASGVPSRFSGSGSGTQFTLTISSLQPEDFATYYCAGYKGGRNDGFAFGGGTKVEIK
```

Fig. 10

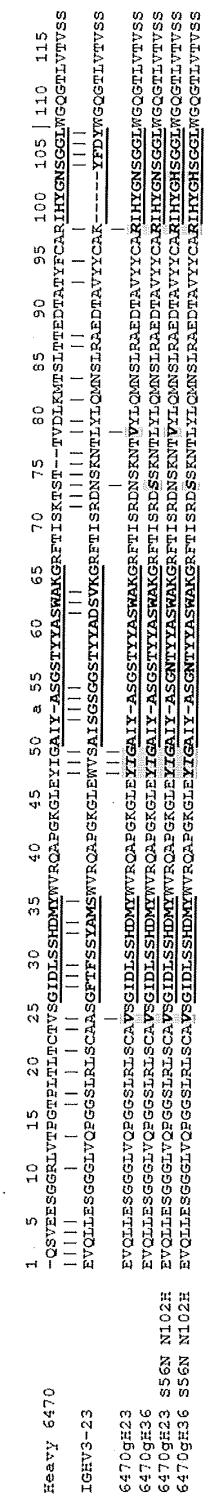

1 5 10 15 20 25 30 35 40 45 50 a 55 60 65 70 75 80 85 90 95 100 105 110 115
Heavy 6470
IGHV3-23
6470gH23
6470gH36
6470gH23 S56N N102H
6470gH36 S56N N102H

Fig. 11

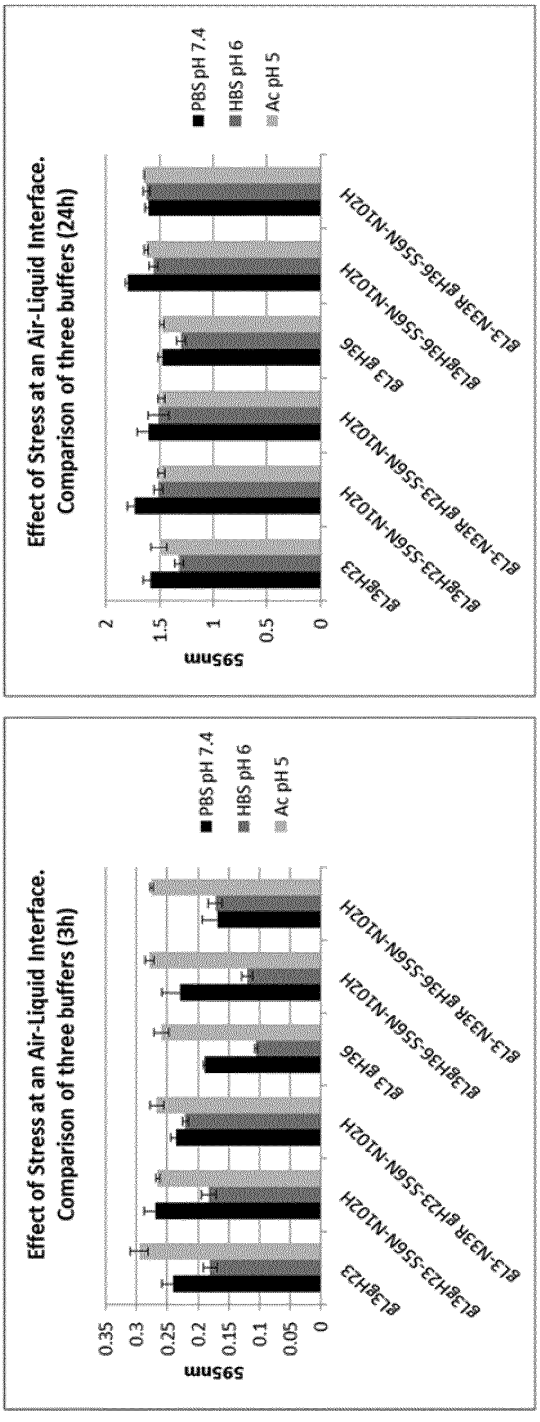

Effect of Stress at an Air-Liquid Interface.
Comparison of three buffers (24h)
PBS pH 7.4
HBS pH 6
Ac pH 5
595nm
0
0.5
1
1.5
2
βL3 βH23
βL3 βH23-S56N-N102H
βL3-N33R βH23-S56N-N102H
βL3 βH36
βL3 βH36-S56N-N102H
βL3-N33R βH36-S56N-N102H
Effect of Stress at an Air-Liquid Interface.
Comparison of three buffers (3h)
PBS pH 7.4
HBS pH 6
Ac pH 5
595nm
0
0.05
0.1
0.15
0.2
0.25
0.3
0.35
βL3 βH23
βL3 βH23-S56N-N102H
βL3-N33R βH23-S56N-N102H
βL3 βH36
βL3 βH36-S56N-N102H
βL3-N33R βH36-S56N-N102H

Fig. 12

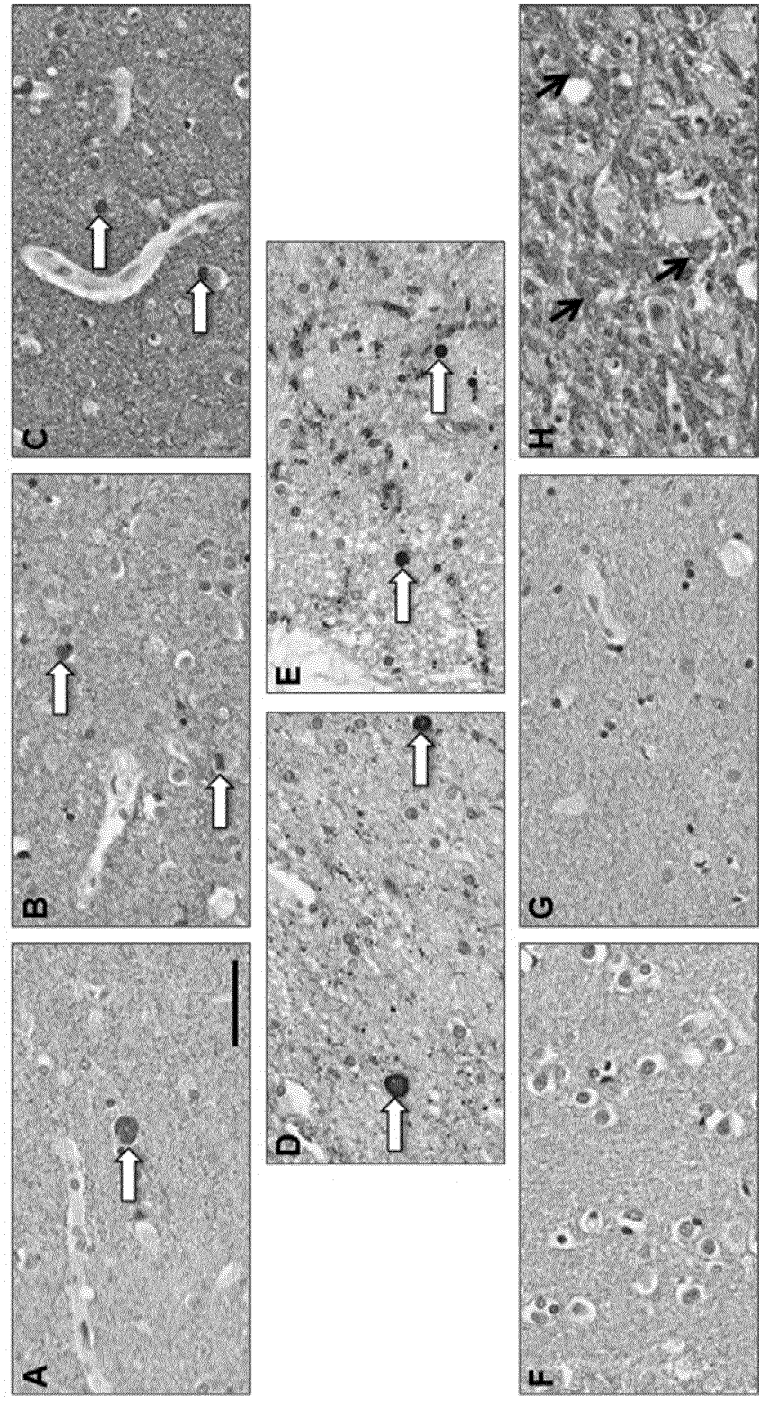


Fig. 13

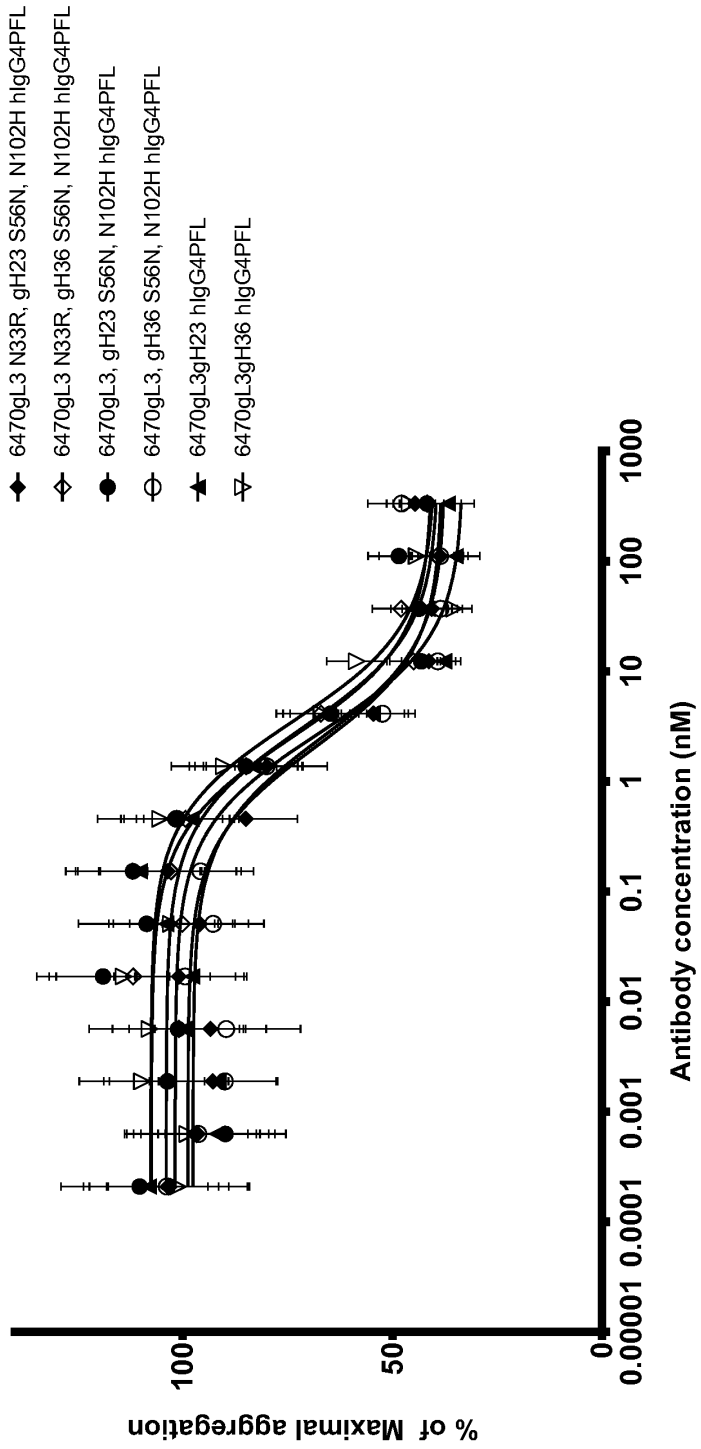

6470gL3 N33R, gH23 S56N, N102H hIgG4PFL
6470gL3 N33R, gH36 S56N, N102H hIgG4PFL
6470gL3, gH23 S56N, N102H hIgG4PFL
6470gL3, gH36 S56N, N102H hIgG4PFL
6470gL3gH23 hIgG4PFL
6470gL3gH36 hIgG4PFL
% of Maximal aggregation
100
50
0
0.00001 0.0001 0.001 0.01 0.1 1 10 100 1000
Antibody concentration (nM)

Fig. 14

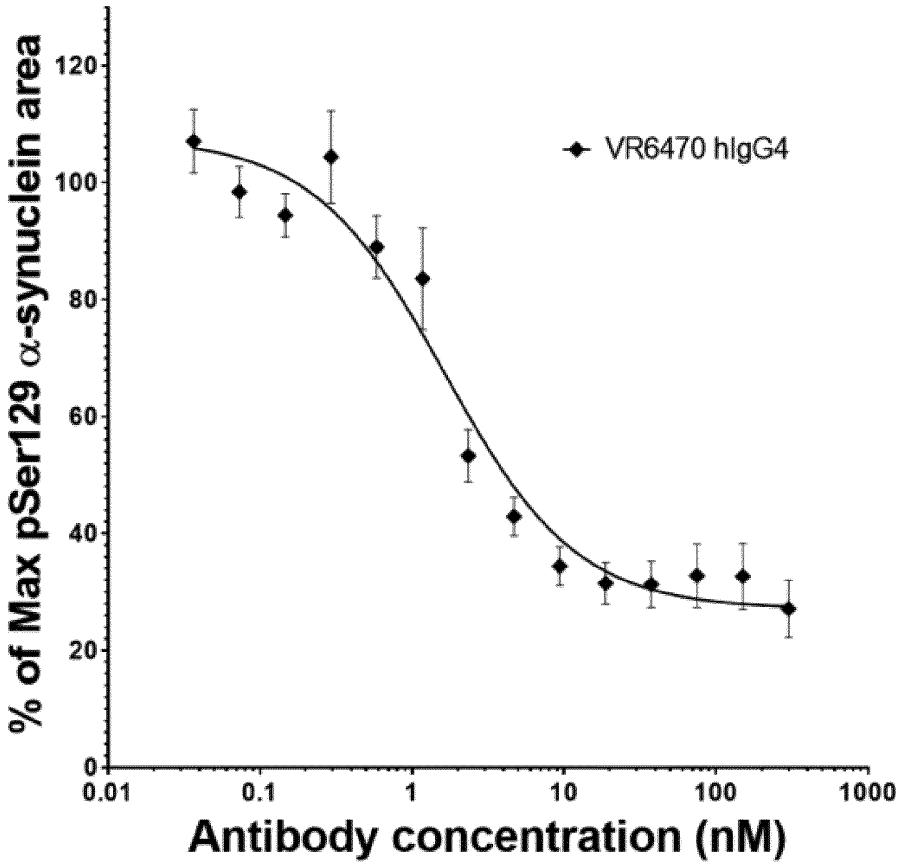

% of Max pSer129 α-synuclein area
120
100
80
60
40
20
0
0.01
0.1
1
10
100
1000
Antibody concentration (nM)
VR6470 hIgG4

Fig. 15

A

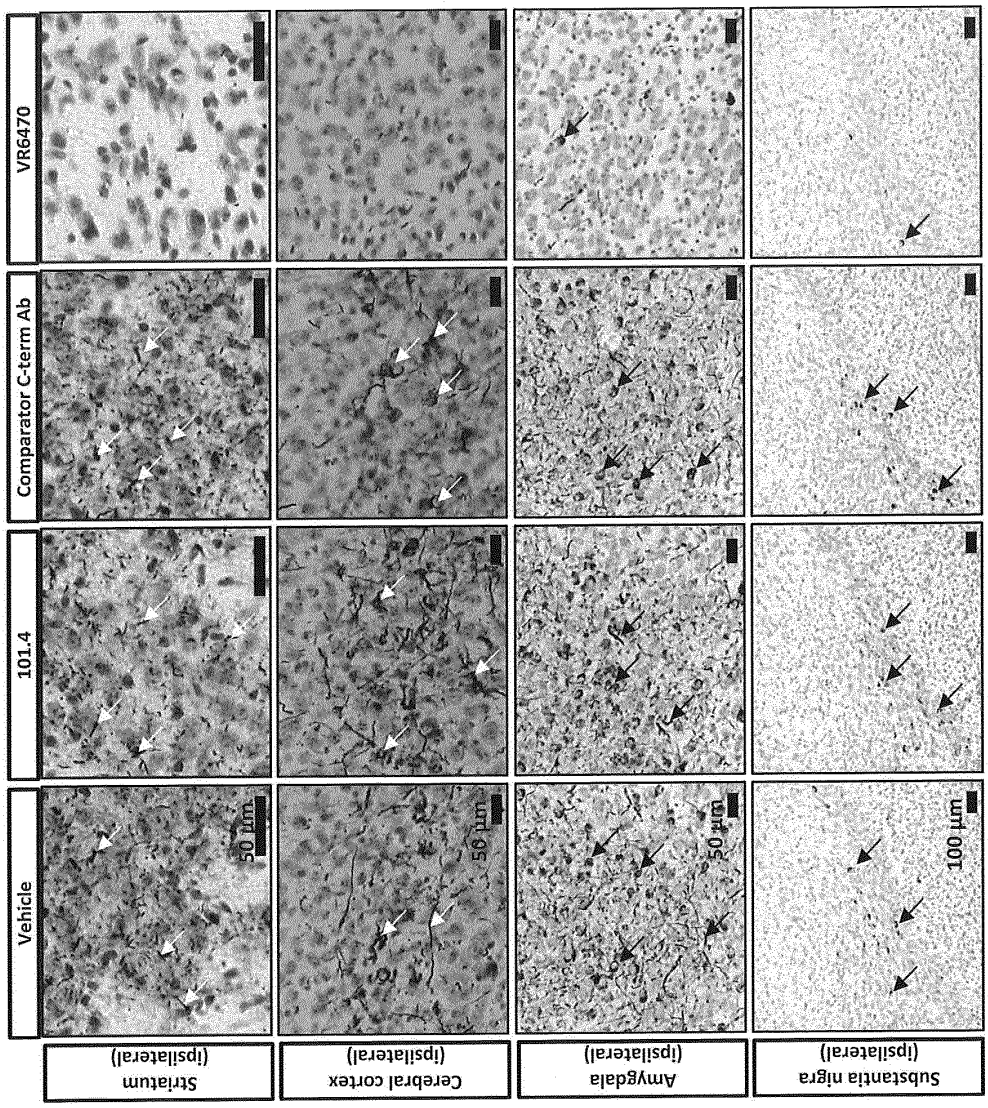

VR6470
Comparator C-term Ab
101.4
Vehicle
50 µm
50 µm
50 µm
100 µm
Striatum (ipsilateral)
Cerebral cortex (ipsilateral)
Amygdala (ipsilateral)
Substantia nigra (ipsilateral)

Fig. 15 (cont.)

B

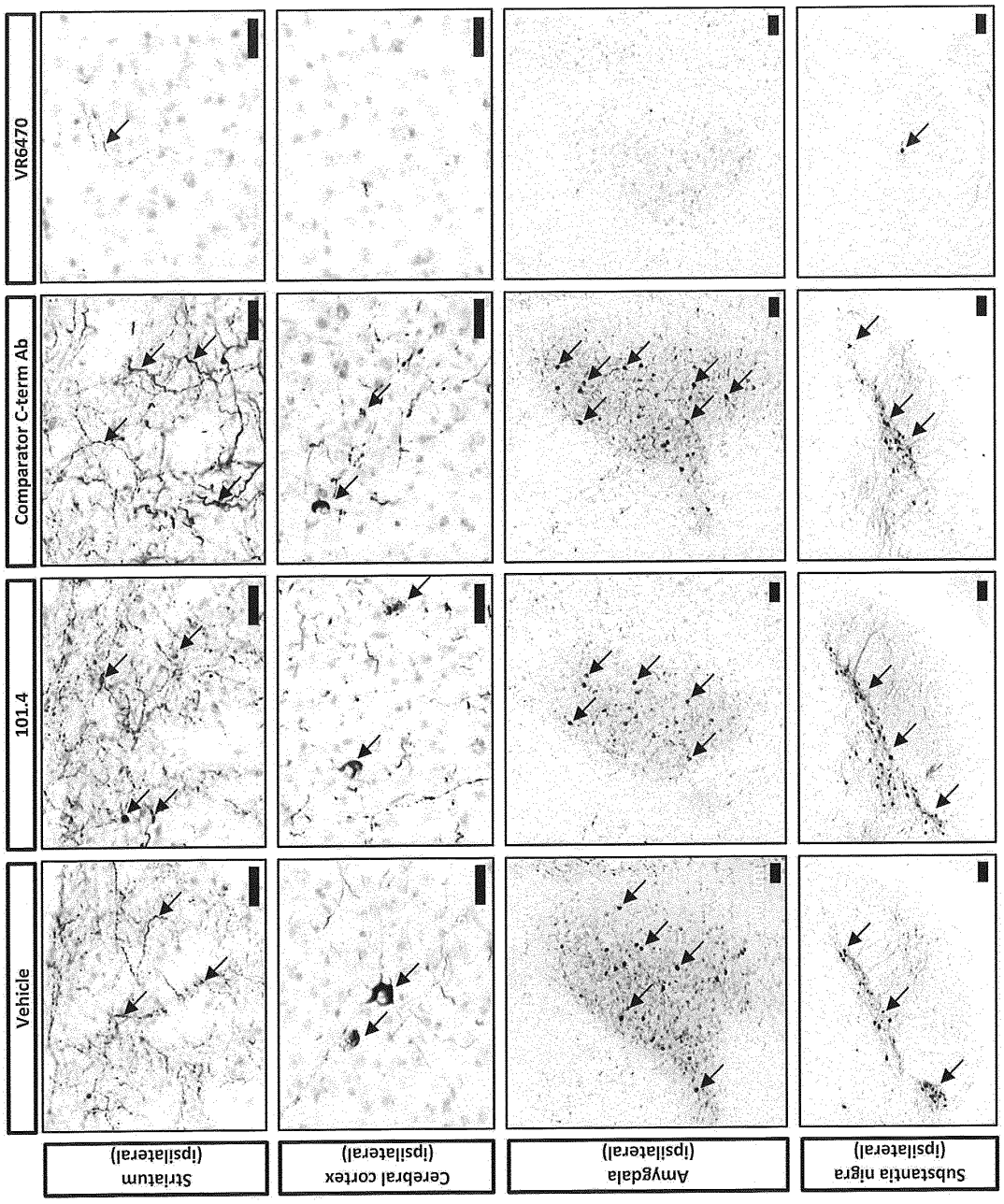

VR6470
Comparator C-term Ab
101.4
Vehicle
Striatum (ipsilateral)
Cerebral cortex (ipsilateral)
Amygdala (ipsilateral)
Substantia nigra (ipsilateral)

Fig. 16

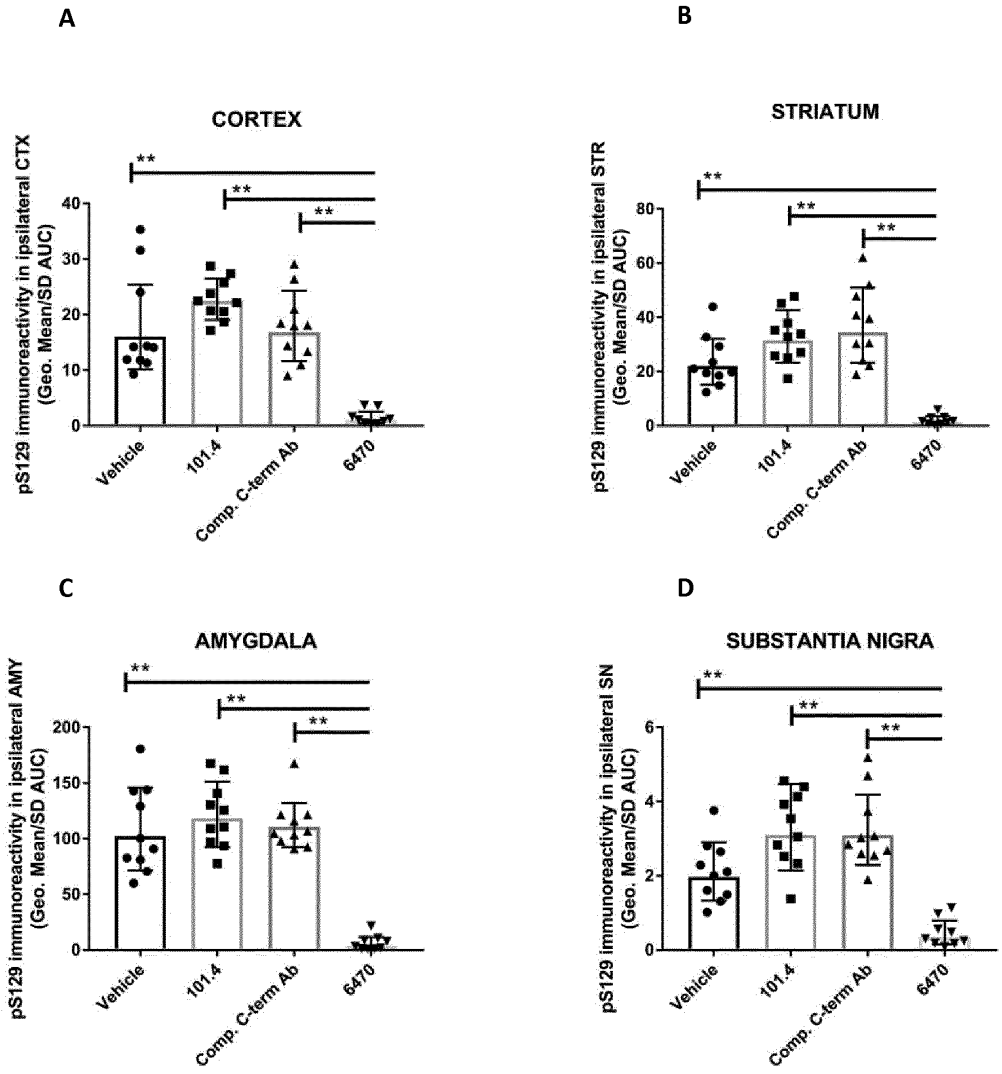
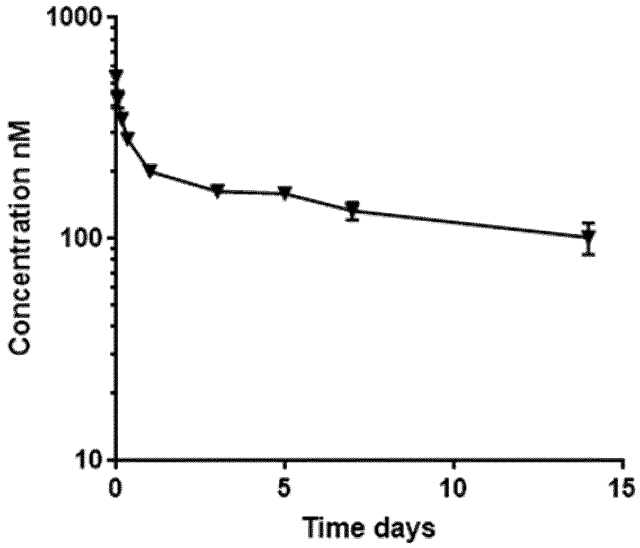
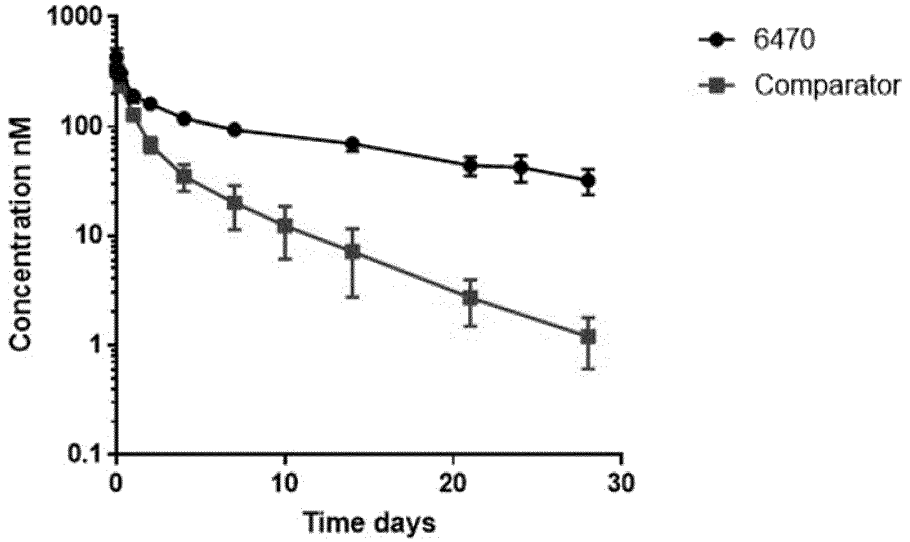

A
CORTEX
pS129 immunoreactivity in ipsilateral CTX (Geo. Mean/SD AUC)
B
STRIATUM
pS129 immunoreactivity in ipsilateral STR (Geo. Mean/SD AUC)
C
AMYGDALA
pS129 immunoreactivity in ipsilateral AMY (Geo. Mean/SD AUC)
D
SUBSTANTIA NIGRA
pS129 immunoreactivity in ipsilateral SN (Geo. Mean/SD AUC)
**
Vehicle
101.4
Comp. C-term Ab
6470

Fig. 17

A


1000
100
10
Concentration nM
0
5
10
15
Time days

B


1000
100
10
1
0.1
Concentration nM
0
10
20
30
Time days
6470
Comparator