FIG. 1A

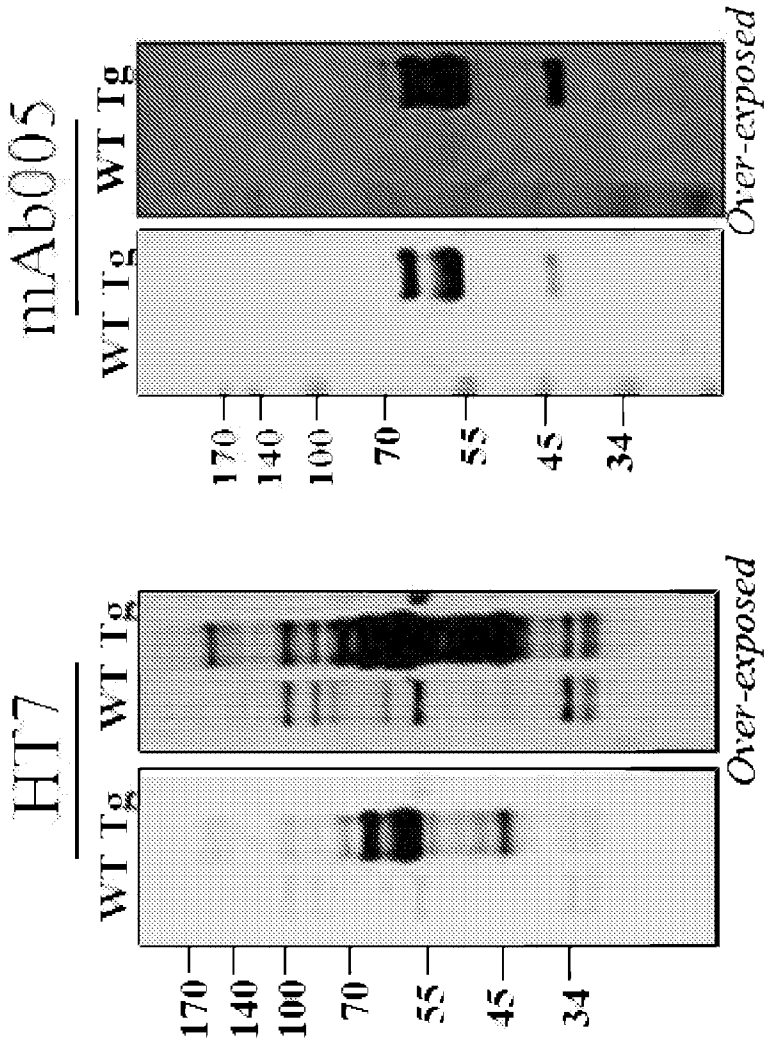

HT7
WT Tg
WT Tg
mAb005
WT Tg
WT Tg
170
140
100
70
55
45
34
Over-exposed
Over-exposed

FIG. 1B

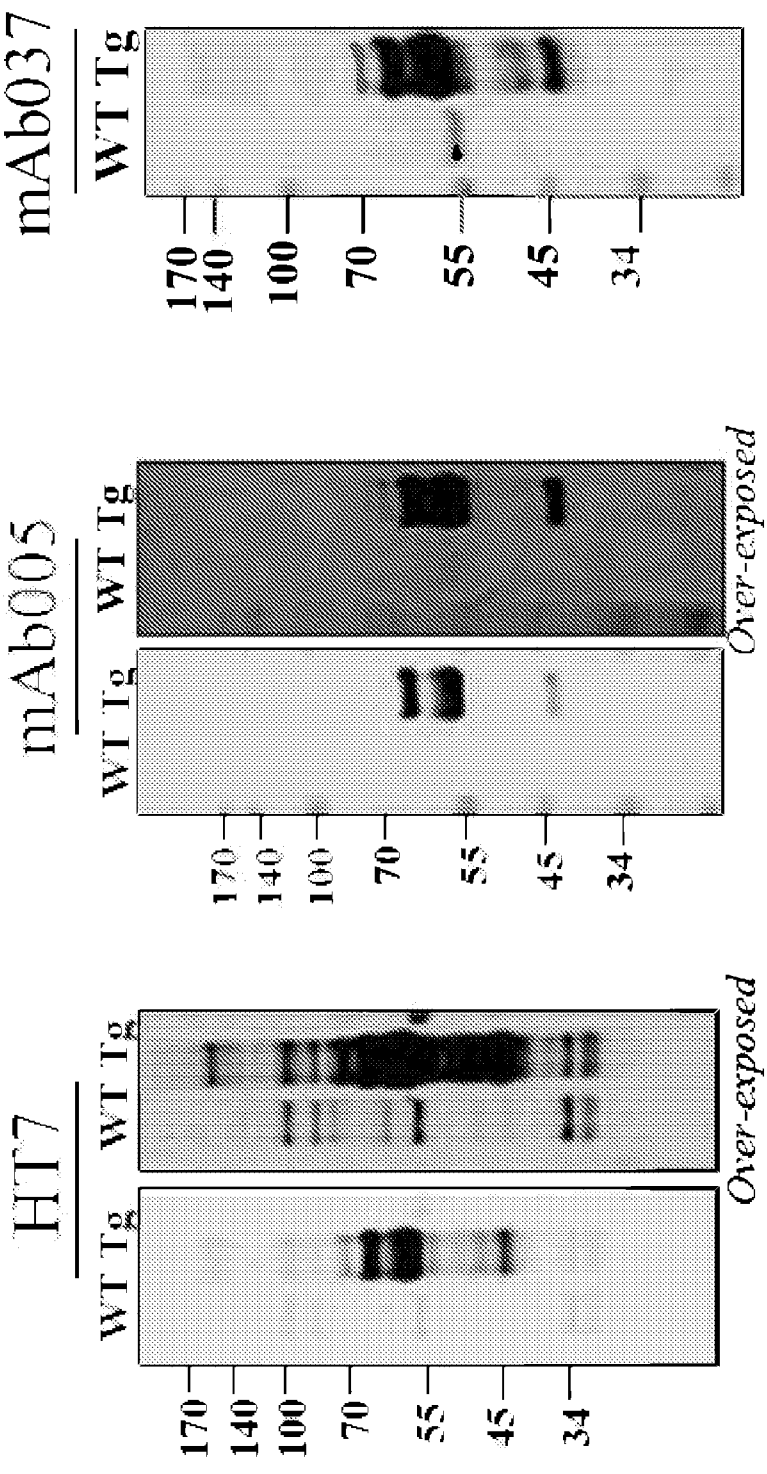

HT7
WT Tg
WT Tg
Over-exposed
mAb005
WT Tg
WT Tg
Over-exposed
mAb037
WT Tg
170
140
100
70
55
45
34

FIG. 2A

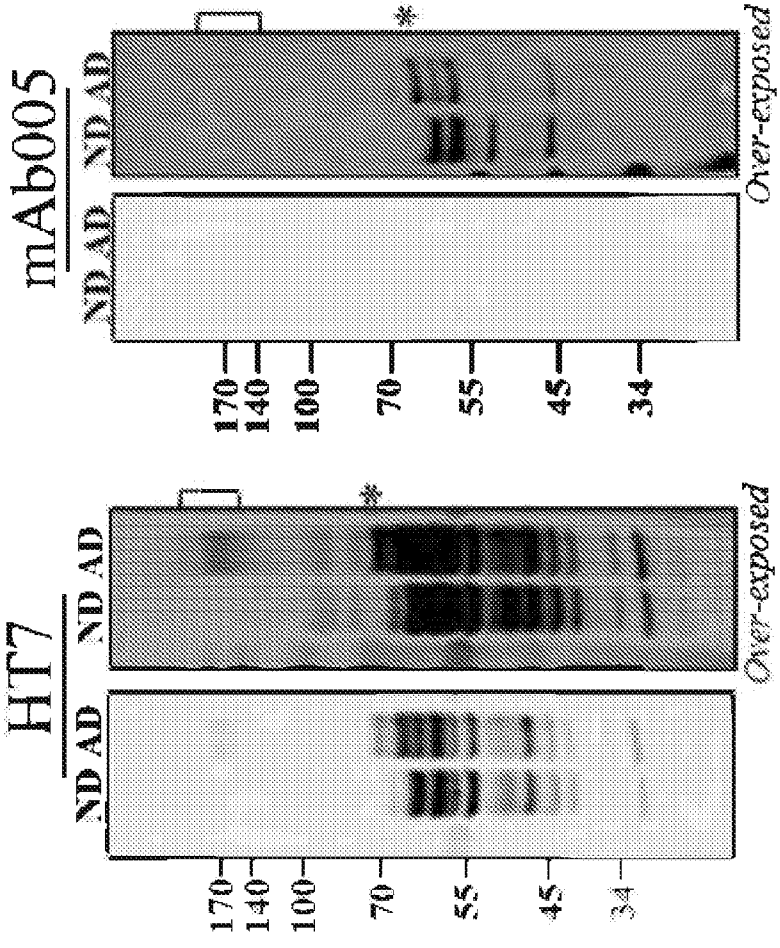

HT7
ND AD
ND AD
170
140
100
70
55
45
34
Over-exposed
mAb005
ND AD
ND AD
170
140
100
70
55
45
34
Over-exposed

FIG. 2B

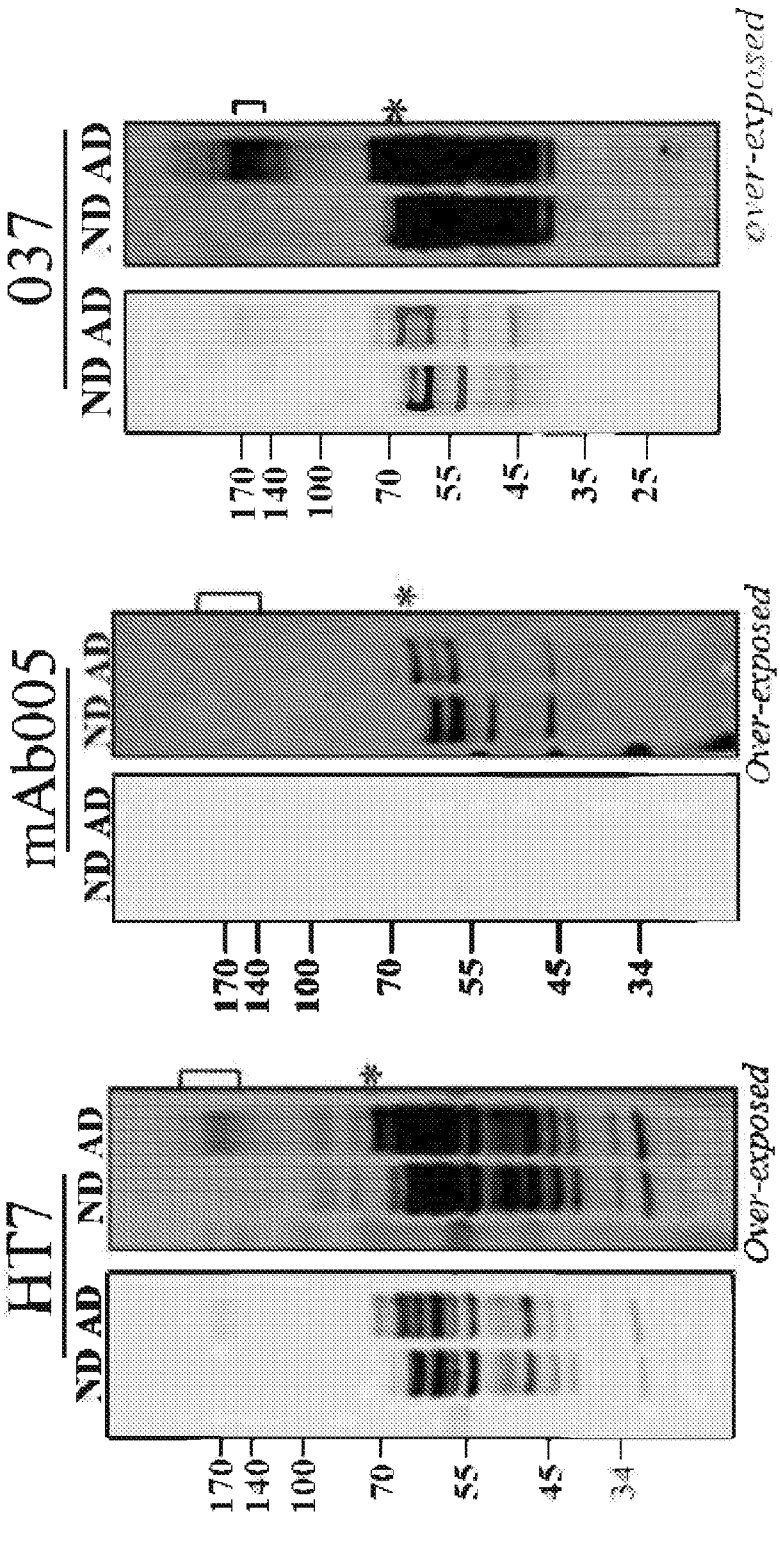

HT7
ND AD
ND AD
170
140
100
70
55
45
34
*
Over-exposed
mAb005
ND AD
ND AD
170
140
100
70
55
45
34
*
Over-exposed
037
ND AD
ND AD
170
140
100
70
55
45
35
25
*
over-exposed

FIG. 3A

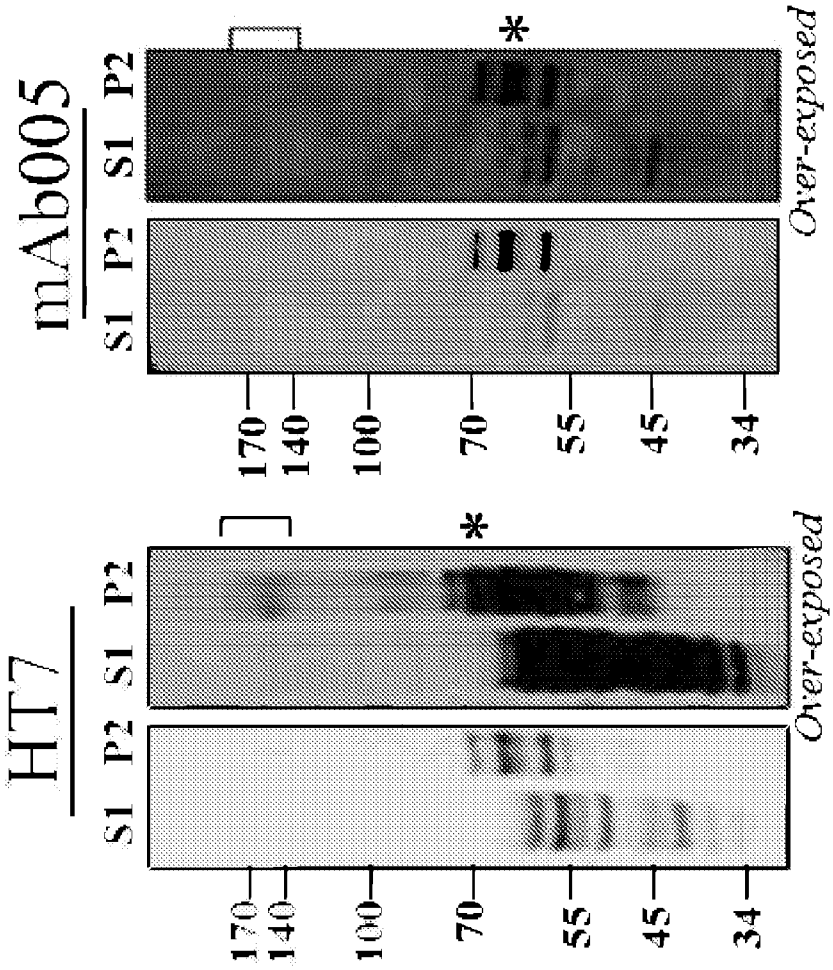

HT7
S1 P2 S1 P2
Over-exposed
mAb005
S1 P2 S1 P2
Over-exposed
170
140
100
70
55
45
34
*
*

FIG. 3B

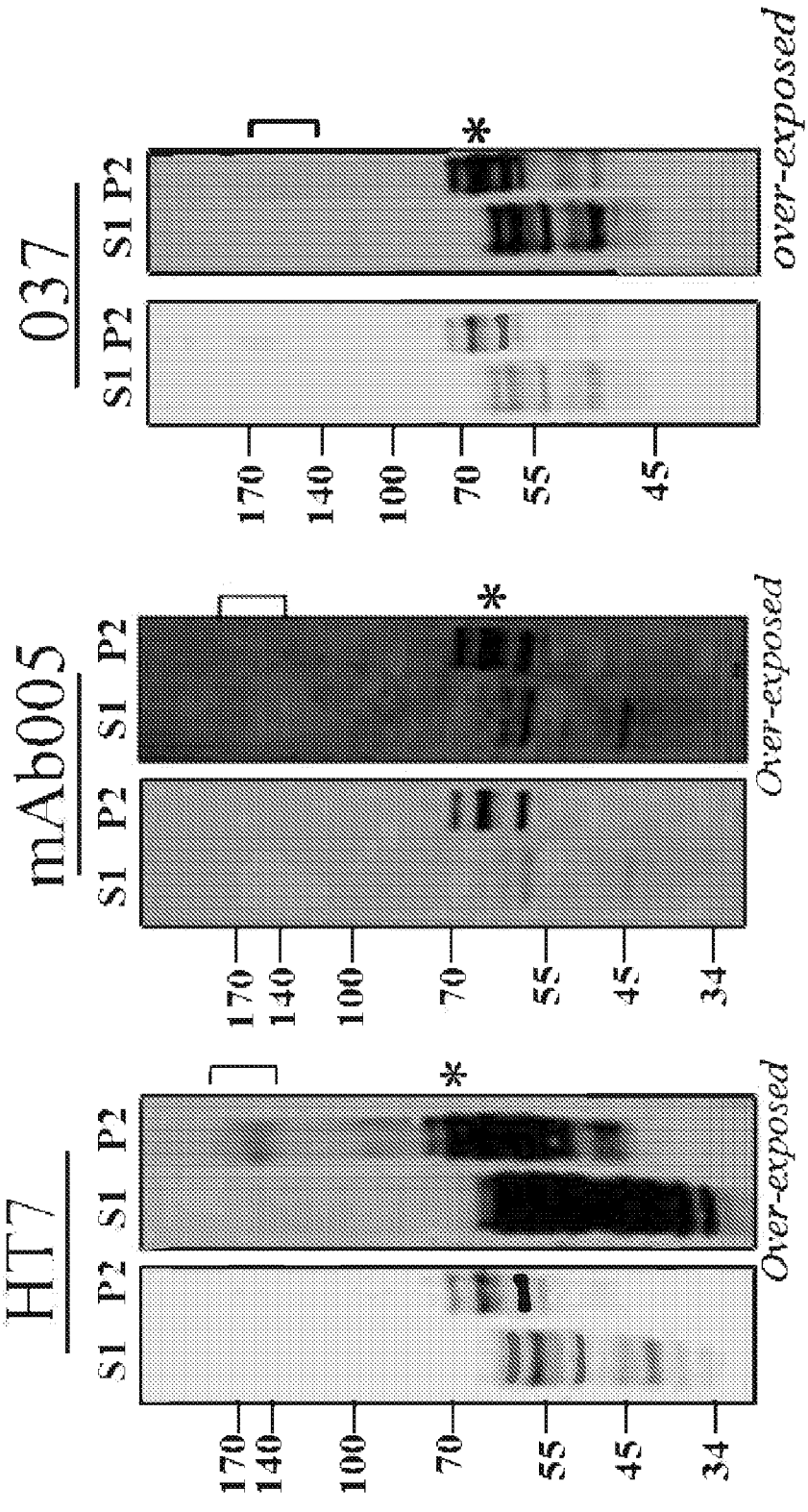

HT7
S1 P2 S1 P2
170
140
100
70
55
45
34
*
Over-exposed
mAb005
S1 P2 S1 P2
170
140
100
70
55
45
34
*
Over-exposed
037
S1 P2 S1 P2
170
140
100
70
55
45
*
over-exposed

FIG. 4A

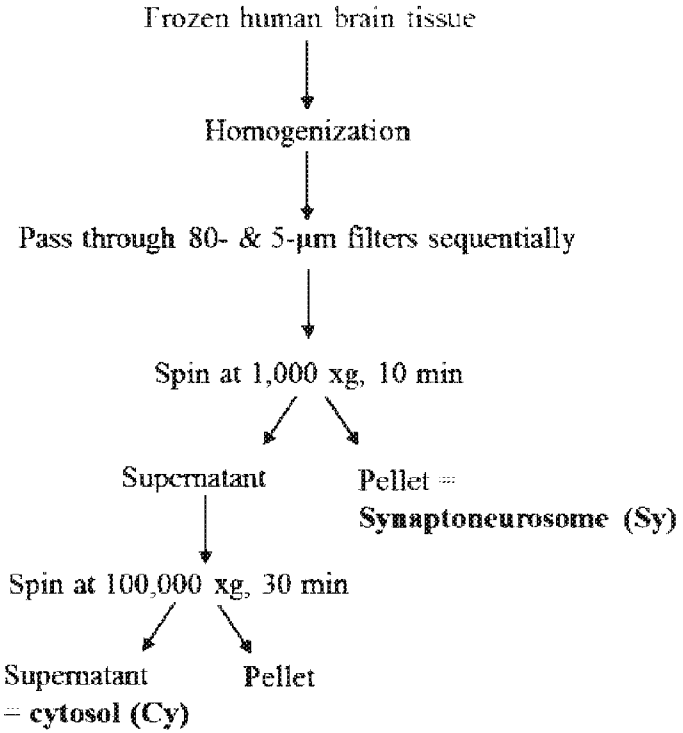

Frozen human brain tissue
Homogenization
Pass through 80- & 5-μm filters sequentially
Spin at 1,000 xg, 10 min
Supernatant
Pellet =
Synaptoneurosome (Sy)
Spin at 100,000 xg, 30 min
Supernatant
= cytosol (Cy)
Pellet

FIG. 4B

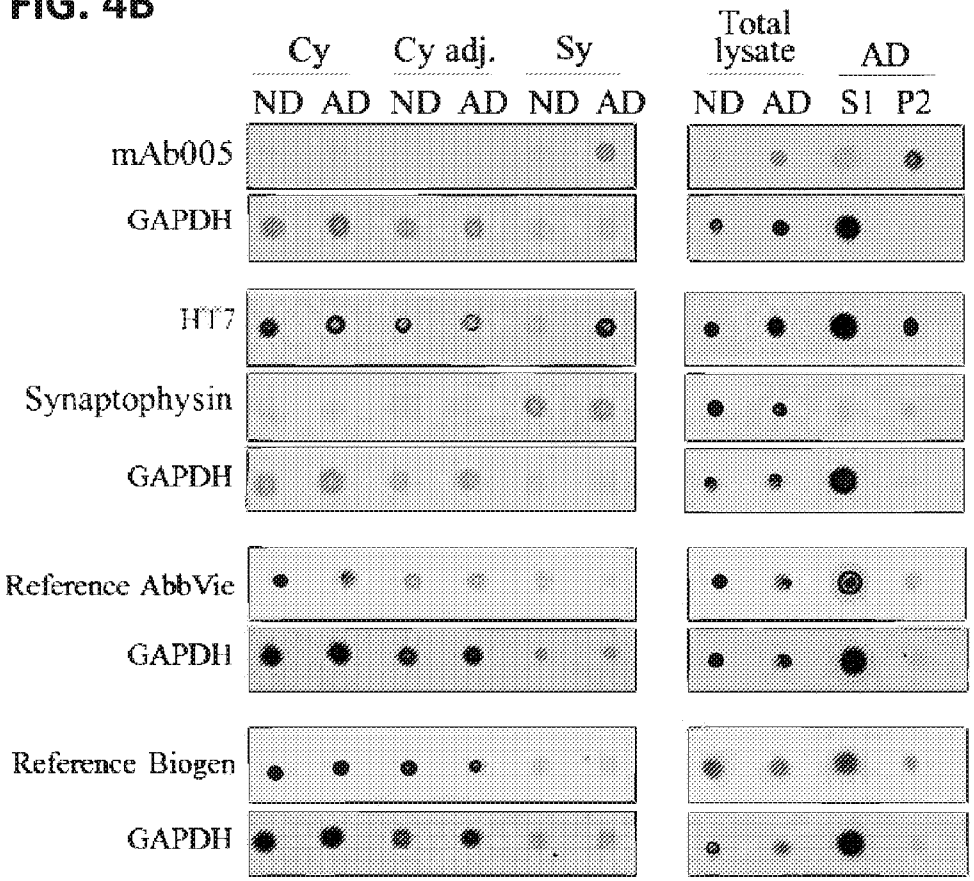
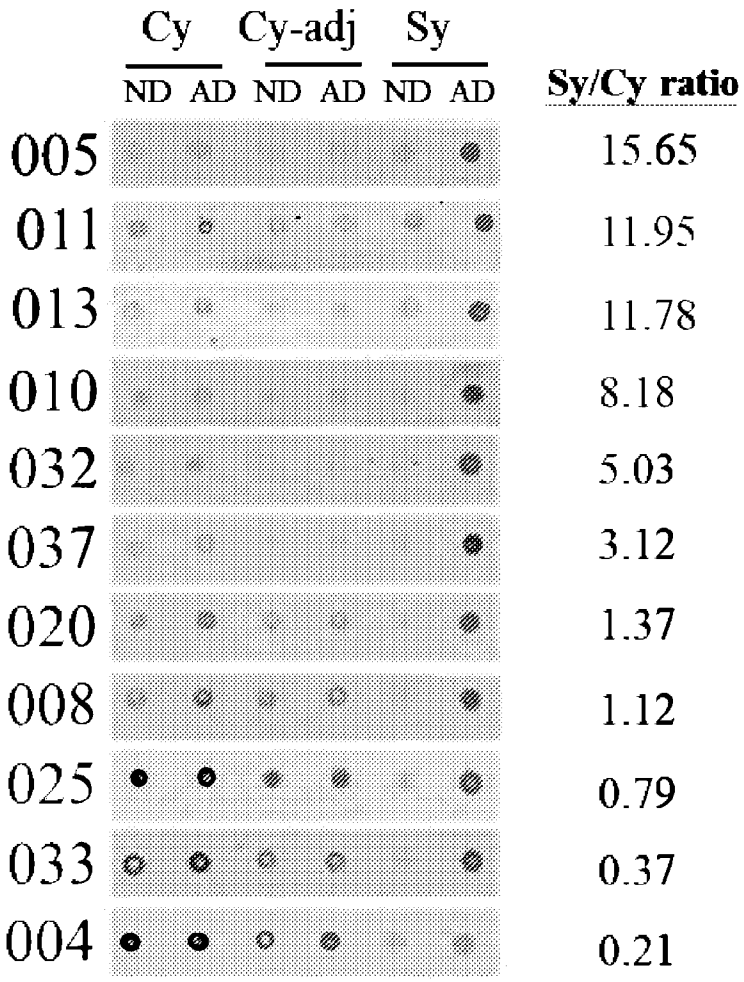

Cy
Cy adj.
Sy
Total lysate
AD
ND AD ND AD ND AD
ND AD S1 P2
mAb005
GAPDH
HT7
Synaptophysin
GAPDH
Reference AbbVie
GAPDH
Reference Biogen
GAPDH

FIG. 4C



Cy: cytosolic fraction
Cy-adj: adjusted cytosolic fraction
Sy: synaptoneurosomic fraction

FIG. 5A

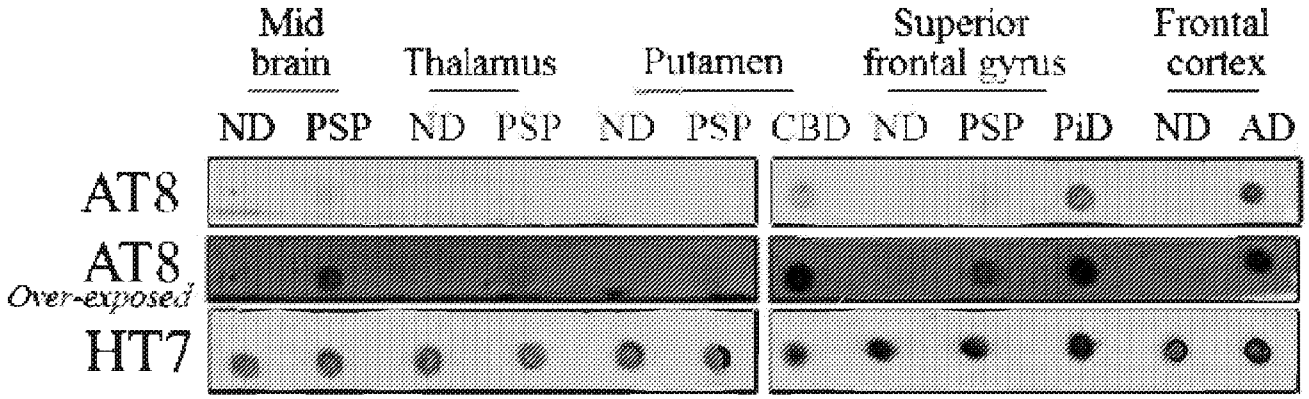

Mid brain
Thalamus
Putamen
Superior frontal gyrus
Frontal cortex
ND PSP ND PSP ND PSP CBD ND PSP PiD ND AD
AT8
AT8 Over-exposed
HT7

FIG. 5B

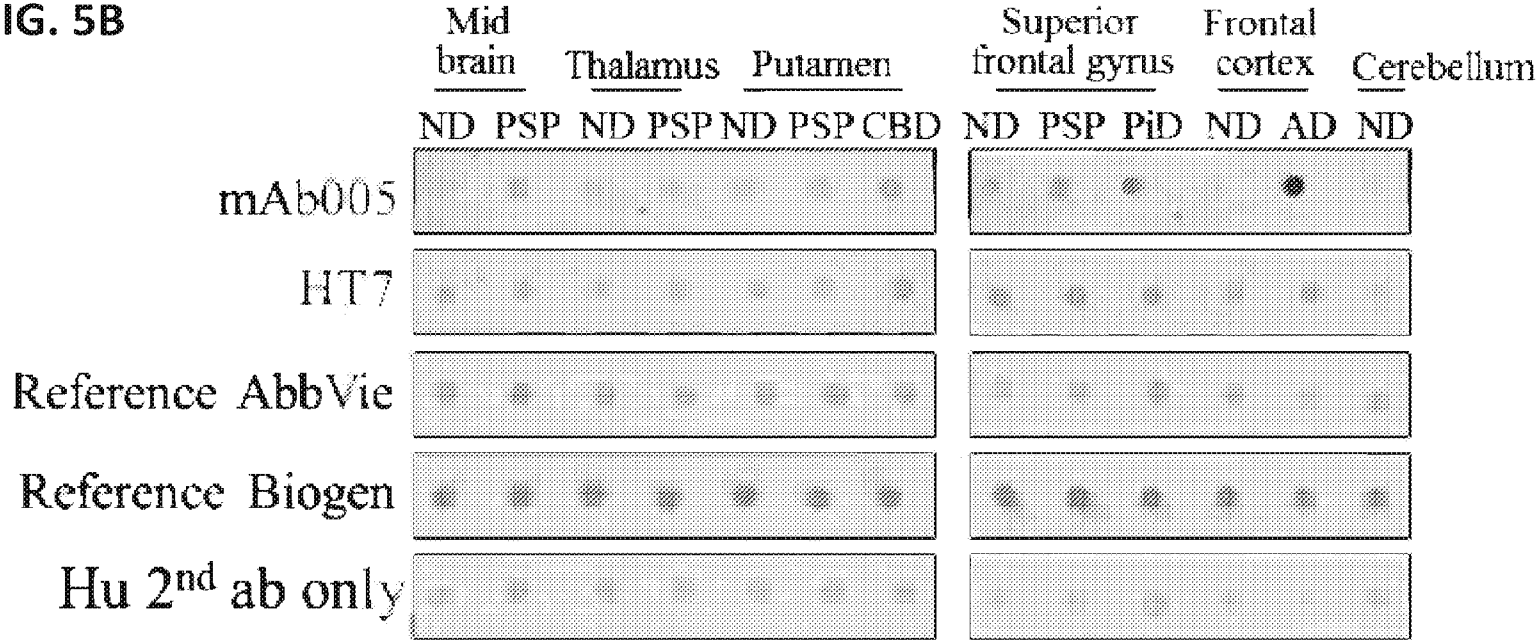

Mid brain
Thalamus
Putamen
Superior frontal gyrus
Frontal cortex
Cerebellum
ND PSP ND PSP ND PSP CBD ND PSP PiD ND AD ND
mAb005
HT7
Reference AbbVie
Reference Biogen
Hu 2nd ab only

FIG. 5C

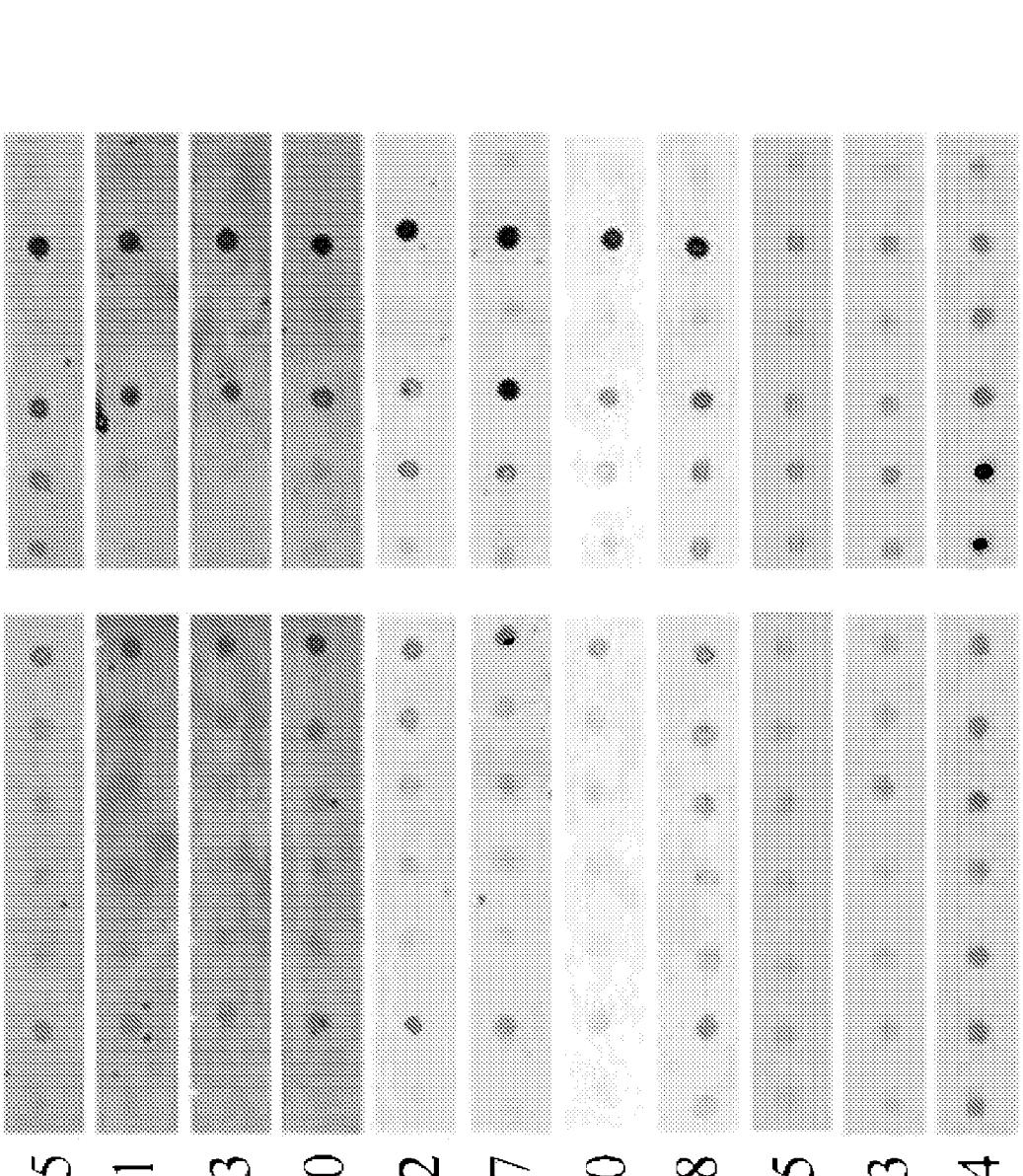

Mid brain
ND PSP
Thalamus
ND PSP
Putamen
ND PSP CBD
Superior frontal gyrus
ND PSP PiD
Frontal cortex
ND AD
Cerebellum
ND
005
011
013
010
032
037
020
008
025
033
004

FIG. 6A

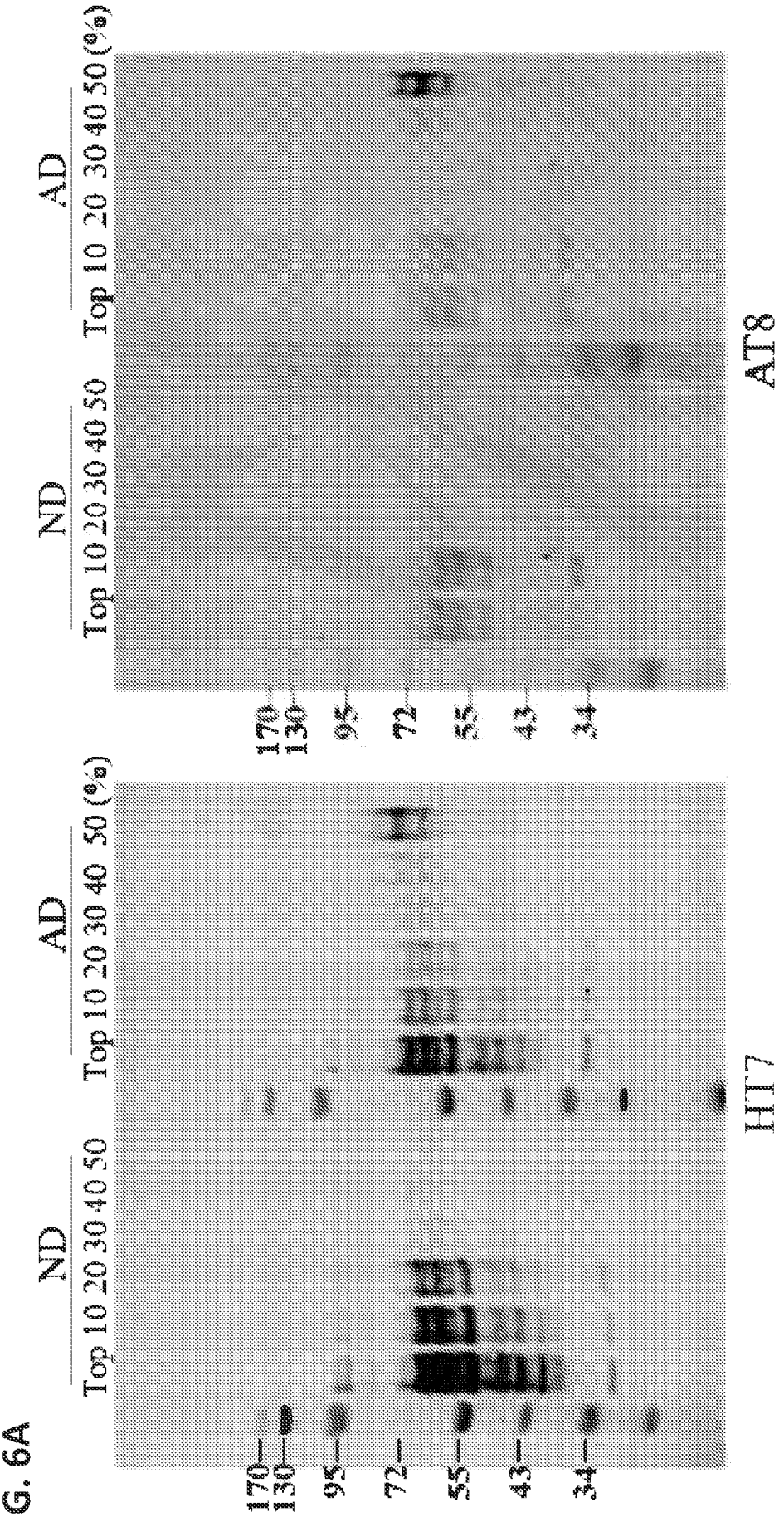

ND
AD
Top 10 20 30 40 50 Top 10 20 30 40 50 (%)
170
130
95
72
55
43
34
HT7
AT8

FIG. 6B

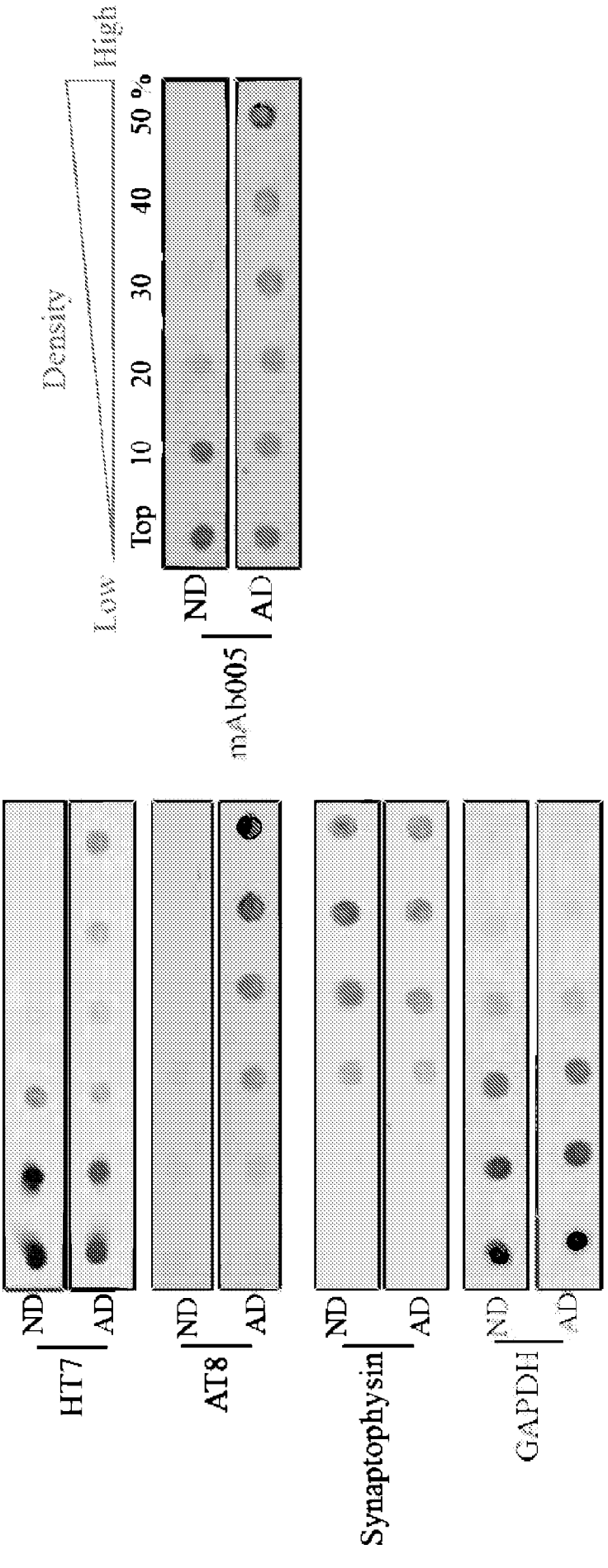

Top
10
20
30
40
50 (%)
ND
AD
HT7
AT8
Synaptophysin
GAPDH
Density
Low
High
Top
10
20
30
40
50 %
mAb005

FIG. 7A

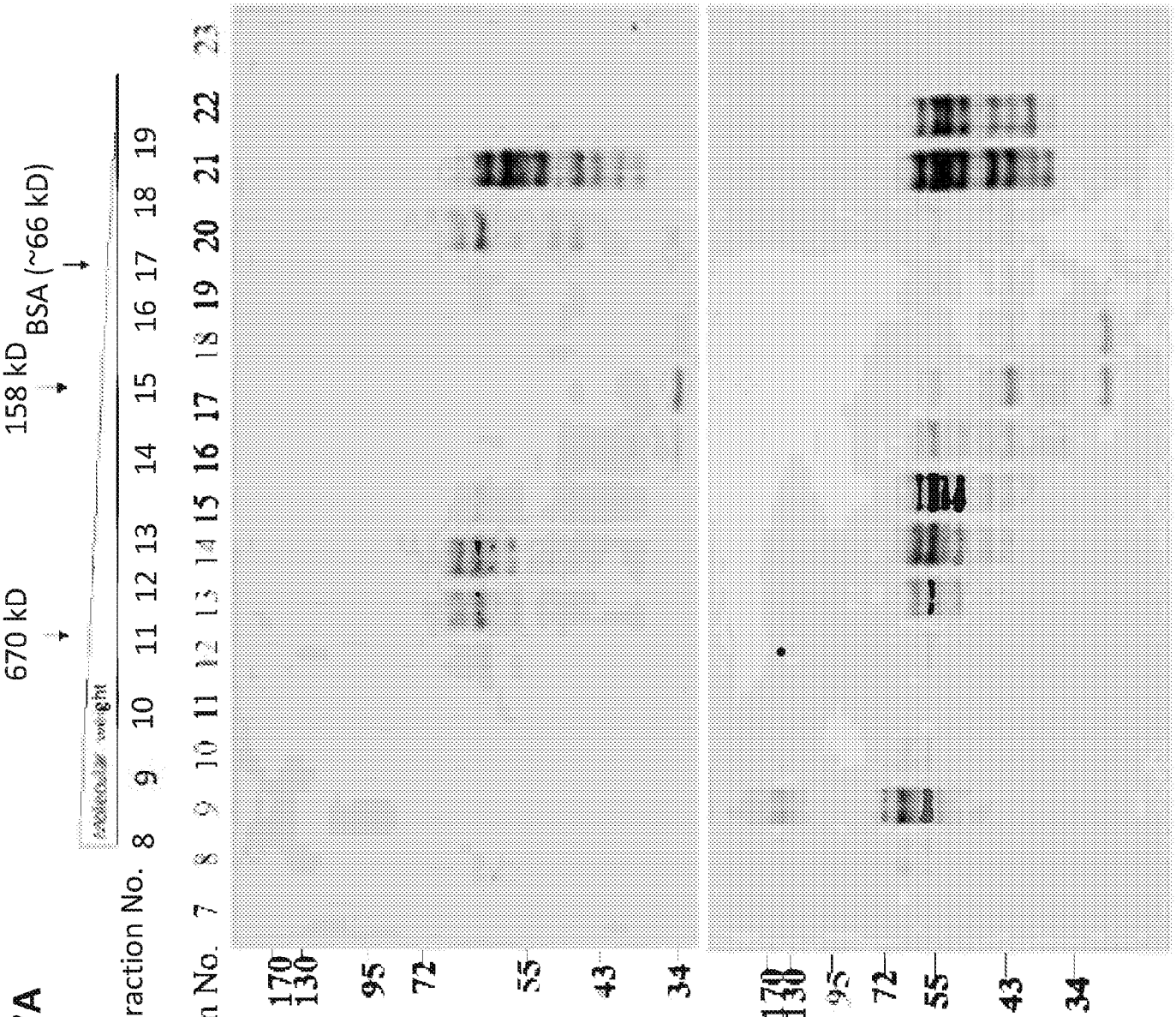

670 kD
158 kD
BSA (~66 kD)
Molecular weight
Fraction No. 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
Fraction No. 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
ND HT7
AD HT7
170
130
95
72
55
43
34

FIG. 7B

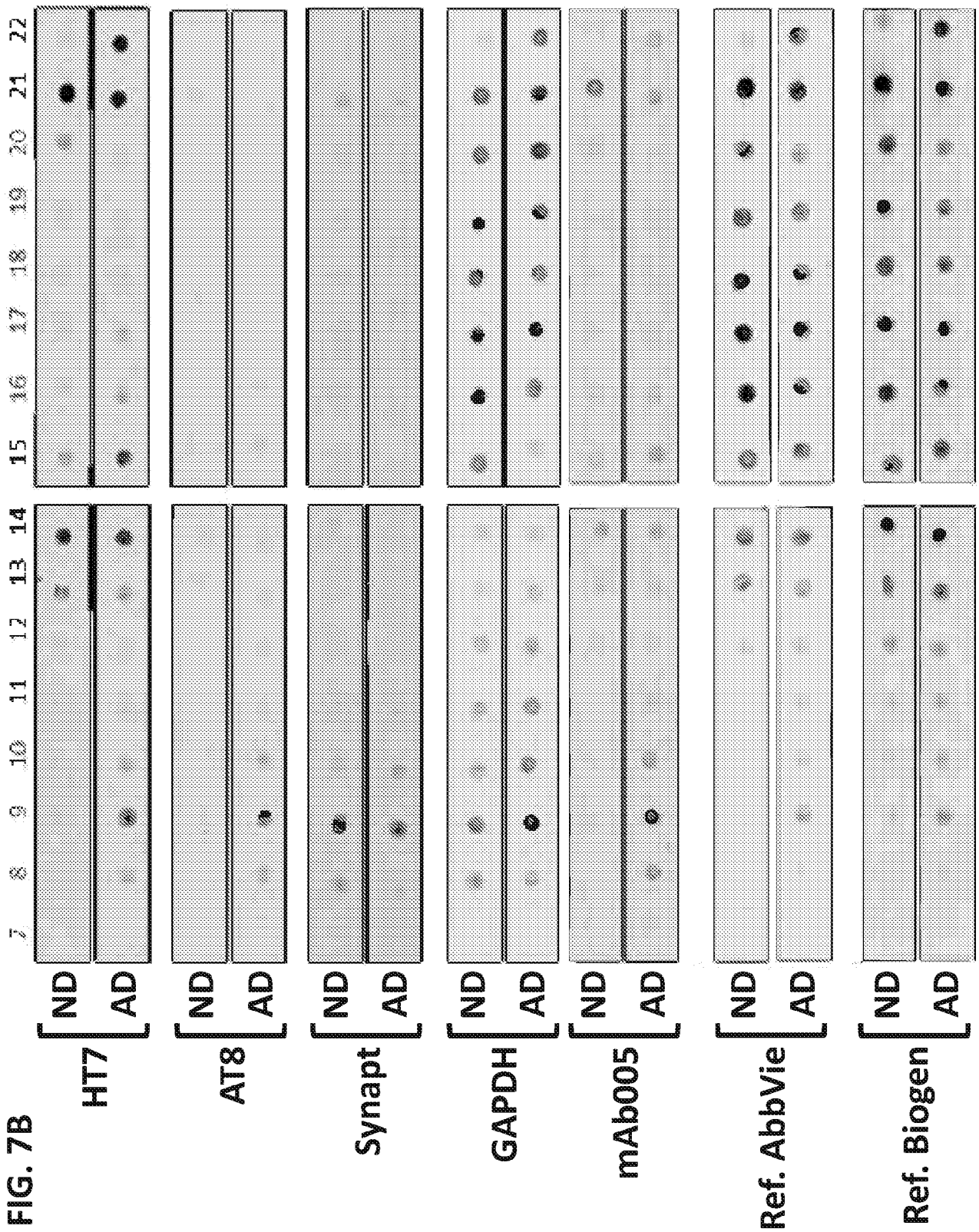

7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22
HT7
AT8
Synapt
GAPDH
mAb005
Ref. AbbVie
Ref. Biogen
ND
AD

FIG. 8A

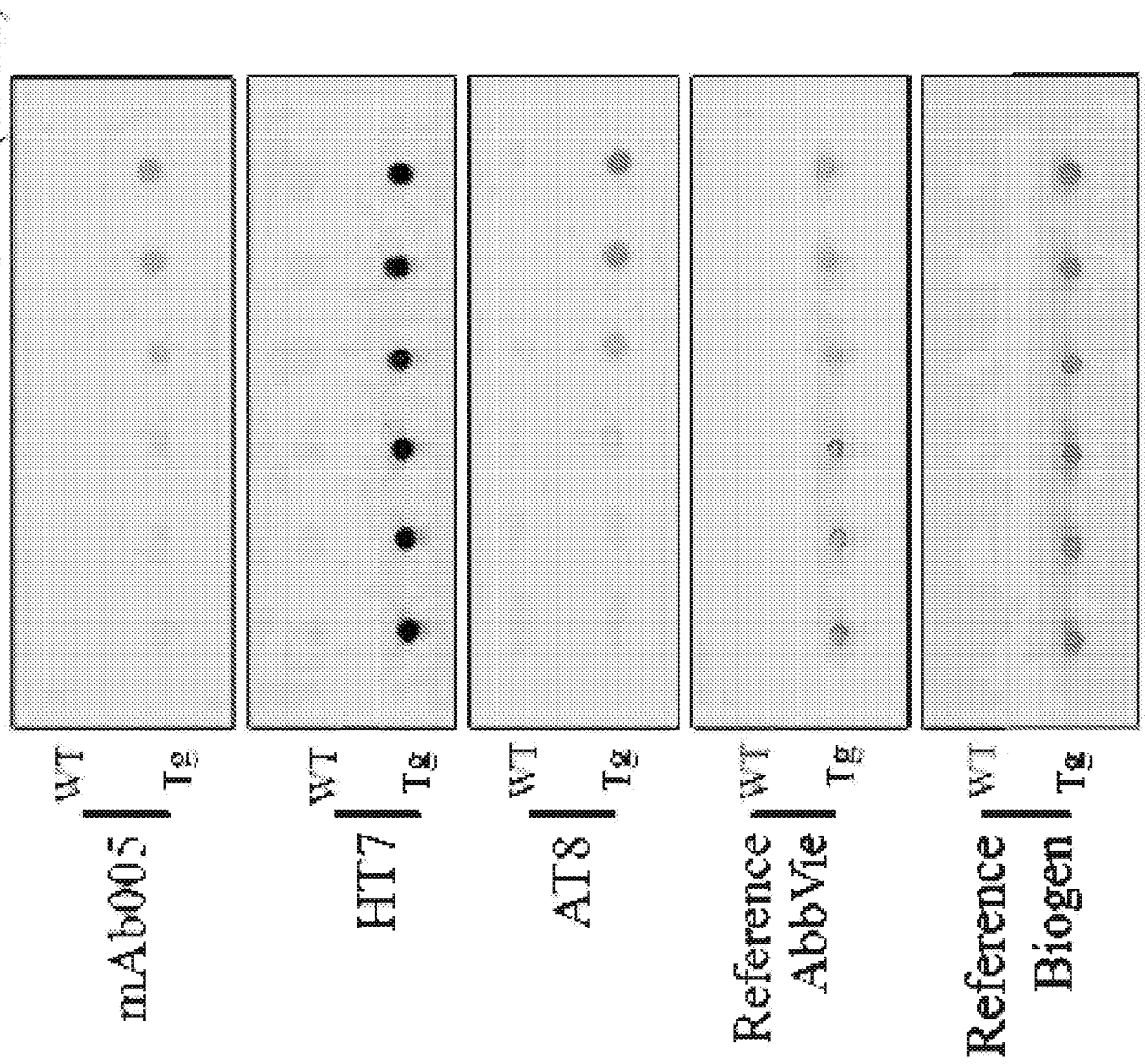
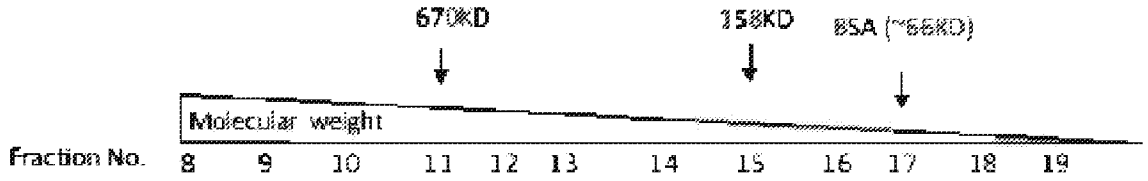
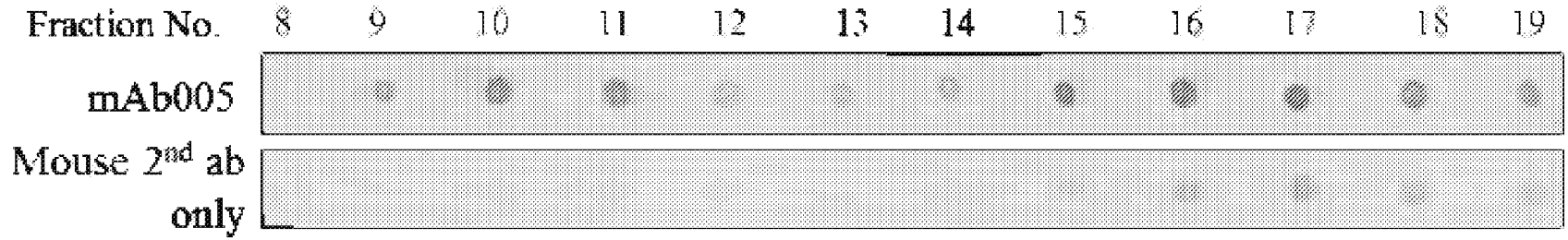

1
2
3
4
5
6 (month)
mAb005
WT
Tg
HT7
WT
Tg
AT8
WT
Tg
Reference
AbbVie
WT
Tg
Reference
Biogen
WT
Tg

FIG. 8B



2.5-mo rTg4510 SEC



6-mo rTg4510 SEC

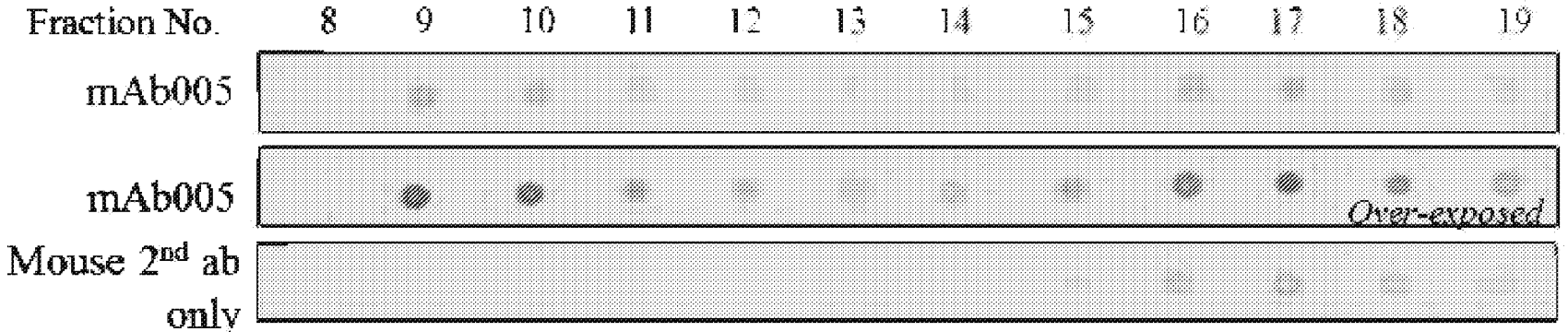


FIG. 9A

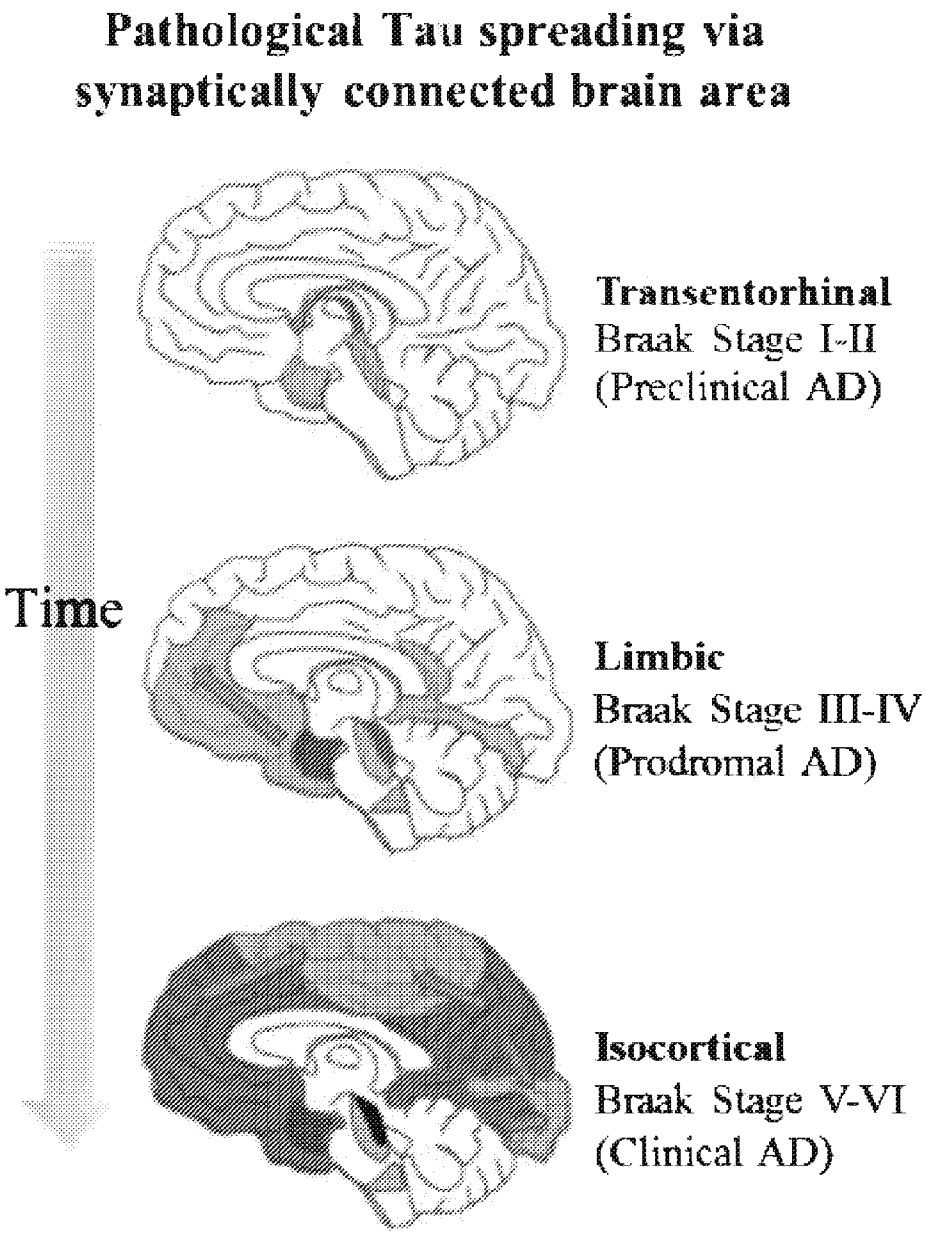

Pathological Tau spreading via synaptically connected brain area
Time
Transentorhinal
Braak Stage I-II
(Preclinical AD)
Limbic
Braak Stage III-IV
(Prodromal AD)
Isocortical
Braak Stage V-VI
(Clinical AD)

FIG. 9B

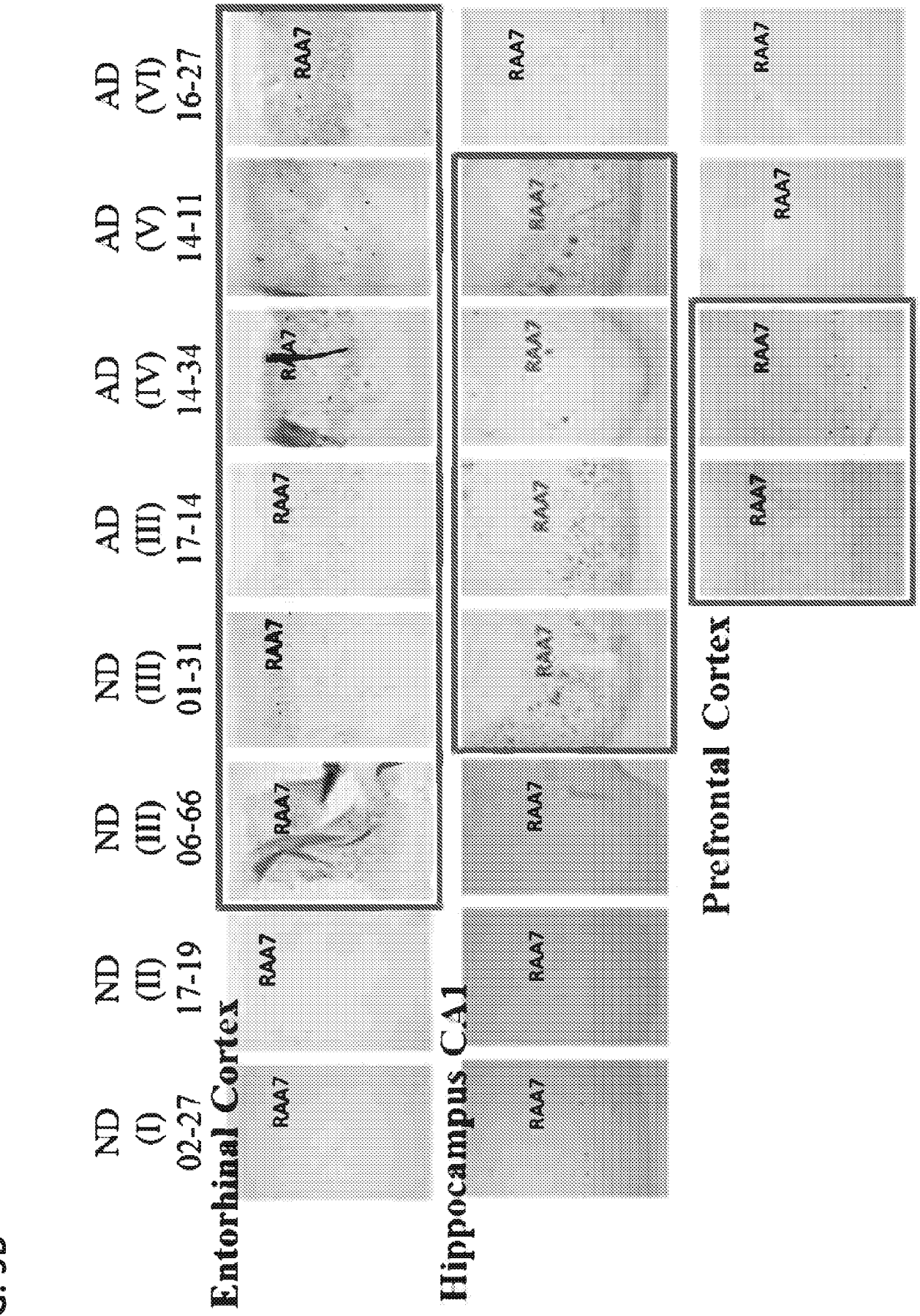

ND (I) 02-27
ND (II) 17-19
ND (III) 06-66
ND (III) 01-31
AD (III) 17-14
AD (IV) 14-34
AD (V) 14-11
AD (VI) 16-27
Entorhinal Cortex
Hippocampus CA1
Prefrontal Cortex
RAA7

FIG. 9C

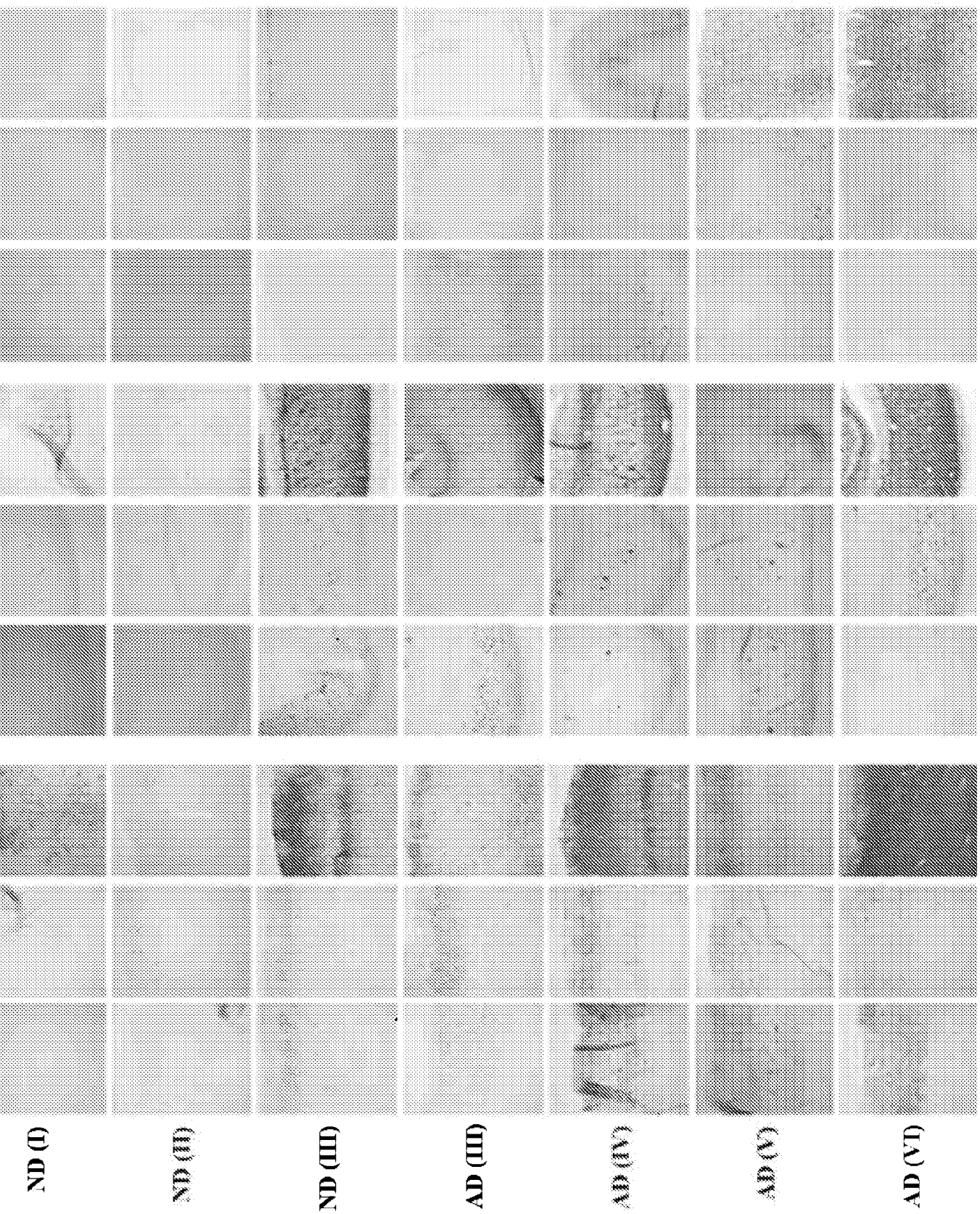

Entorhinal cortex
mAb005
mAb037
AT8
Hippocampus CA1
mAb005
mAb037
AT8
Prefrontal Cortex
mAb005
mAb037
AT8
ND (I)
ND (II)
ND (III)
AD (III)
AD (IV)
AD (V)
AD (VI)

FIG. 9D

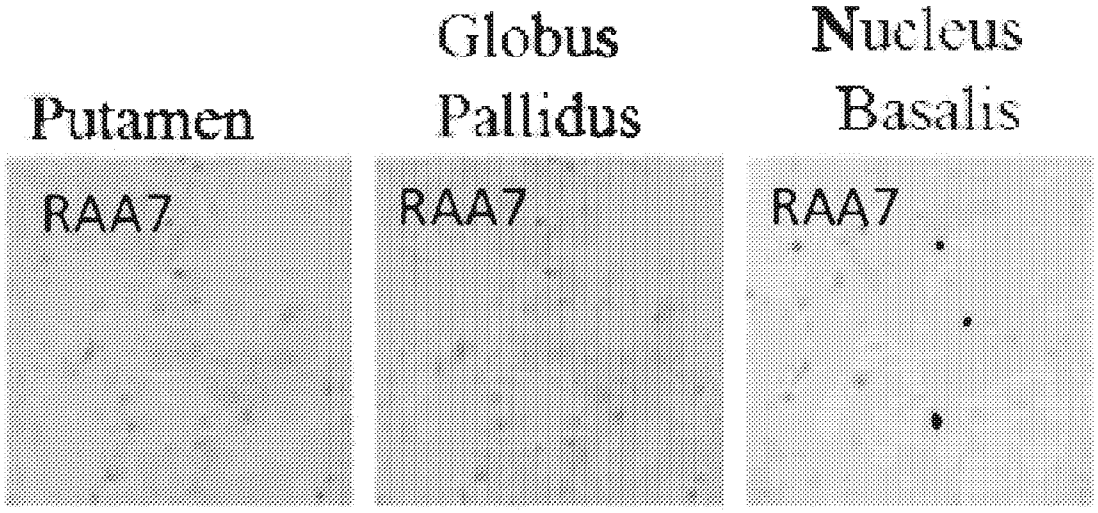


FIG. 9E

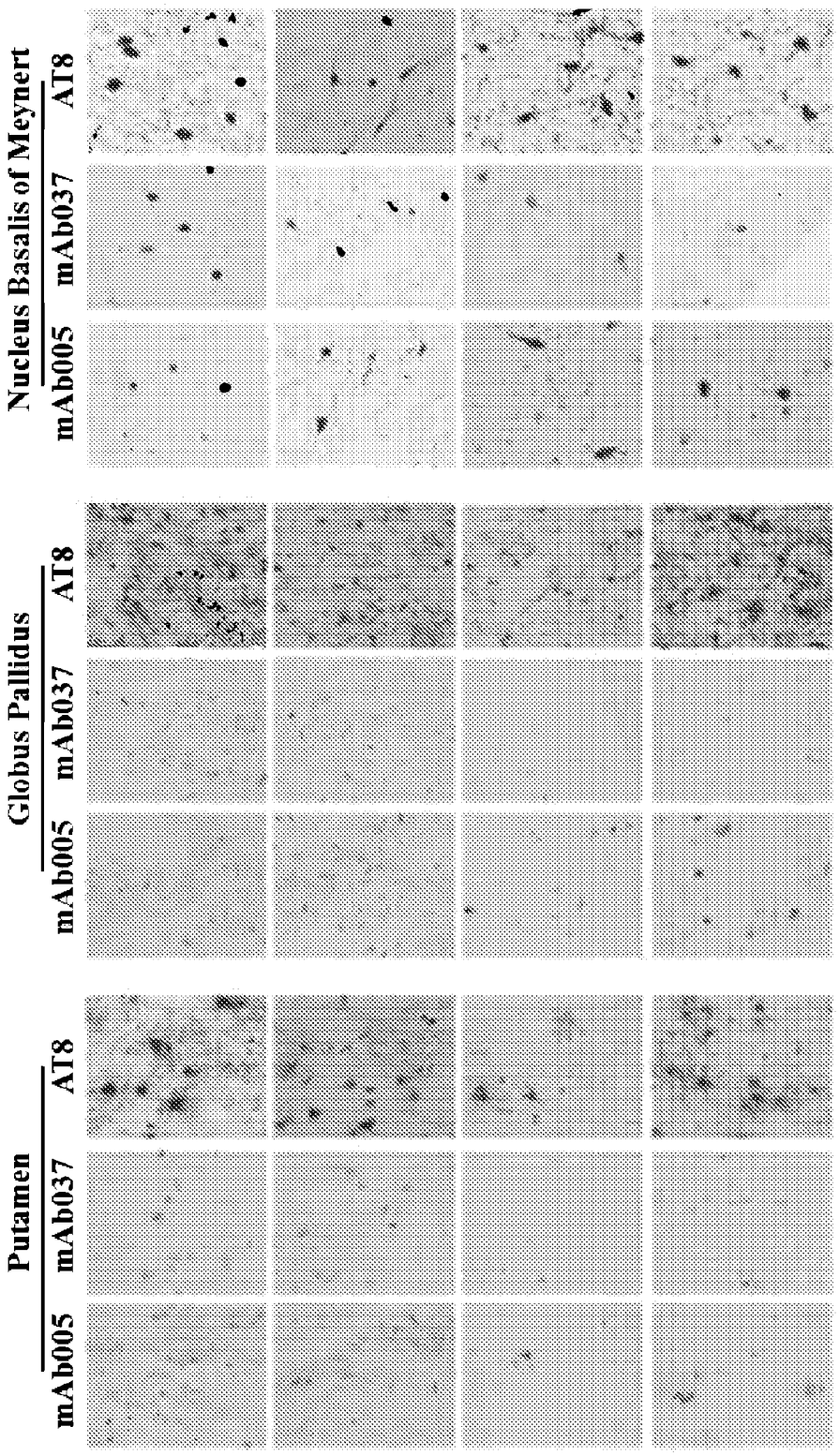

Putamen
mAb005
mAb037
AT8
Globus Pallidus
mAb005
mAb037
AT8
Nucleus Basalis of Meynert
mAb005
mAb037
AT8
PSP-1
PSP-2
PSP-3
PSP-4

FIG. 10A

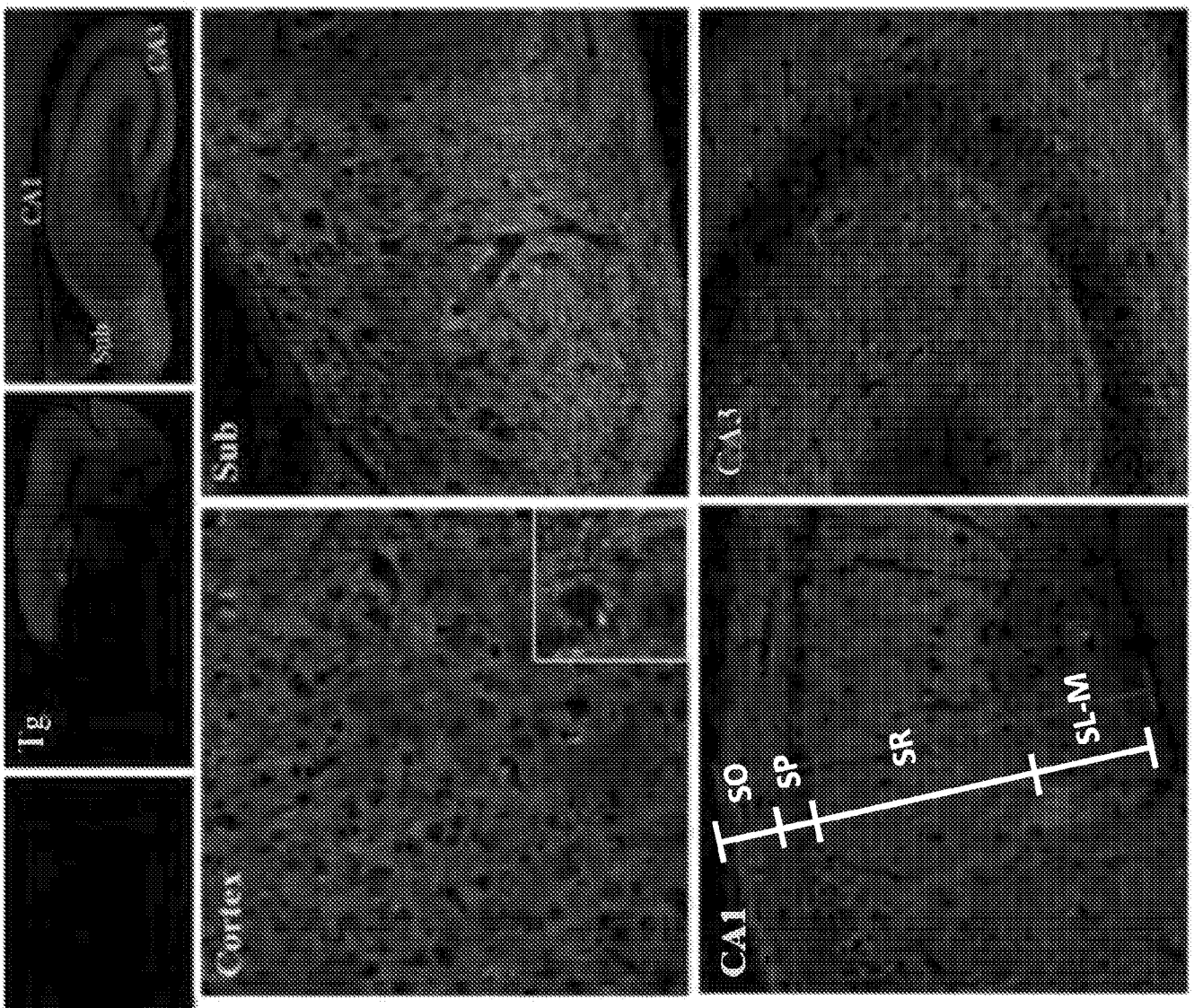


FIG. 10B

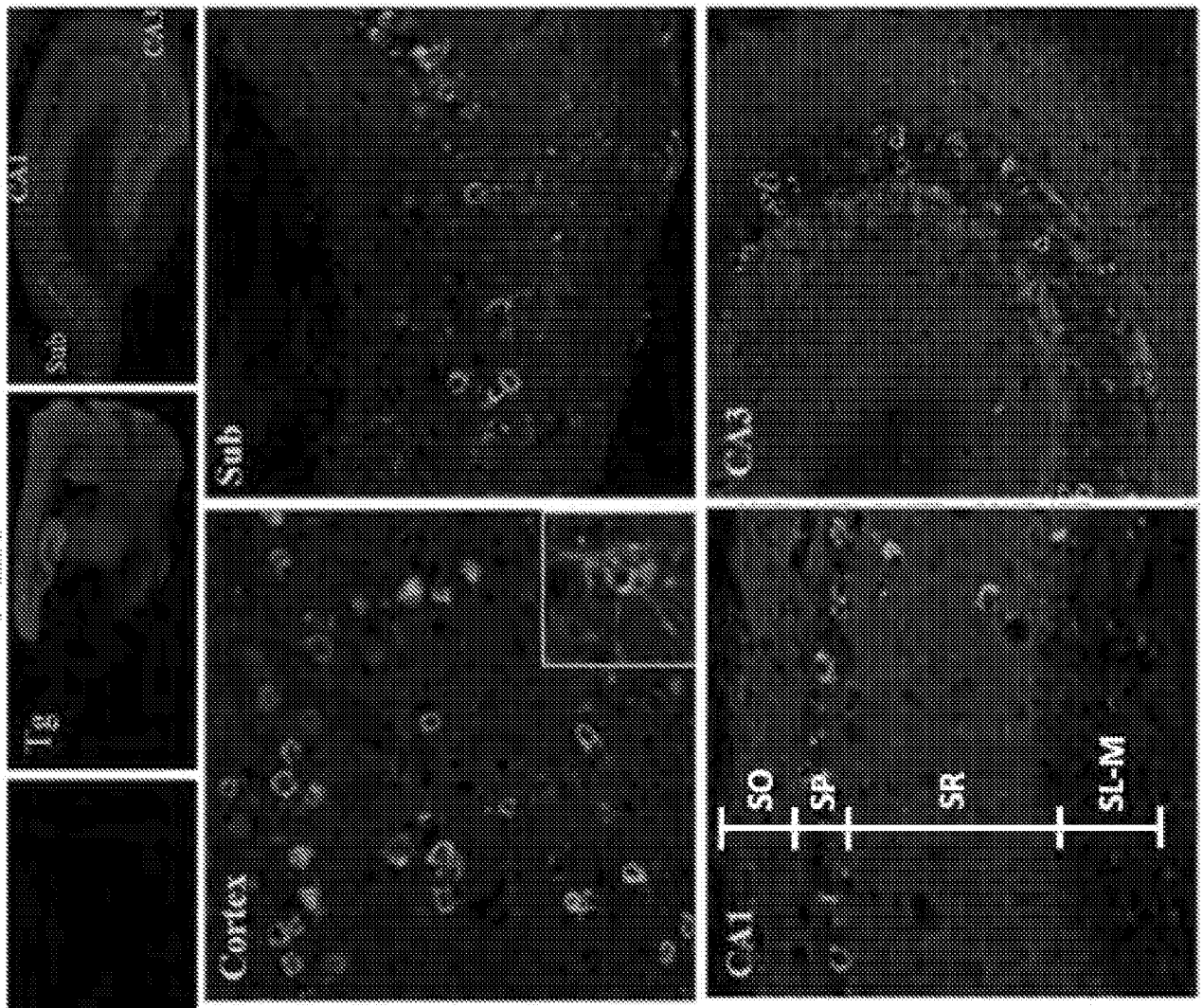


FIG. 11A

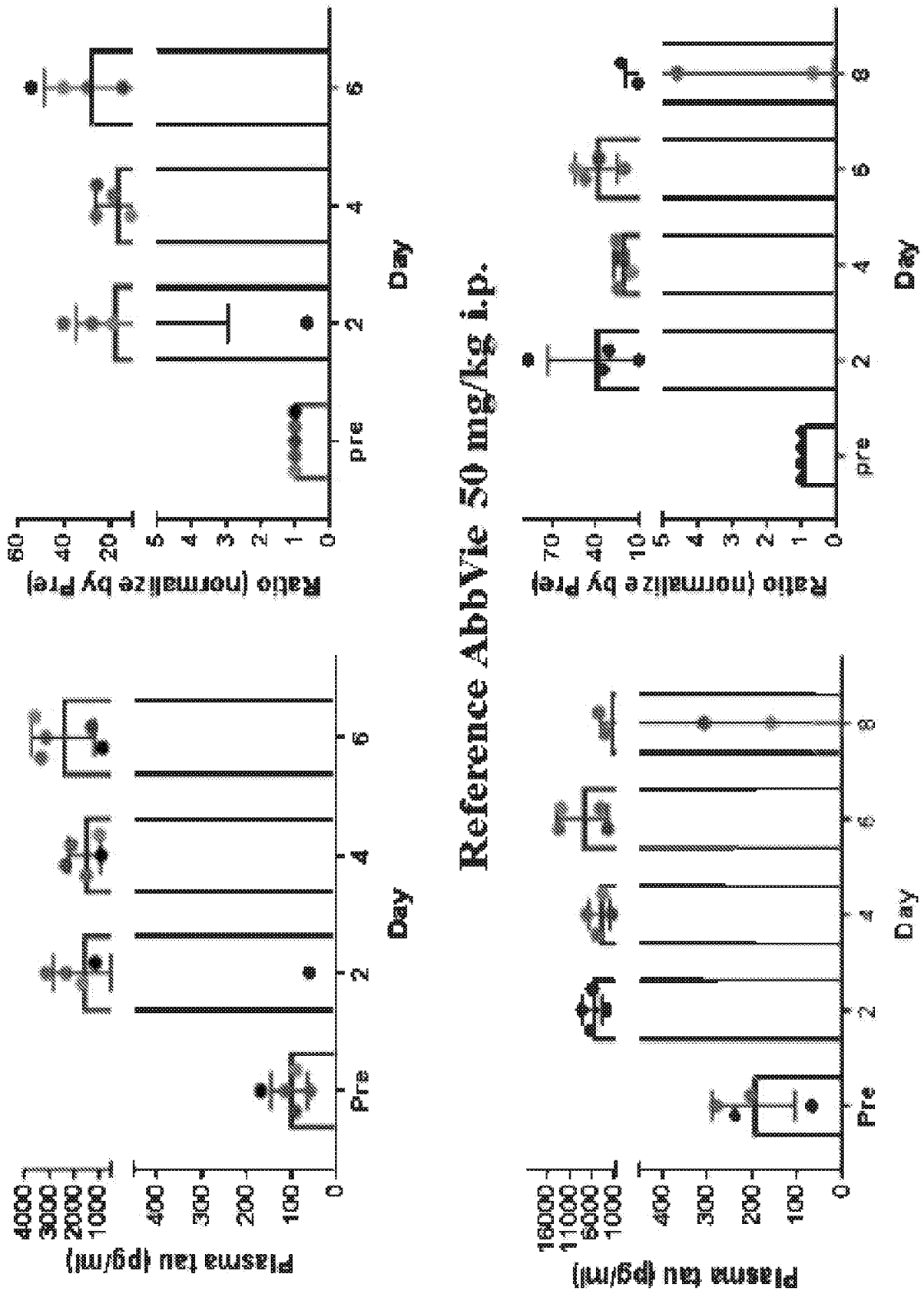

Reference AbbVie 10 mg/kg i.p.
Plasma tau (pg/ml)
Pre
Day
Ratio (normalize by Pre)
pre
Day
Reference AbbVie 50 mg/kg i.p.
Plasma tau (pg/ml)
Pre
Day
Ratio (normalize by Pre)
pre
Day

FIG. 11B

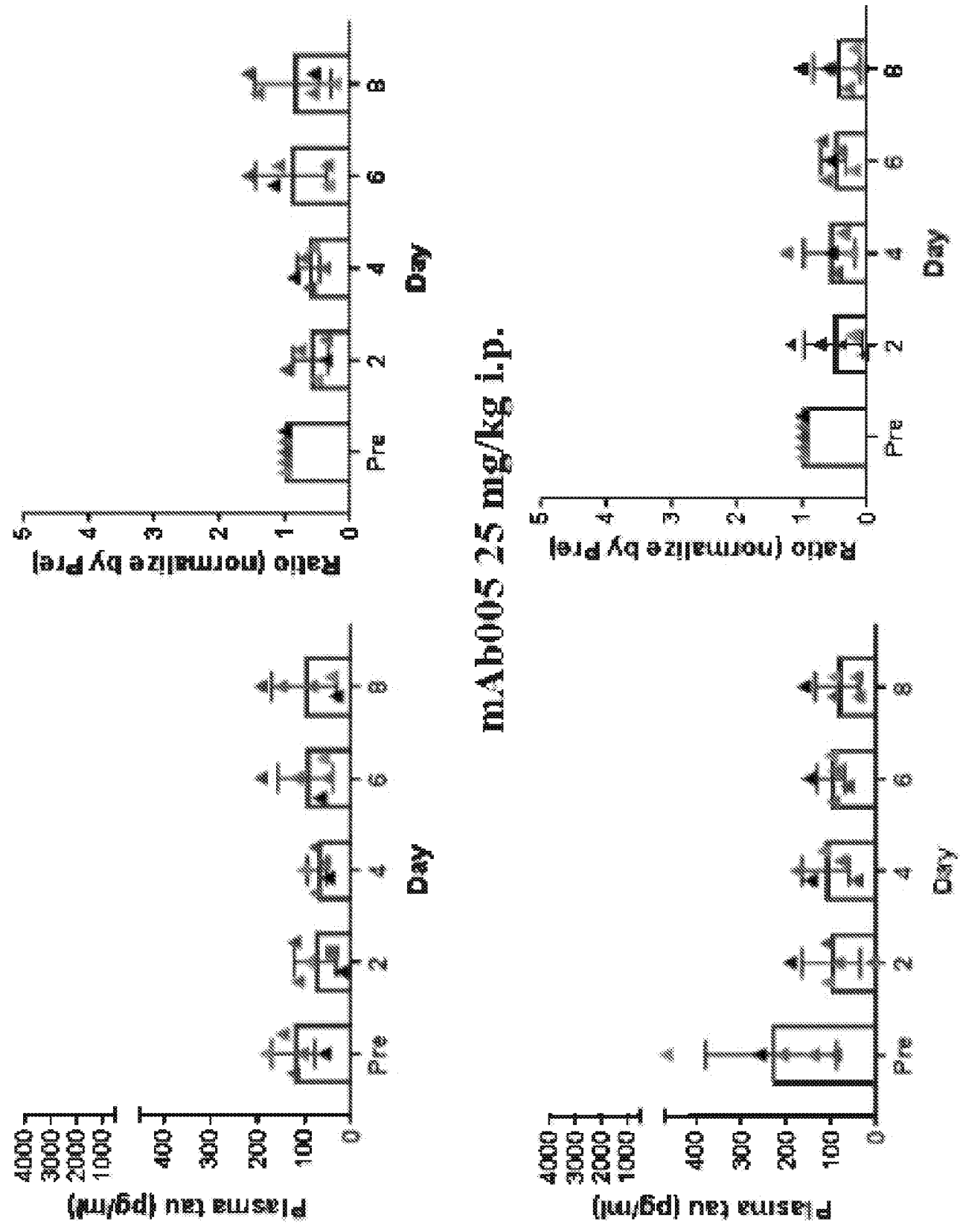

mAb005 10 mg/kg i.p.
Ratio (normalize by Pre)
Pre
Day
Plasma tau (pg/ml)
mAb005 25 mg/kg i.p.

FIG. 12A

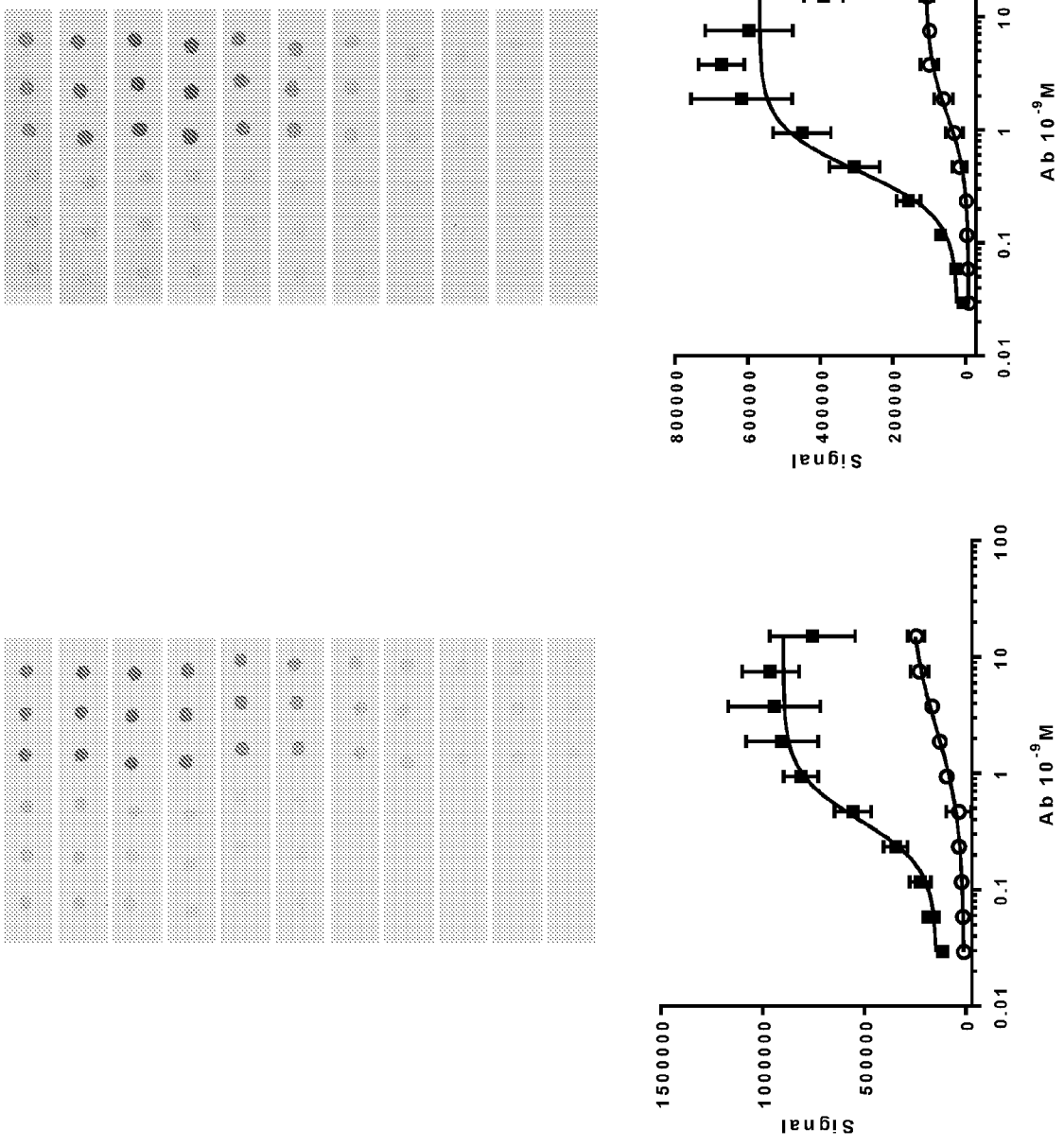

Mouse mAb005
ND
AD
Humanized mAb005
ND
AD
ND total lysate
AD total lysate
Signal
Ab 10 -9 M
0
500000
1000000
1500000
0.01
0.1
1
10
100
200000
400000
600000
800000

FIG. 12B

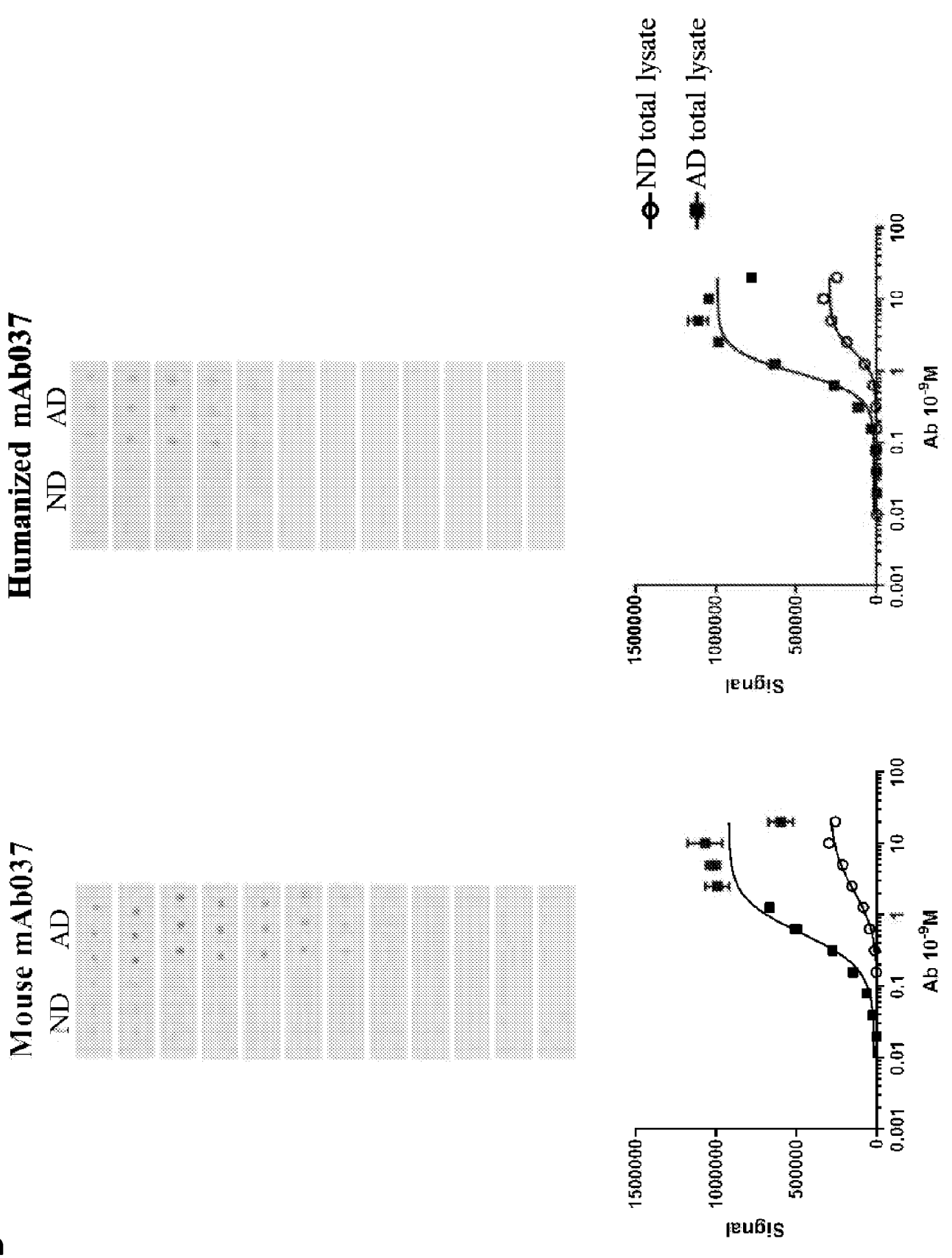

Humanized mAb037
ND
AD
Mouse mAb037
ND
AD
ND total lysate
AD total lysate
Signal
Ab 10^{-9}M
0
500000
1000000
1500000
0.001
0.01
0.1
1
10
100

FIG. 13A

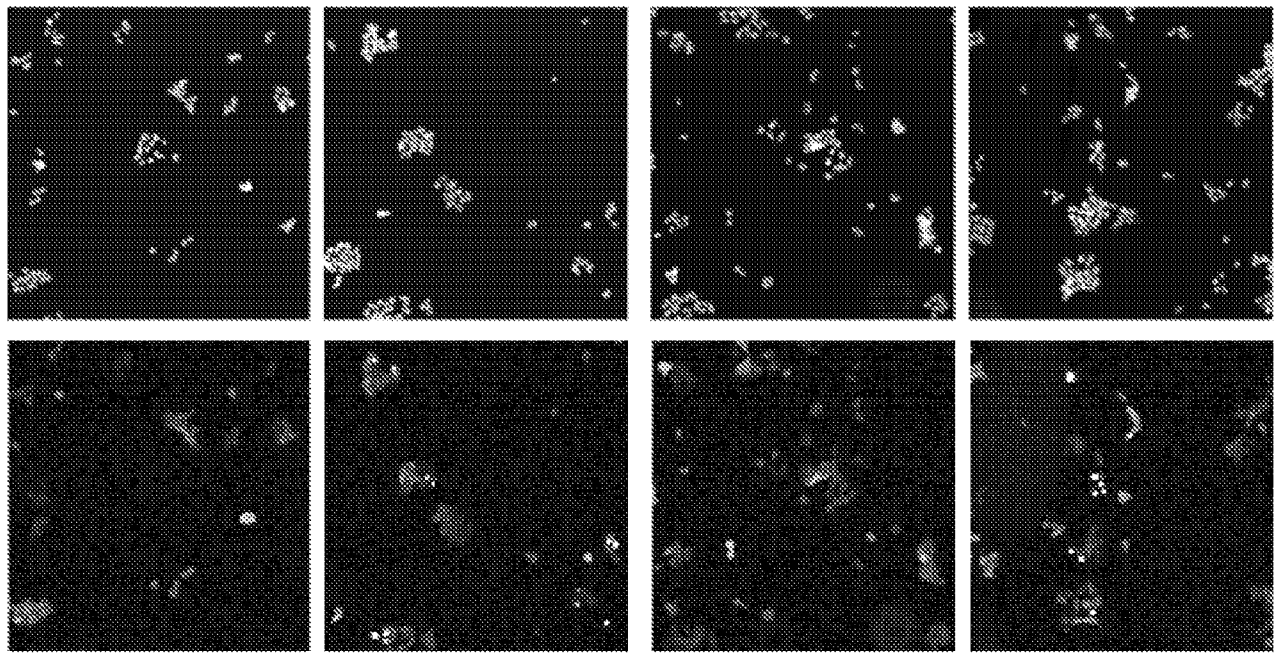

Tau
DAPI
No lysate
Lysate (control group)
Lysate + 133.3 nM mAb005
Lysate + 133.3 nM mIgG

FIG. 13B

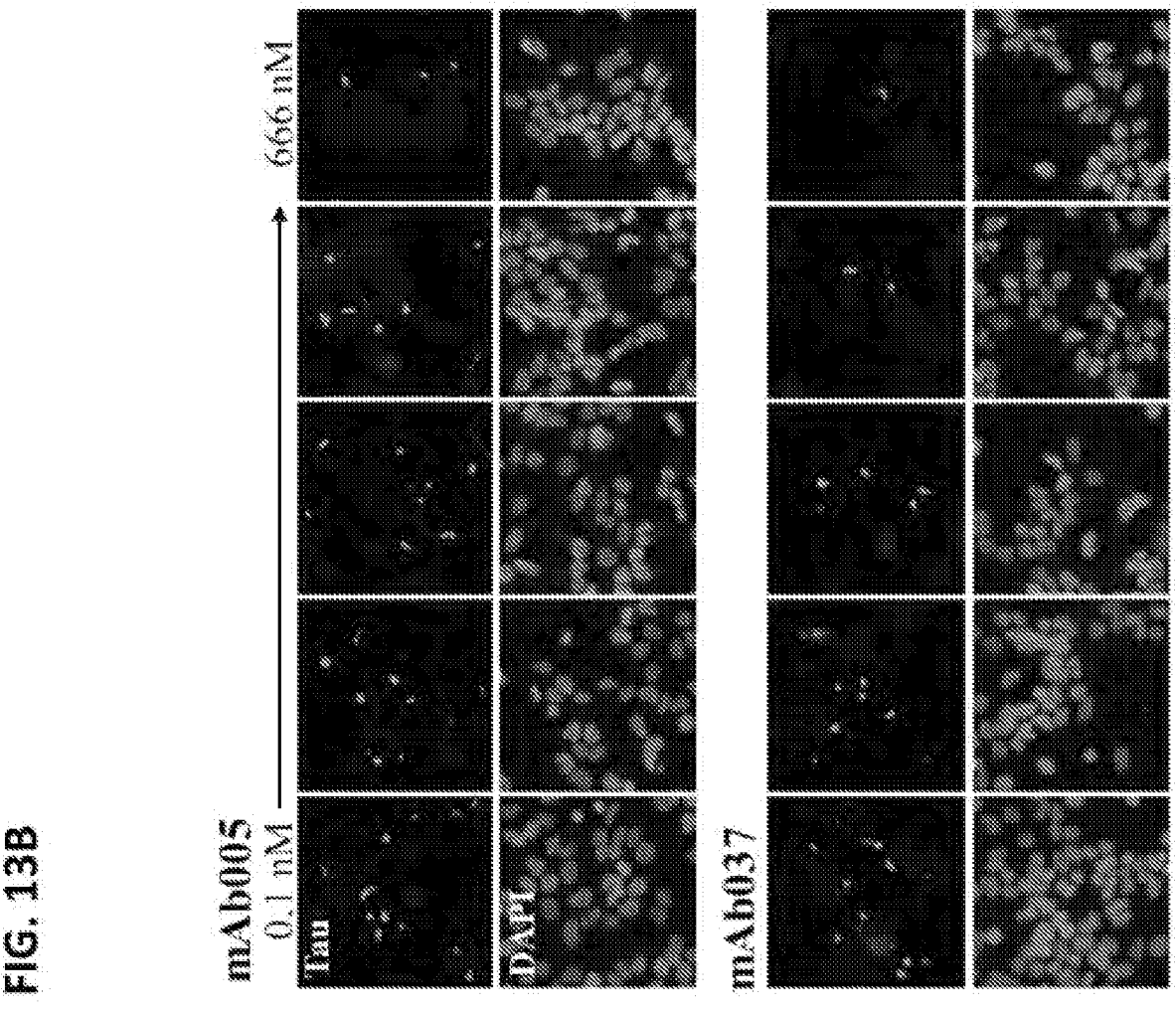

mAb005
0.1 nM
666 nM
Tau
DAPI
mAb037
% Inhibition of control
80
60
40
20
0
-20
0.1
1
10
100
1000
Antibody conc (nM)
mAb037
mAb005
mIgG

FIG. 13C

	mIgG	mAb005
EC50		0.6215

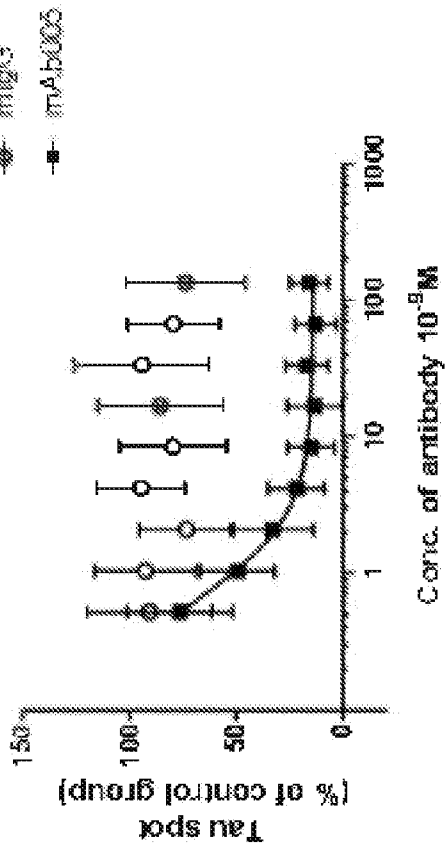


FIG. 13E

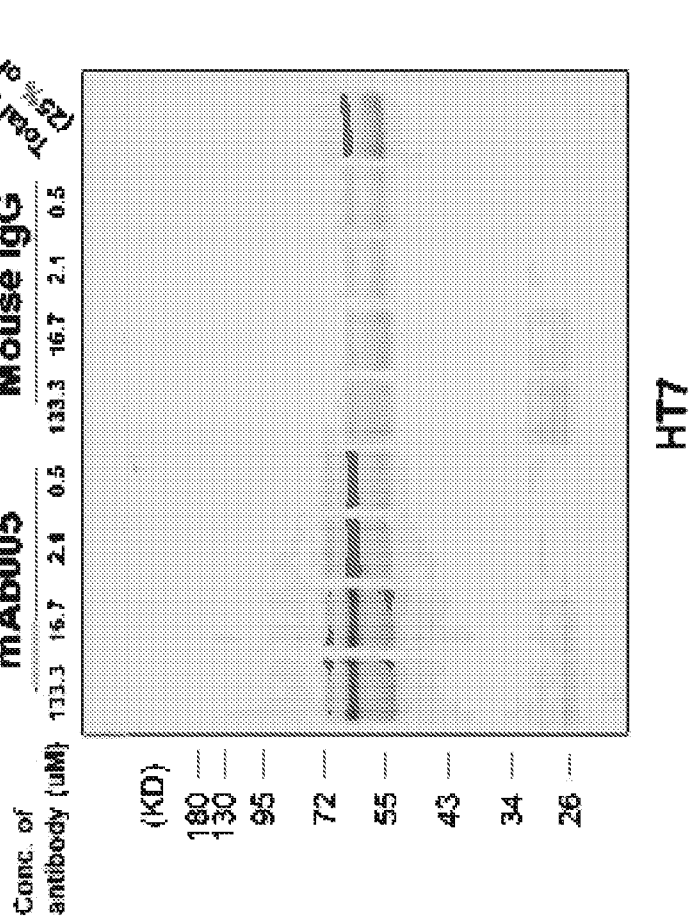


FIG. 13D

	mIgG	mAb005
EC50		1.12

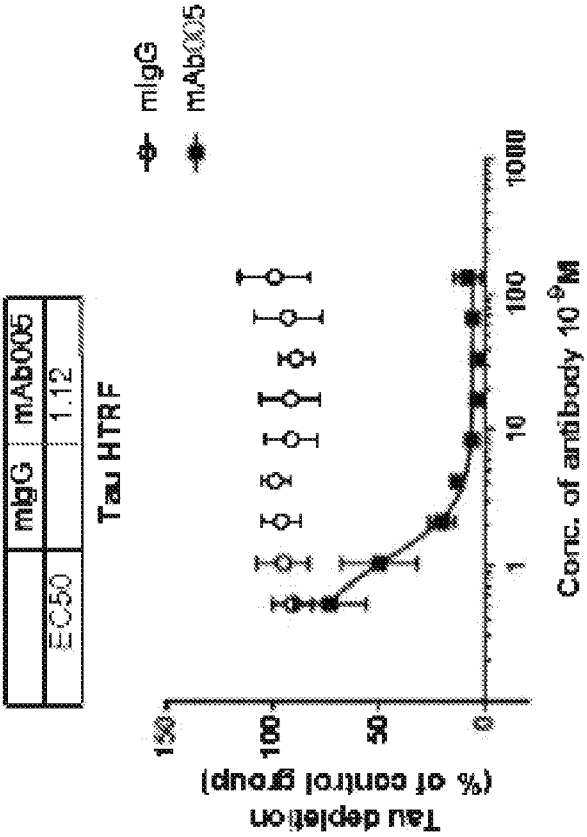
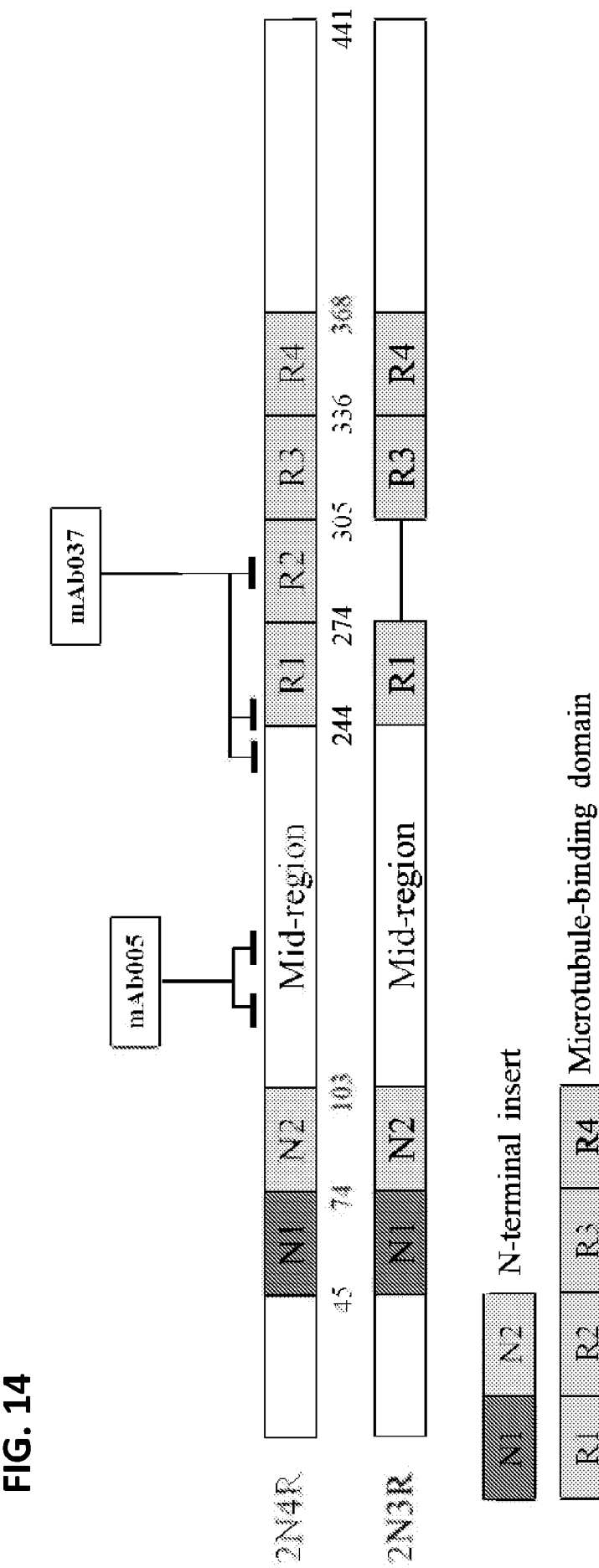


FIG. 14


mAb037
mAb005
2N4R
2N3R
N1
N2
Mid-region
R1
R2
R3
R4
45
74
103
244
274
305
336
368
441
N-terminal insert
Microtubule-binding domain