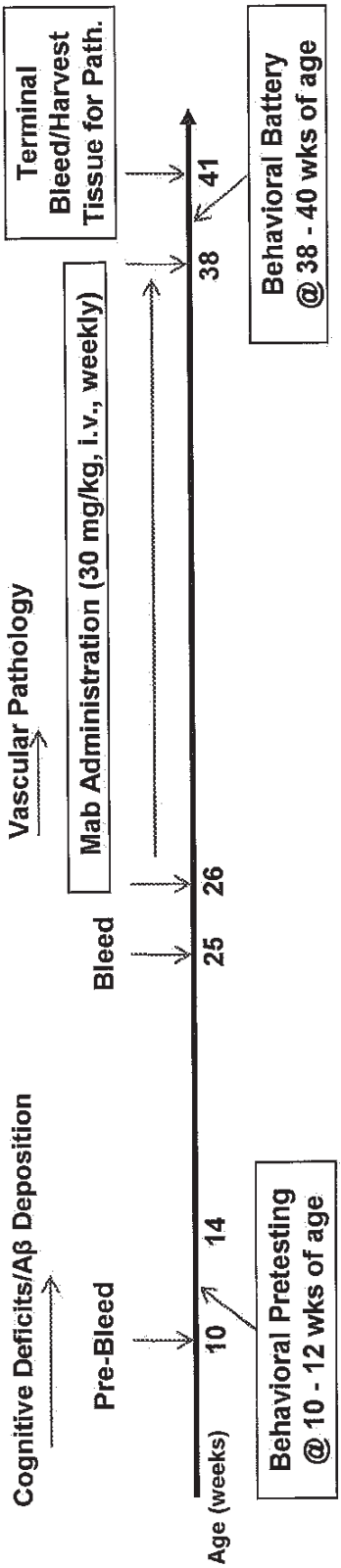

Cognitive Deficits/Aβ Deposition
Vascular Pathology
Pre-Bleed
Bleed
Mab Administration (30 mg/kg, i.v., weekly)
Terminal Bleed/Harvest Tissue for Path.
Behavioral Pretesting @ 10 - 12 wks of age
Behavioral Battery @ 38 - 40 wks of age
Age (weeks)
10
14
25
26
38
41

FIG. 1

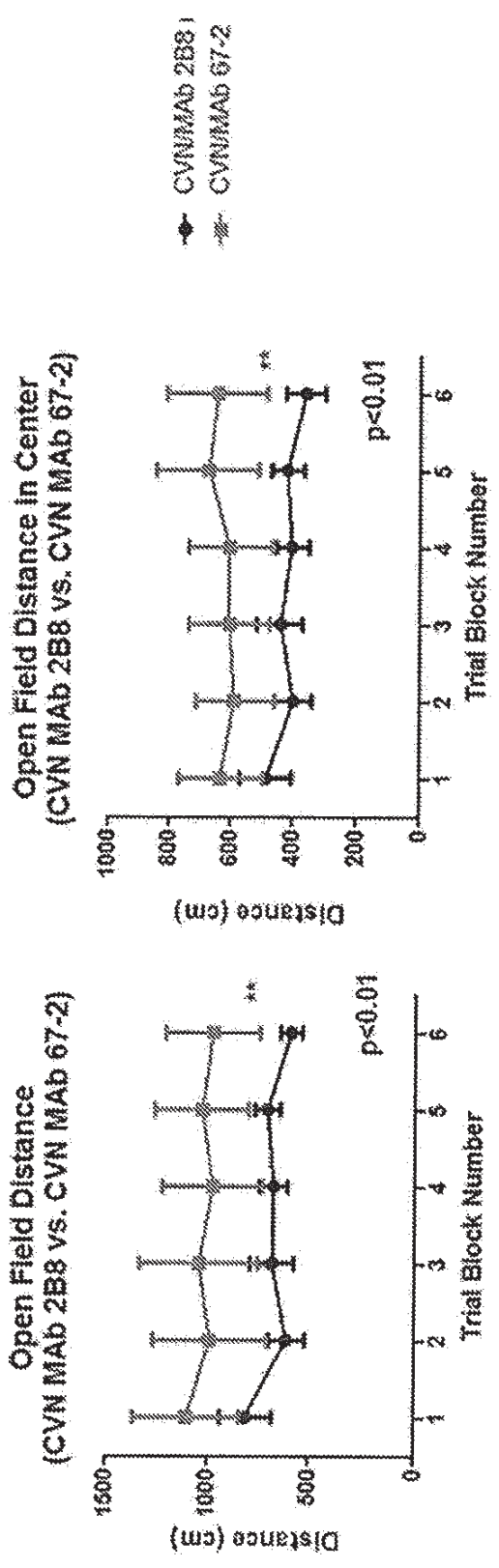
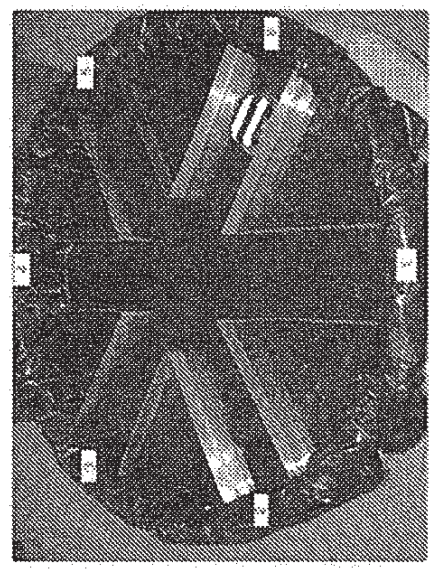

Open Field Distance
(CVN MAb 2B8 vs. CVN MAb 67-2)
Distance (cm)
1500
1000
500
0
1
2
3
4
5
6
Trial Block Number
**
p<0.01
Open Field Distance in Center
(CVN MAb 2B8 vs. CVN MAb 67-2)
Distance (cm)
1000
800
600
400
200
0
1
2
3
4
5
6
Trial Block Number
**
p<0.01
CVNMAb 2B8
CVNMAb 67-2

FIG. 2A

FIG. 2B



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FIG. 3A

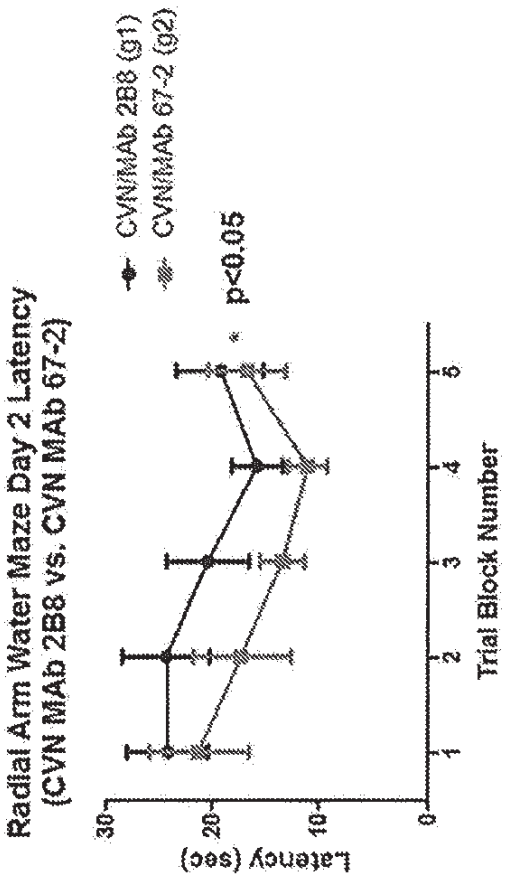



FIG. 3B

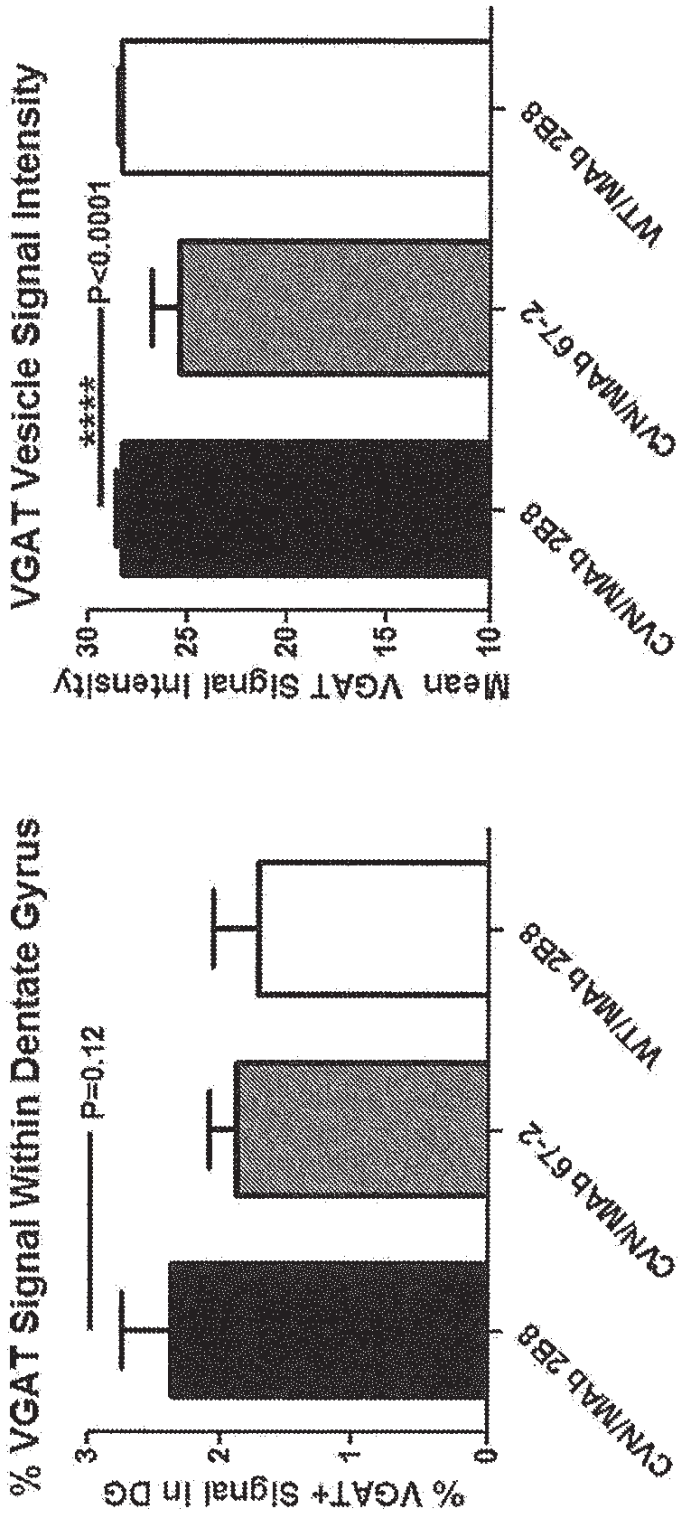

VGAT Vesicle Signal Intensity
Mean VGAT Signal Intensity
30
25
20
15
10
****
P<0.0001
CVN/MAb 2B8
CVN/MAb 67-2
WT/MAb 2B8
% VGAT Signal Within Dentate Gyrus
% VGAT+ Signal in DG
3
2
1
0
P=0.12
CVN/MAb 2B8
CVN/MAb 67-2
WT/MAb 2B8

FIG. 4

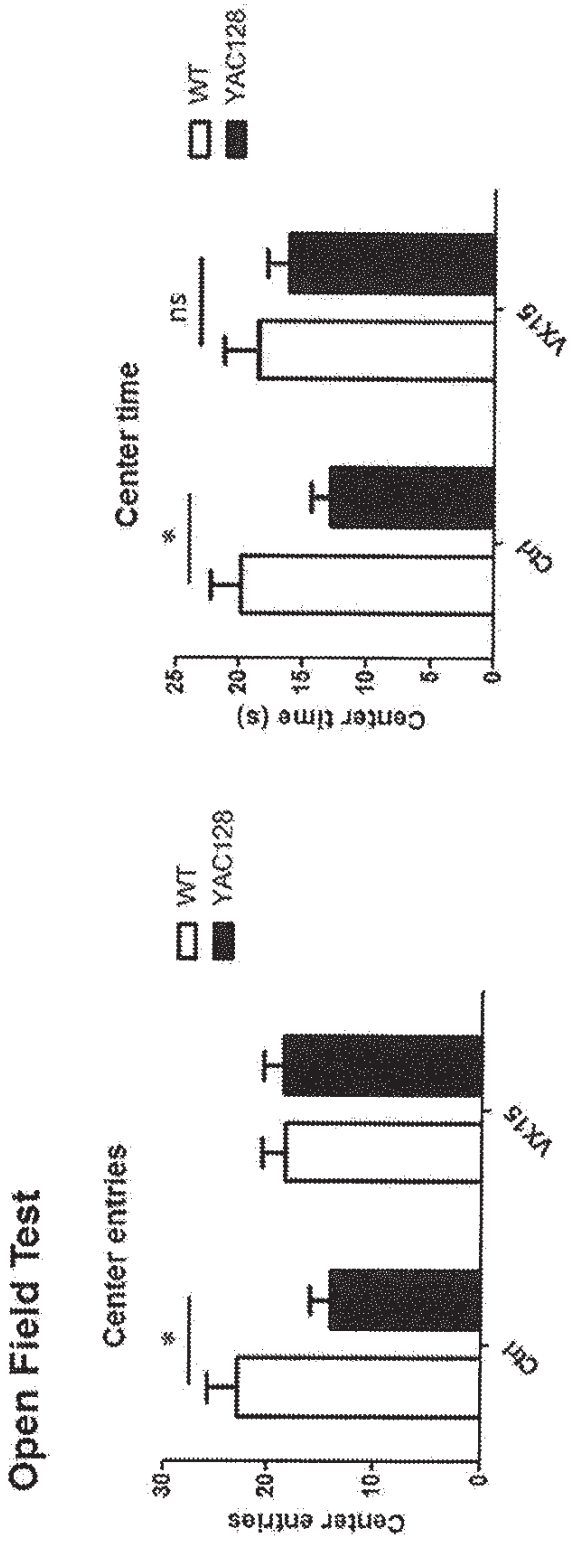

Open Field Test
Center entries
WT
YAC128
*
Cdf
YX15
Center entries
0
10
20
30

FIG. 5A


Center time
WT
YAC128
*
ns
Cdf
YX15
Center time (s)
0
5
10
15
20
25

FIG. 5B

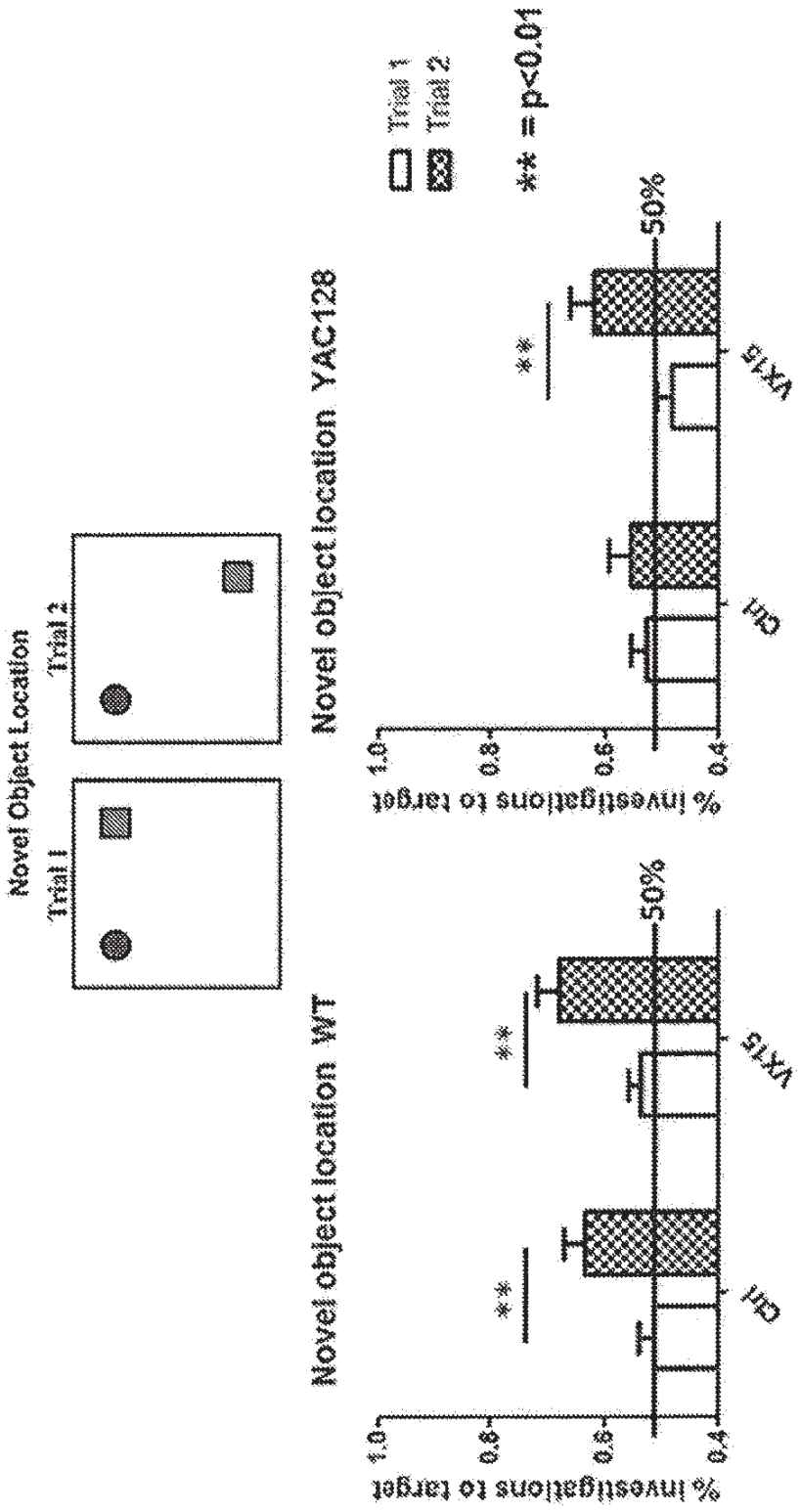
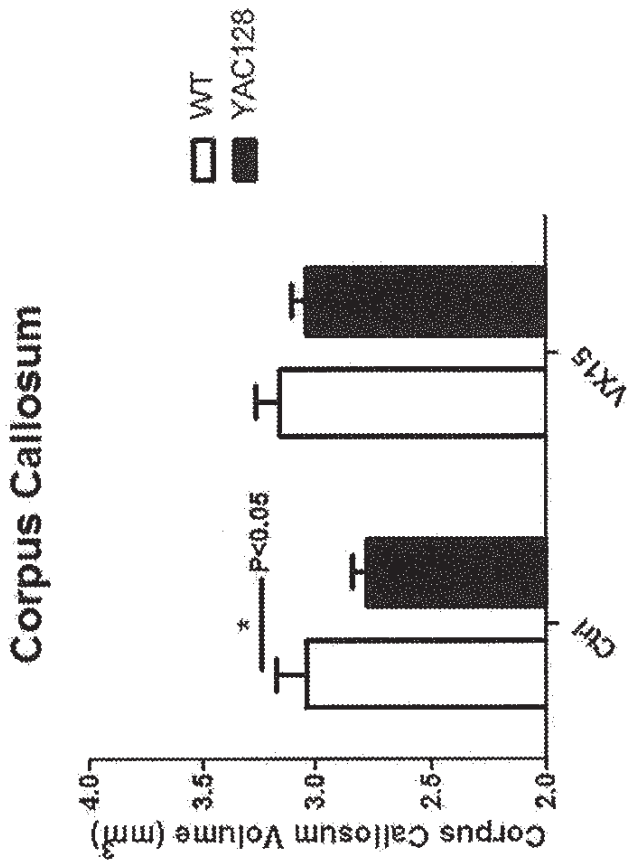
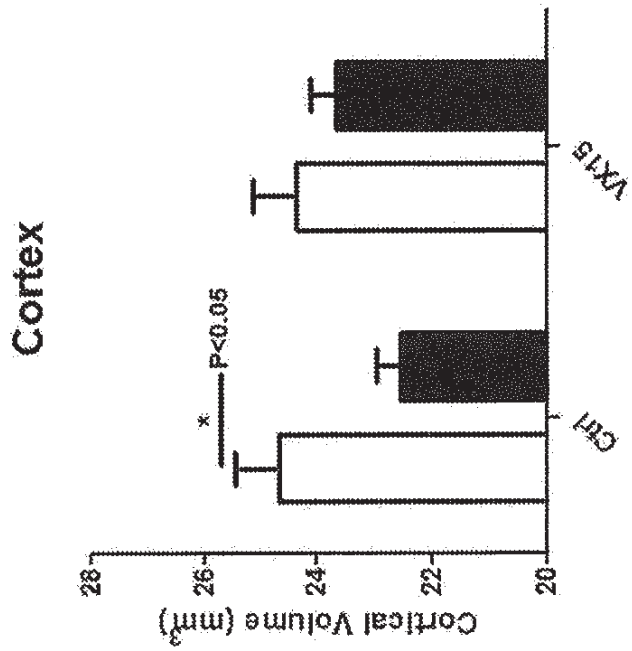

Novel Object Location
Trial 1
Trial 2
Novel object location WT
Novel object location YAC128
Trial 1
Trial 2
** = p<0.01
% investigations to target
1.0
0.8
0.6
0.4
50%
**
Ctl
Vk15

FIG. 6A

FIG. 6B


Corpus Callosum
WT
YAC128
Corpus Callosum Volume (mm³)
4.0
3.5
3.0
2.5
2.0
*
P<0.05
Ctrl
YAC
FIG. 7B


Cortex
Cortical Volume (mm³)
28
26
24
22
20
*
P<0.05
Ctrl
YAC
FIG. 7A

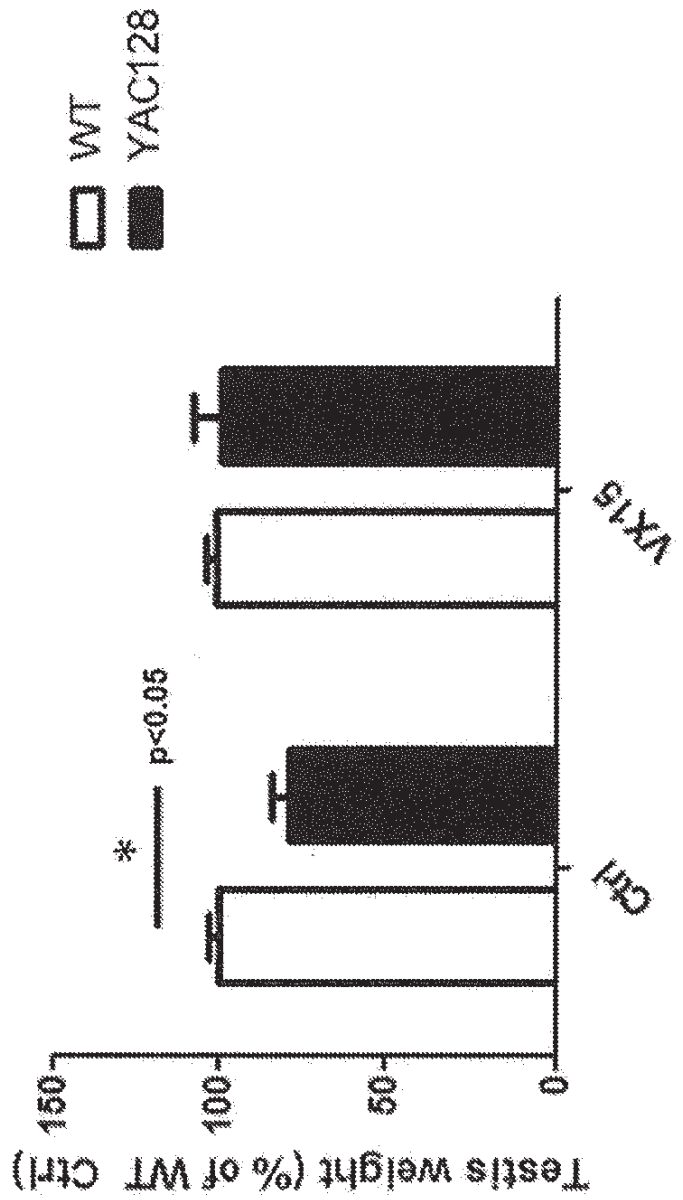



FIG. 8

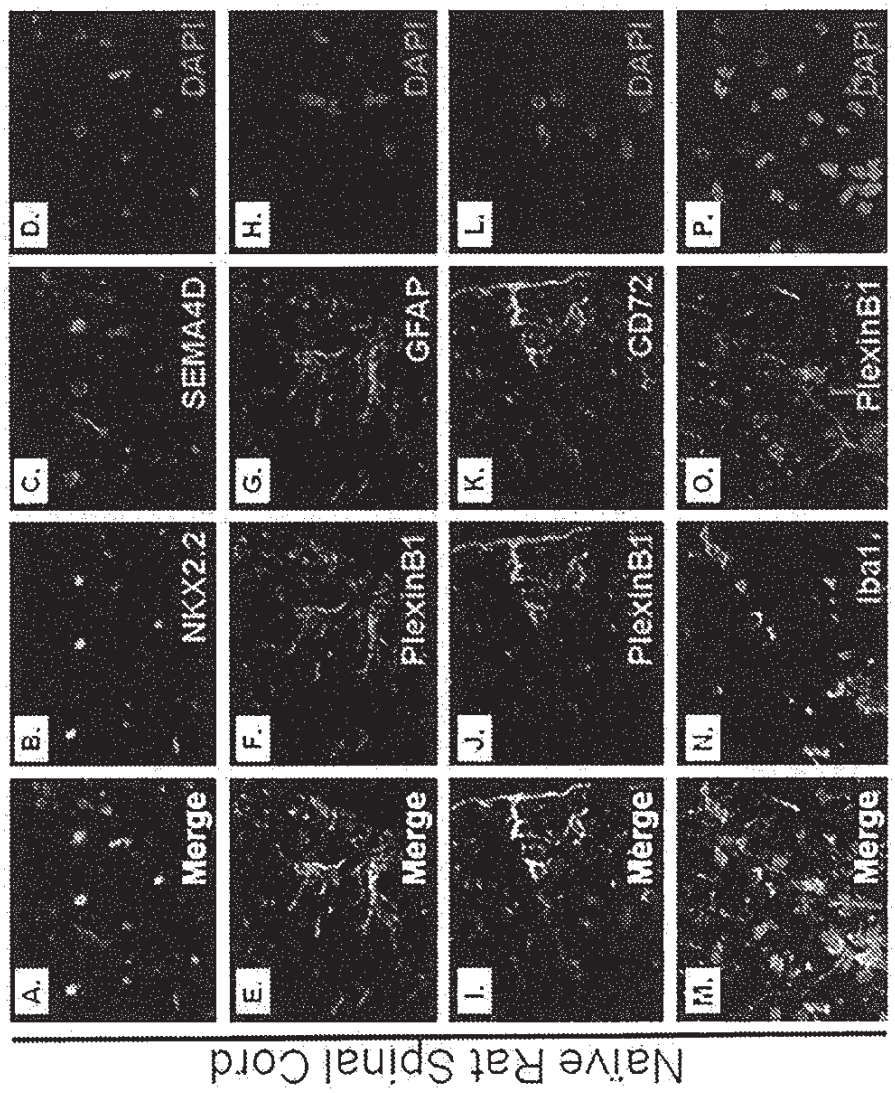



FIG. 9A, B, C, D, E, F, G, H, I, J, K, L, M, N, O, P

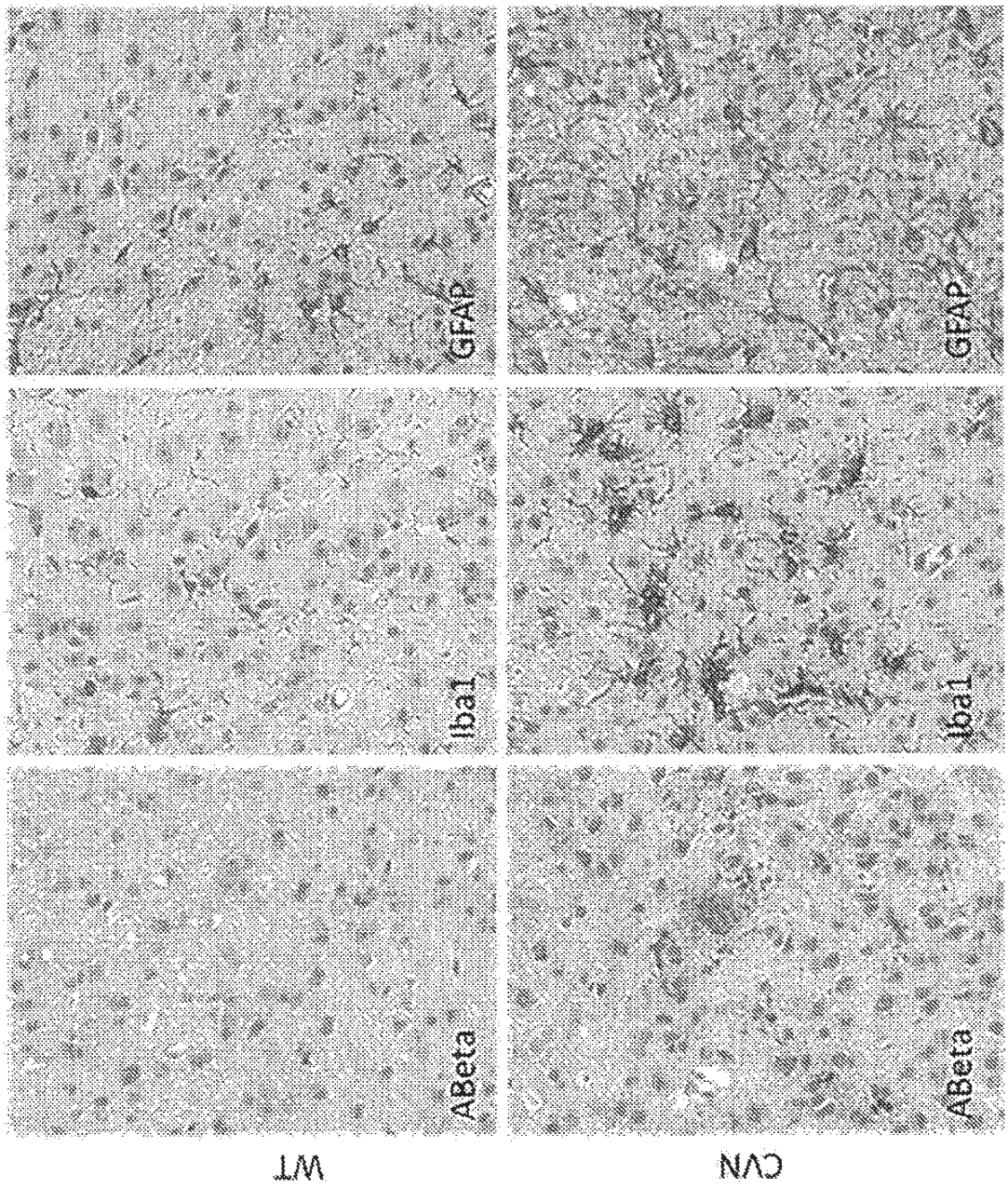



FIG. 10

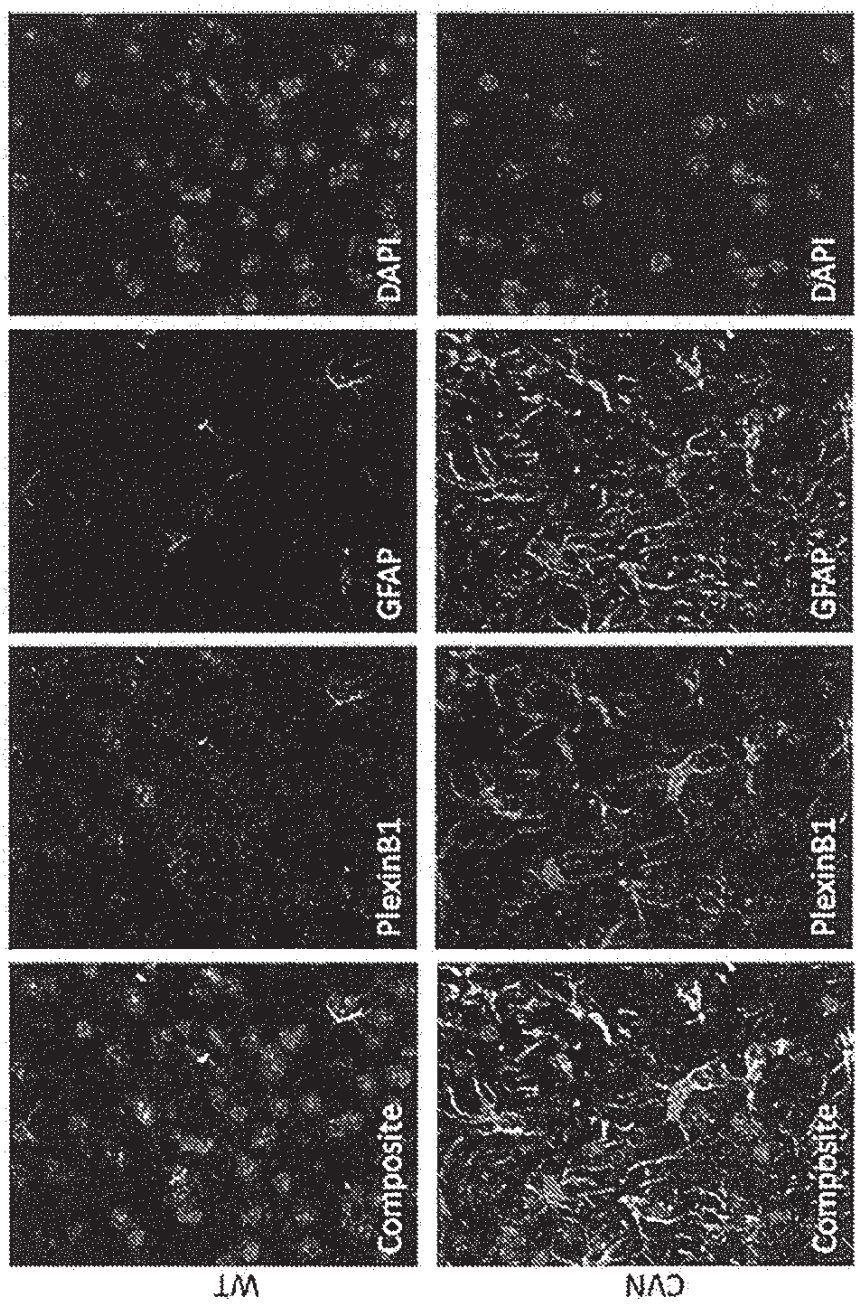



FIG. 11A

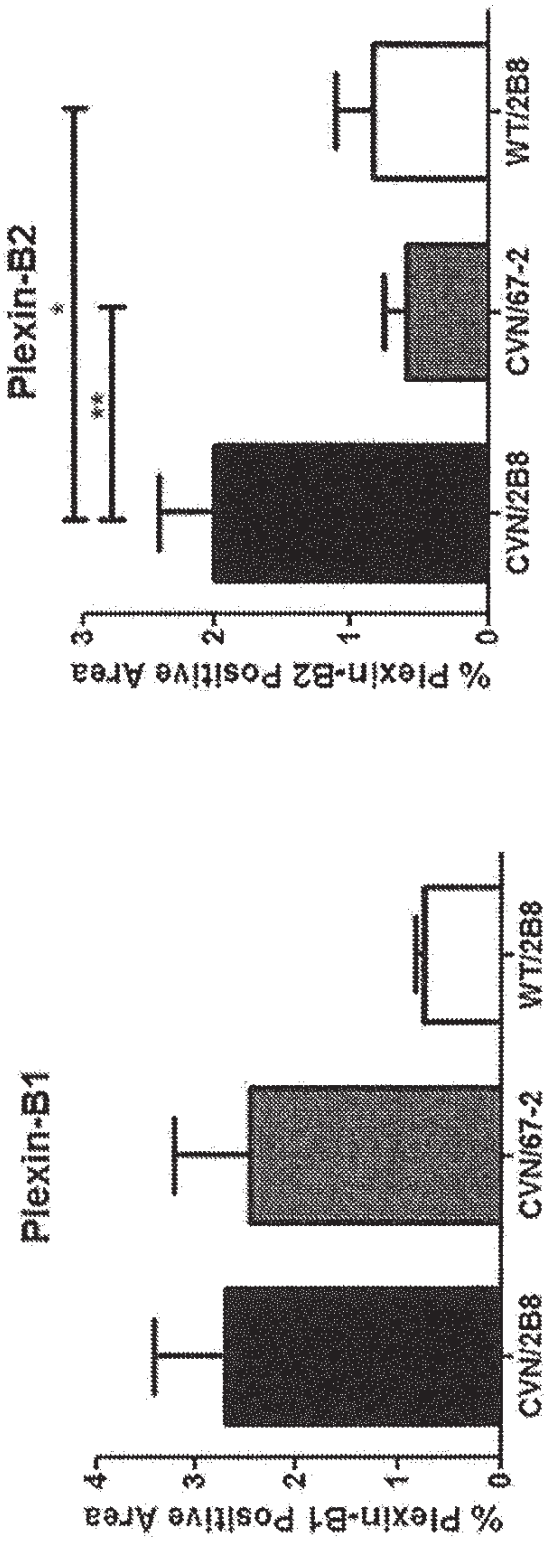

Plexin-B2
*
**
% Plexin-B2 Positive Area
0
1
2
3
CVN/2B8
CVN/67-2
WT/2B8
Plexin-B1
% Plexin-B1 Positive Area
0
1
2
3
4
CVN/2B8
CVN/67-2
WT/2B8

FIG. 11B

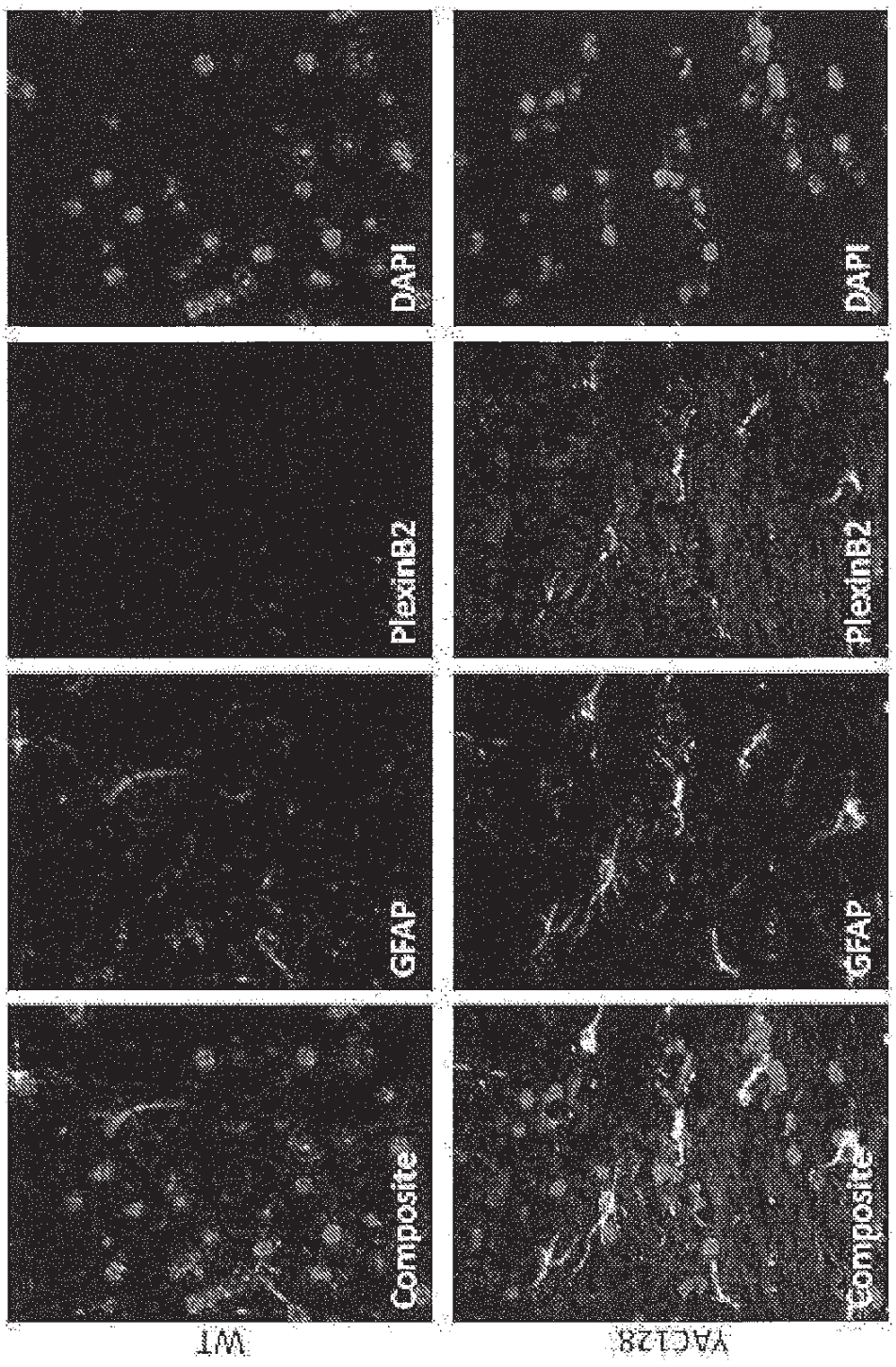

WT
YAC128
Composite
GFAP
PlexinB2
DAPI
Composite
GFAP
PlexinB2
DAPI

FIG. 12

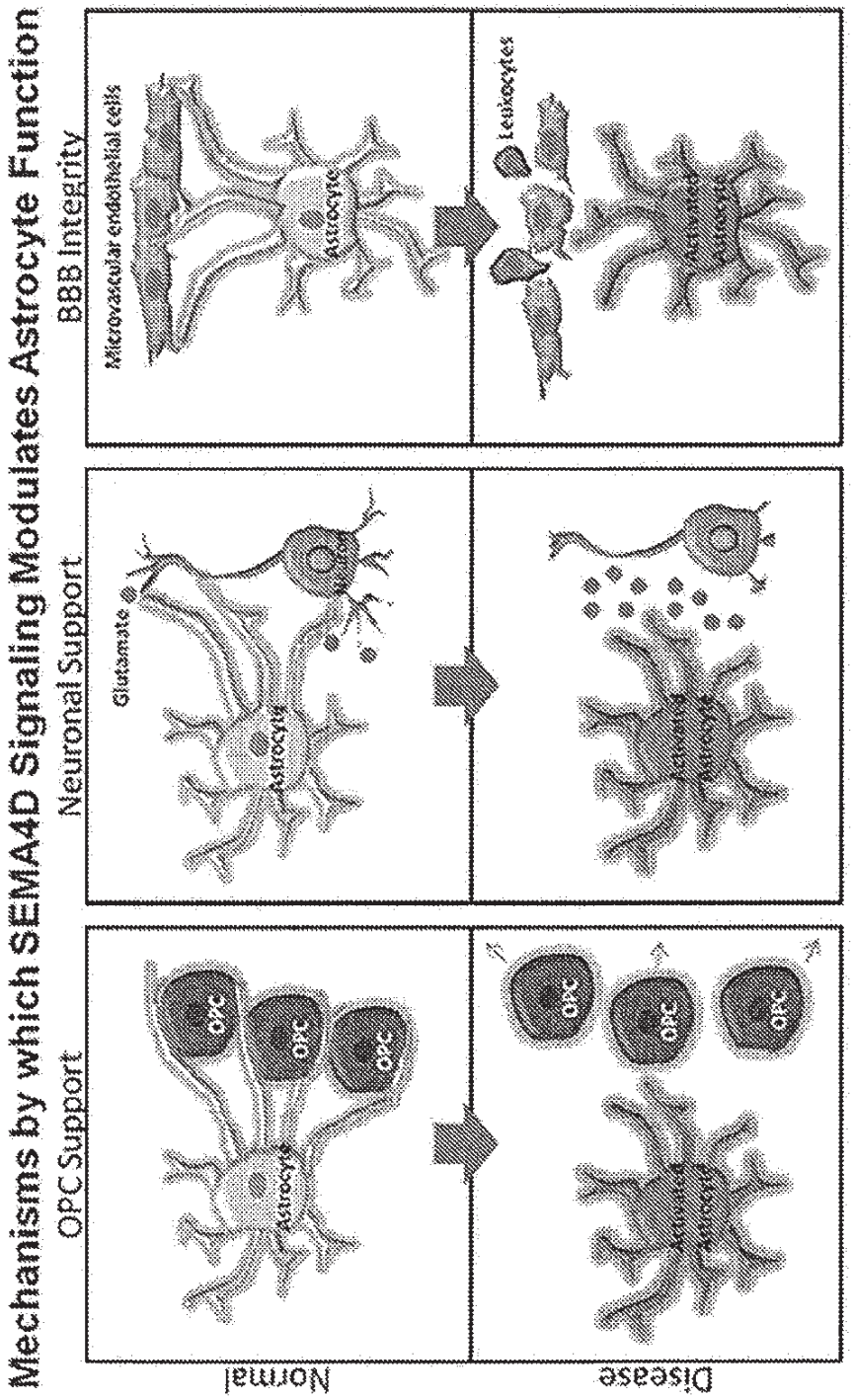

Mechanisms by which SEMA4D Signaling Modulates Astrocyte Function
OPC Support
Neuronal Support
BBB Integrity
Normal
Disease
OPC
Astrocyte
Glutamate
Activated Astrocyte
Microvascular endothelial cells
Leukocytes

FIG. 13

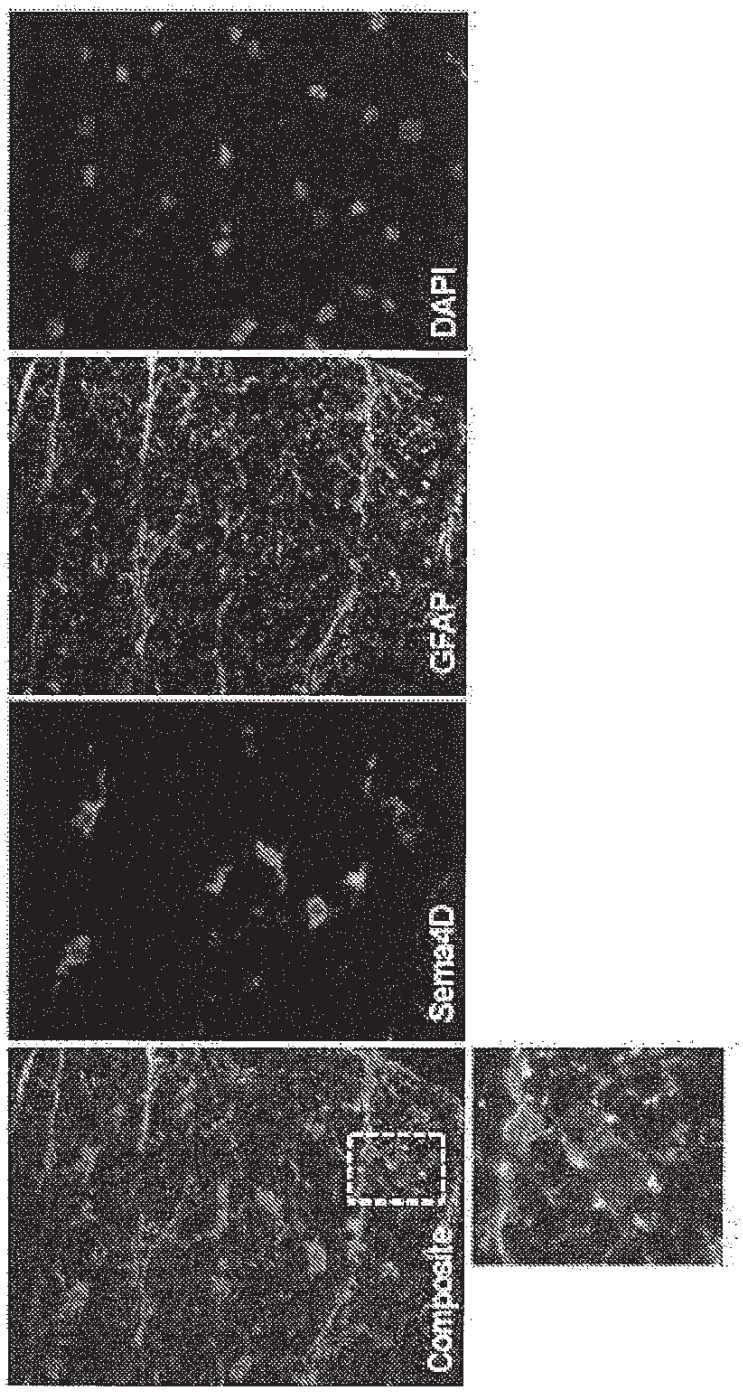



FIG. 14

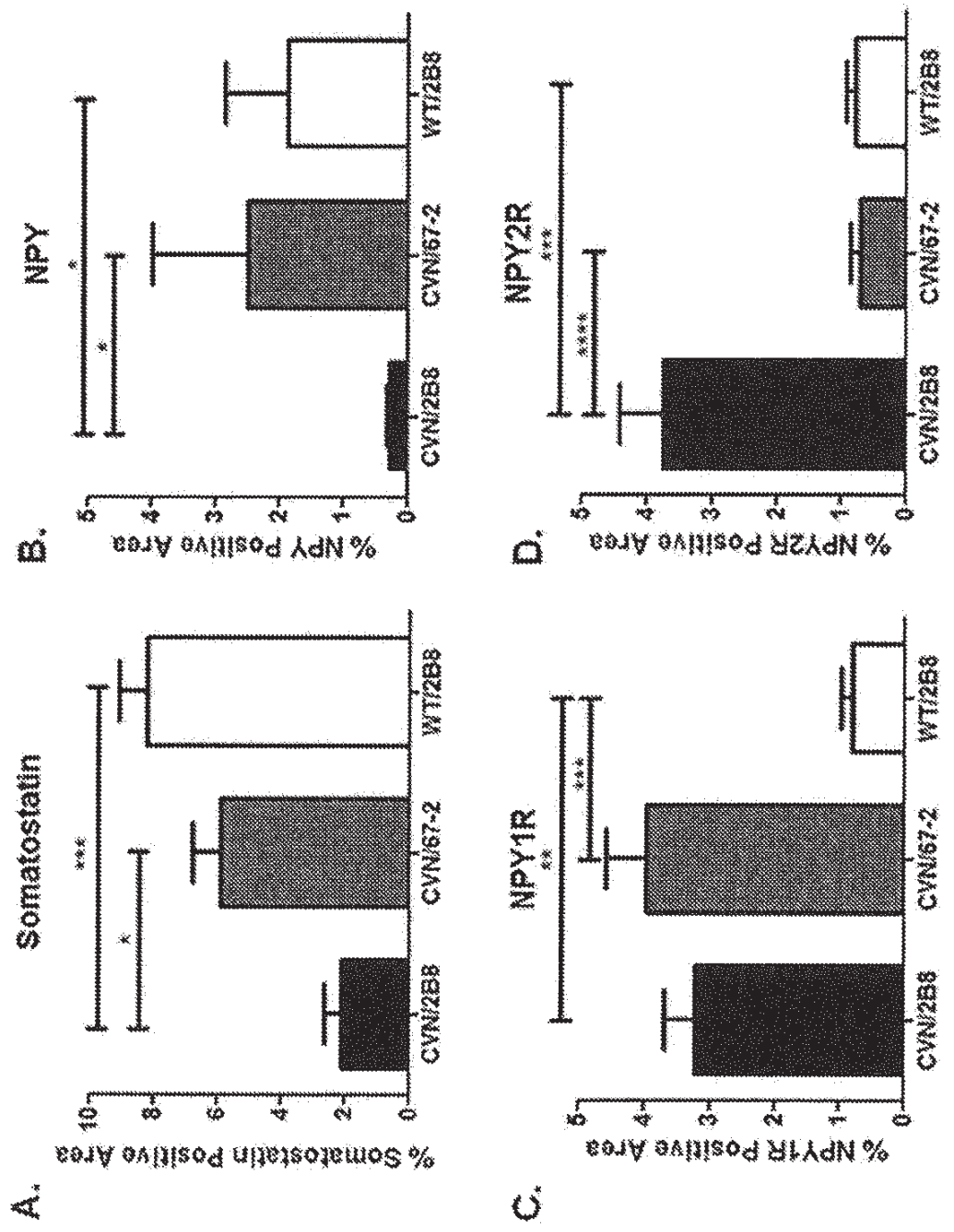

A.
Somatostatin
% Somatostatin Positive Area
CVN/2B8
CVN/67-2
WT/2B8
B.
NPY
% NPY Positive Area
C.
NPY1R
% NPY1R Positive Area
D.
NPY2R
% NPY2R Positive Area

FIG. 15A, B, C, D

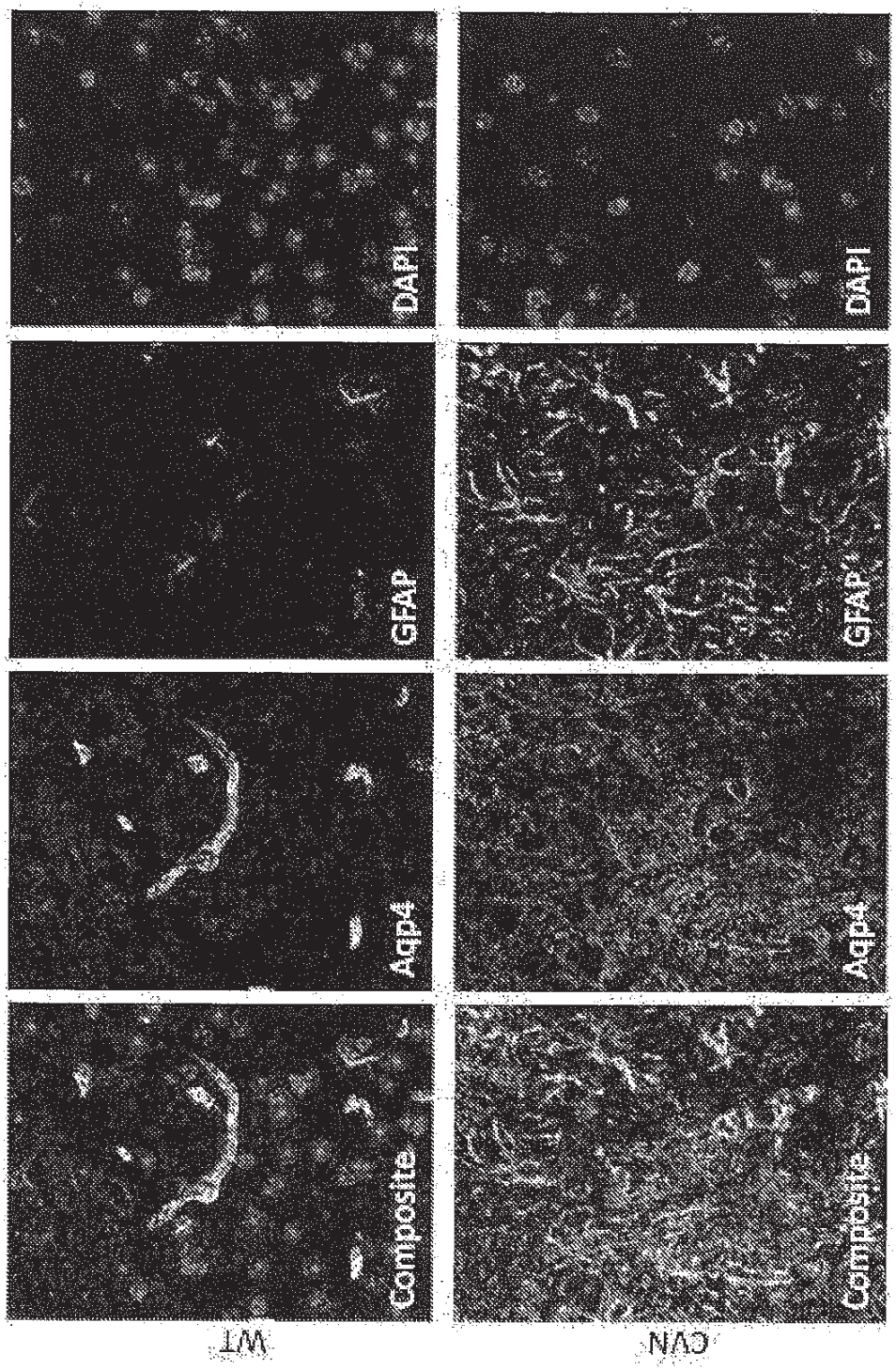



FIG. 16

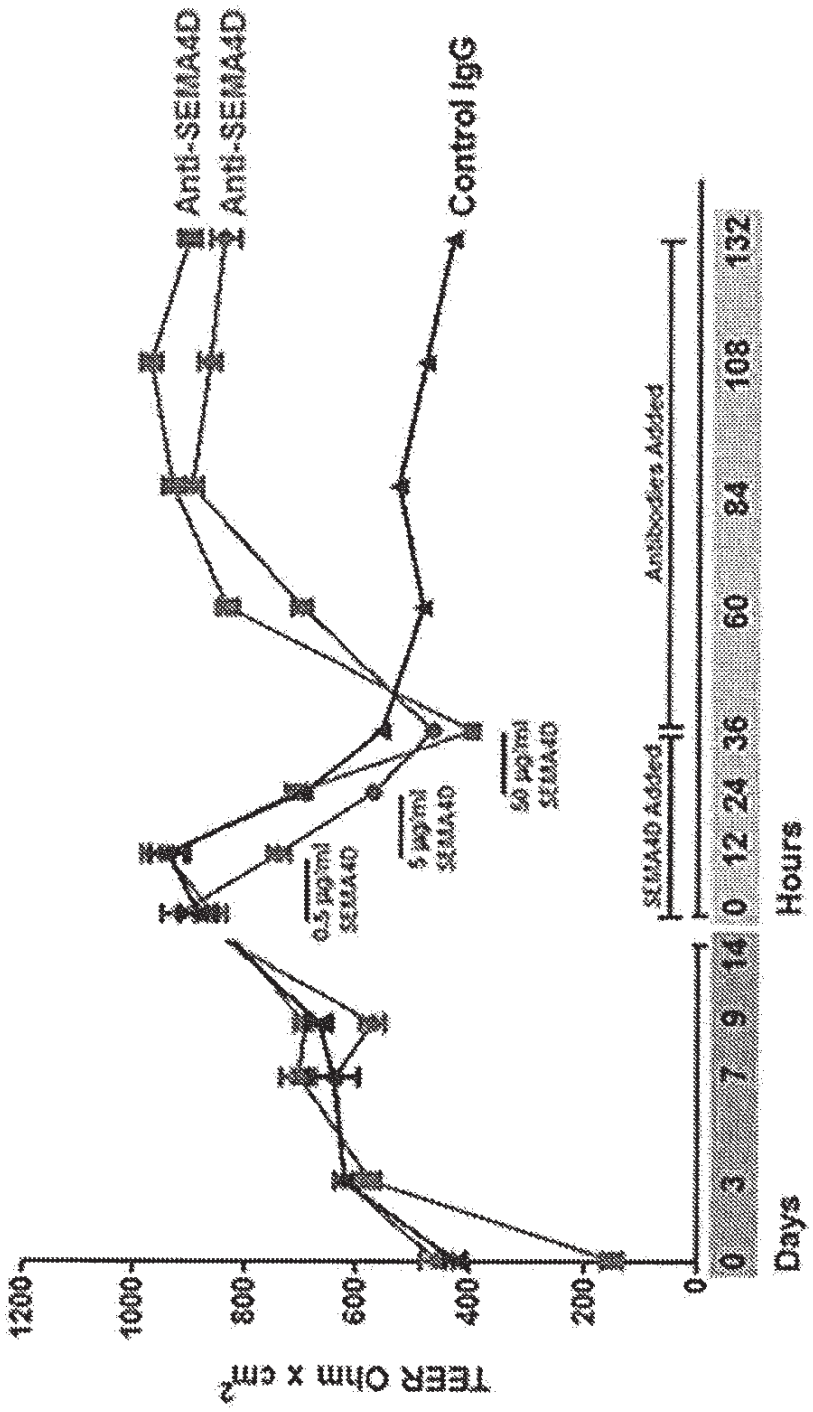

TEER Ohm x cm²
1200
1000
800
600
400
200
0
Days
0 3 7 9 14
Hours
0 12 24 36 60 84 108 132
SEMA4D Added
Antibodies Added
0.5 µg/ml SEMA4D
5 µg/ml SEMA4D
50 µg/ml SEMA4D
Anti-SEMA4D
Anti-SEMA4D
Control IgG

FIG. 17

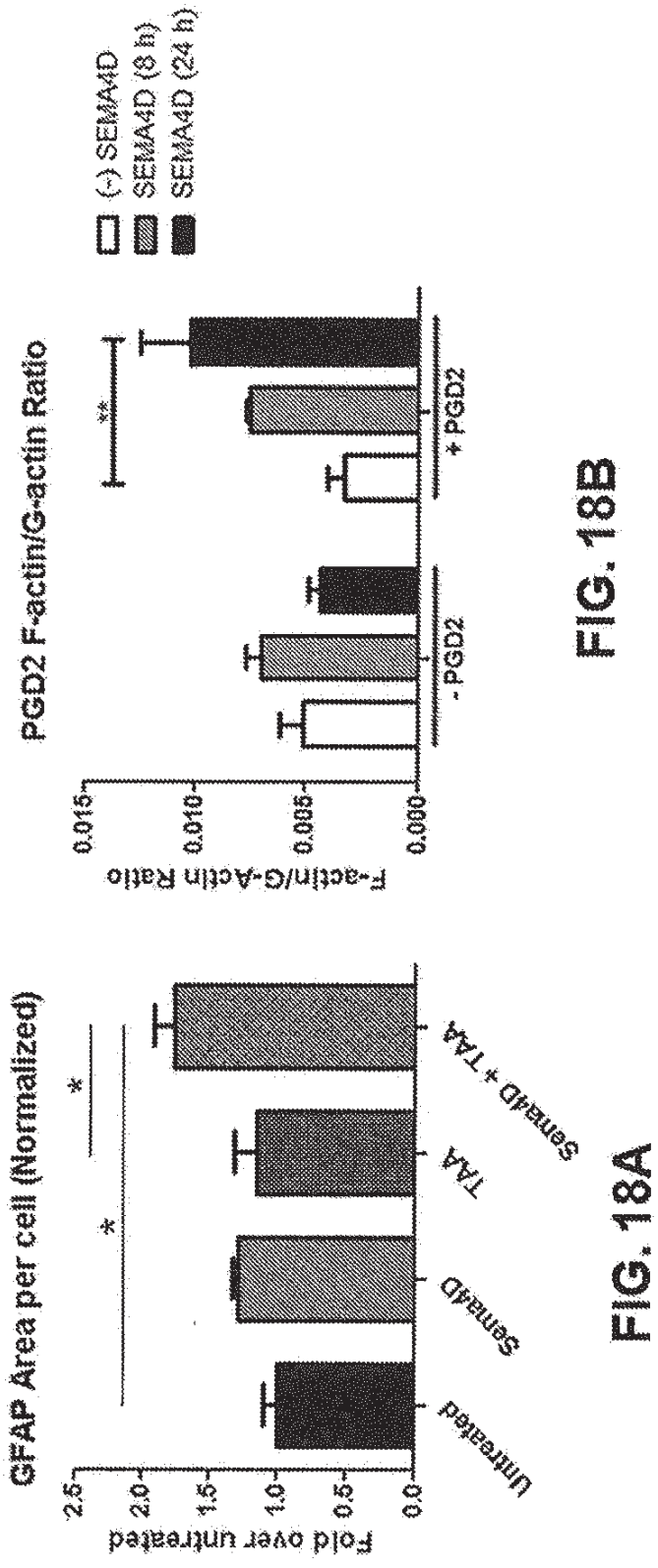



FIG. 18A

FIG. 18B