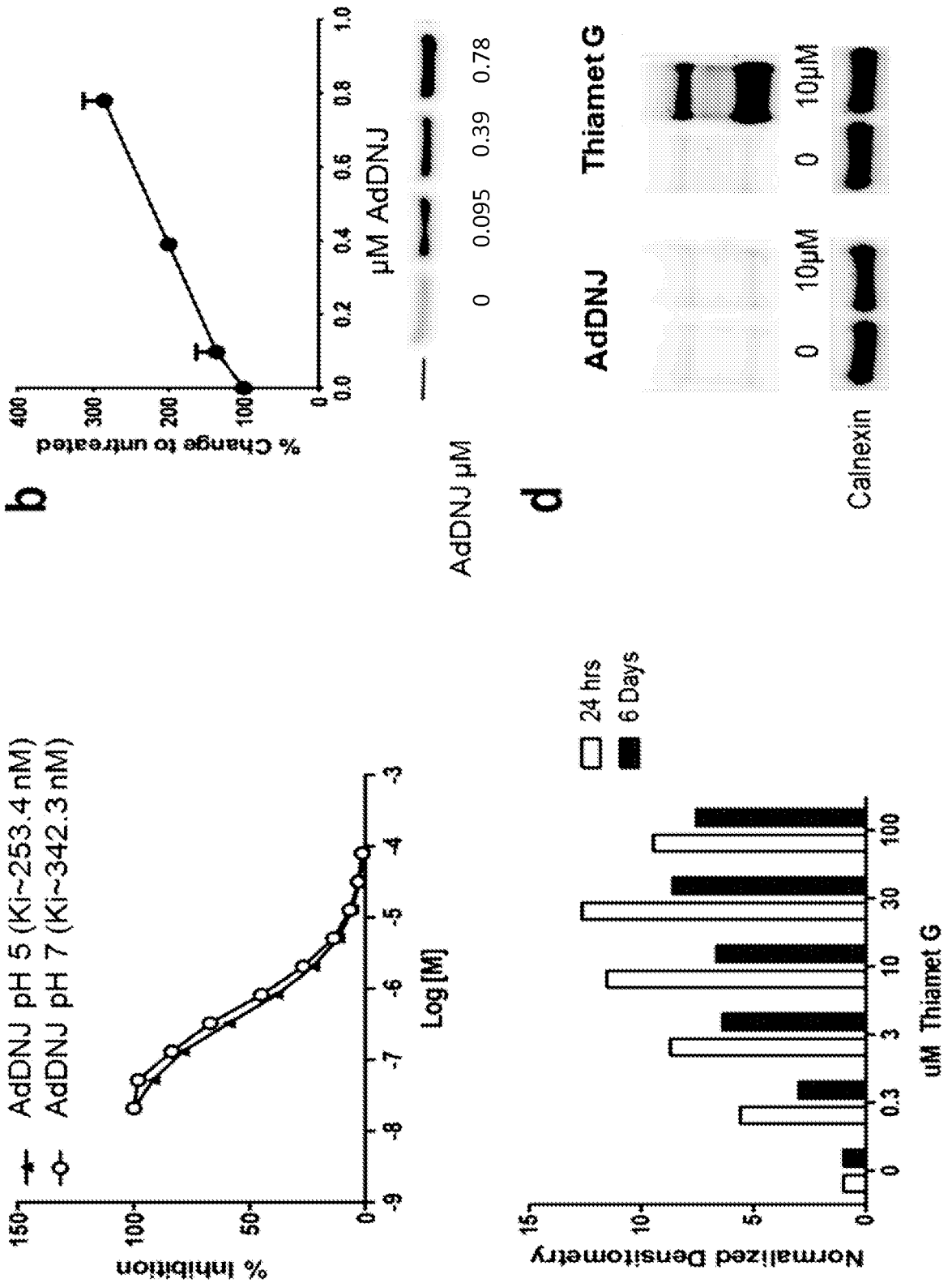
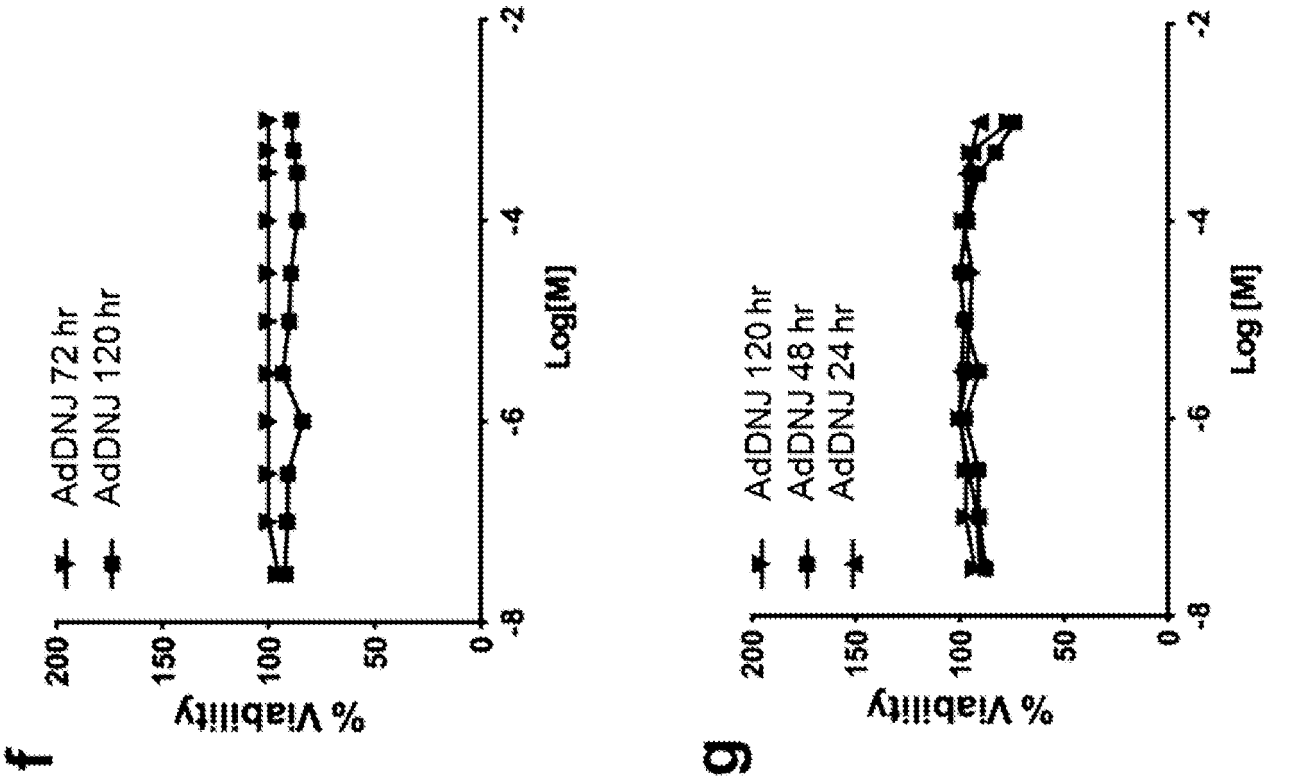
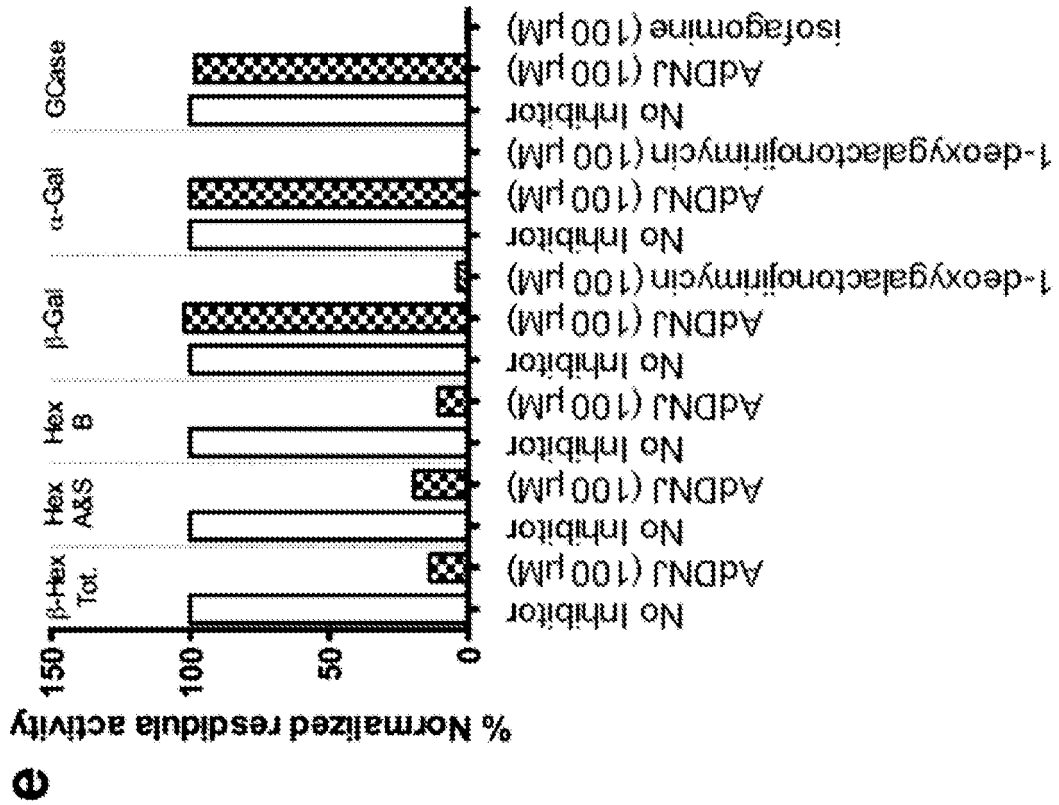
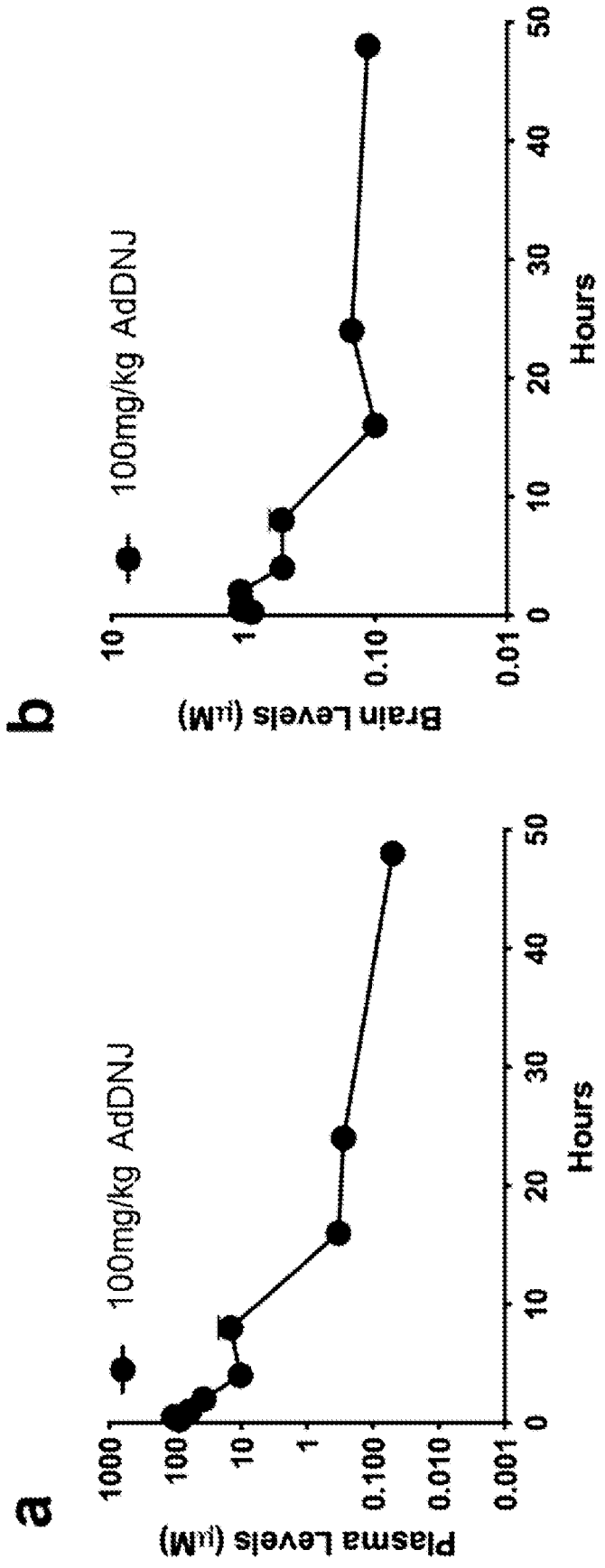

a
AdDNJ pH 5 (Ki~253.4 nM)
AdDNJ pH 7 (Ki~342.3 nM)
% Inhibition
Log [M]
b
% Change to untreated
µM AdDNJ
AdDNJ µM
0 0.095 0.39 0.78
c
24 hrs
6 Days
Normalized Densitometry
uM Thiamet G
d
AdDNJ
Thiamet G
0 10µM 0 10µM
Calnexin

FIGS. 1 a-d

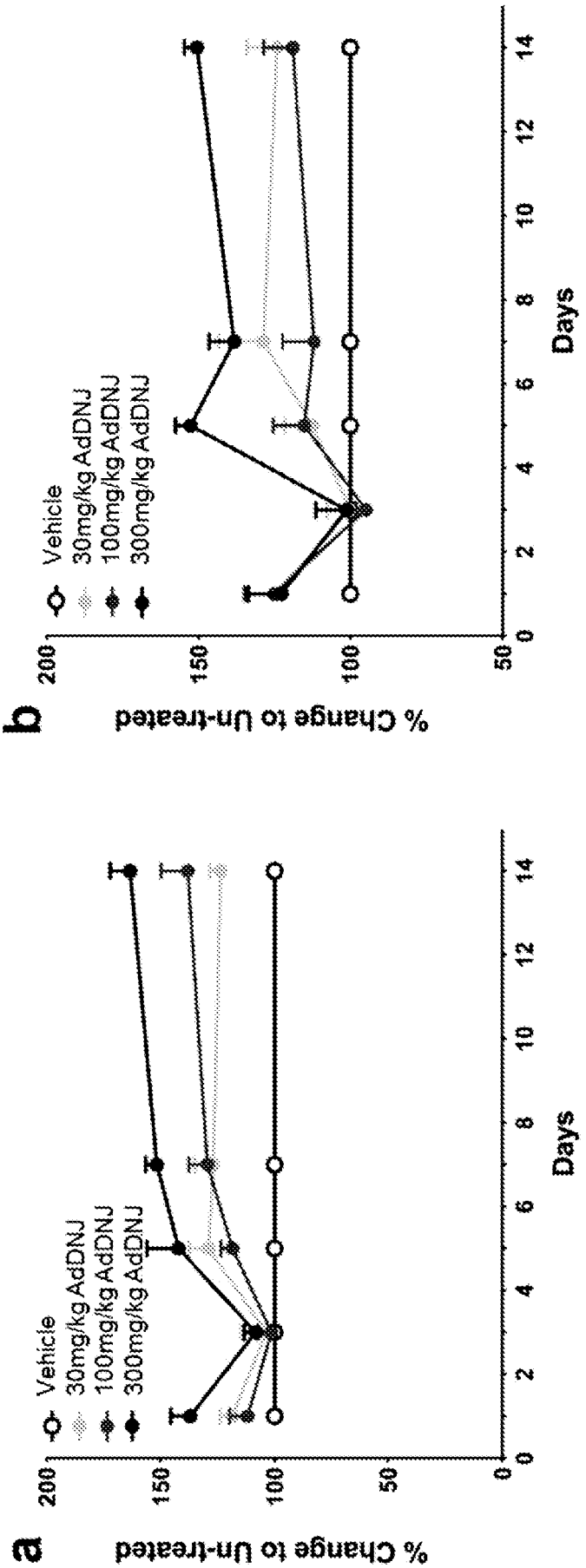

f
% Viability
200
150
100
50
0
-8
-6
-4
-2
Log[M]
AdDNJ 72 hr
AdDNJ 120 hr
g
% Viability
200
150
100
50
0
-8
-6
-4
-2
Log [M]
AdDNJ 120 hr
AdDNJ 48 hr
AdDNJ 24 hr


e
% Normalized resdidula activity
150
100
50
0
β-Hex Tot.
Hex A&S
Hex B
β-Gal
α-Gal
GCase
No Inhibitor
AdDNJ (100 μM)
No Inhibitor
AdDNJ (100 μM)
No Inhibitor
AdDNJ (100 μM)
No Inhibitor
AdDNJ (100 μM)
1-deoxygalactonojirimycin (100 μM)
No Inhibitor
AdDNJ (100 μM)
1-deoxygalactonojirimycin (100 μM)
No Inhibitor
AdDNJ (100 μM)
isofagomine (100 μM)

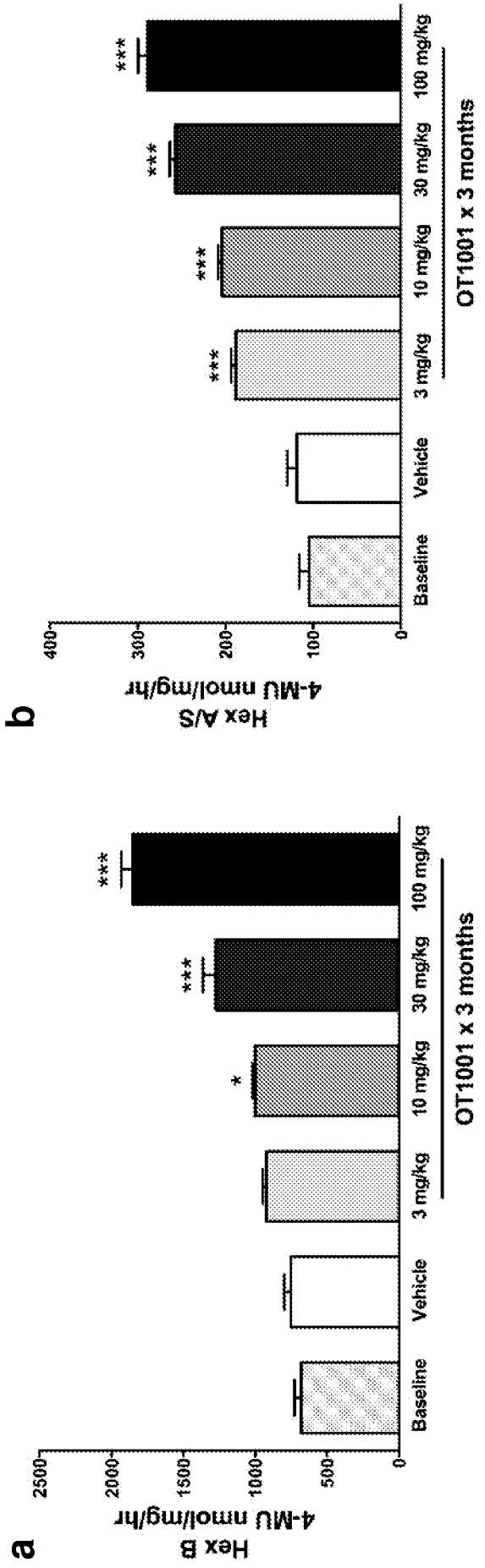
FIGS. 1 e-g


a
Plasma Levels (μM)
1000
100
10
1
0.100
0.010
0.001
0
10
20
30
40
50
Hours
100mg/kg AdDNJ
b
Brain Levels (μM)
10
1
0.10
0.01
0
10
20
30
40
50
Hours
100mg/kg AdDNJ

FIGS. 2 a-b


a
% Change to Un-treated
200
150
100
50
0
0
2
4
6
8
10
12
14
Days
Vehicle
30mg/kg AdDNJ
100mg/kg AdDNJ
300mg/kg AdDNJ
b
% Change to Un-treated
200
150
100
50
0
0
2
4
6
8
10
12
14
Days
Vehicle
30mg/kg AdDNJ
100mg/kg AdDNJ
300mg/kg AdDNJ

FIGS. 3 a-b


a
Hex B
4-MU nmol/mg/hr
2500
2000
1500
1000
500
0
Baseline
Vehicle
3 mg/kg
10 mg/kg
30 mg/kg
100 mg/kg
OT1001 x 3 months
*
***
***
***
b
Hex A/S
4-MU nmol/mg/hr
400
300
200
100
0
Baseline
Vehicle
3 mg/kg
10 mg/kg
30 mg/kg
100 mg/kg
OT1001 x 3 months
***
***
***
***

FIGS. 4 a-b

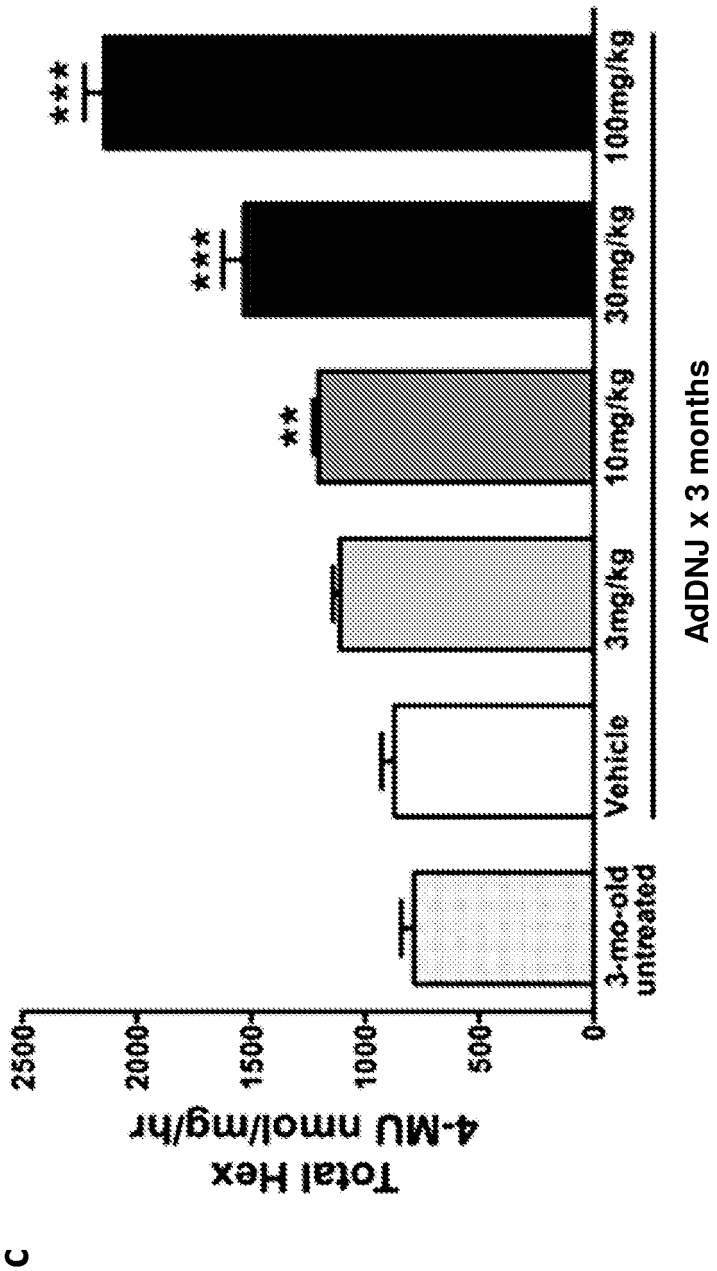
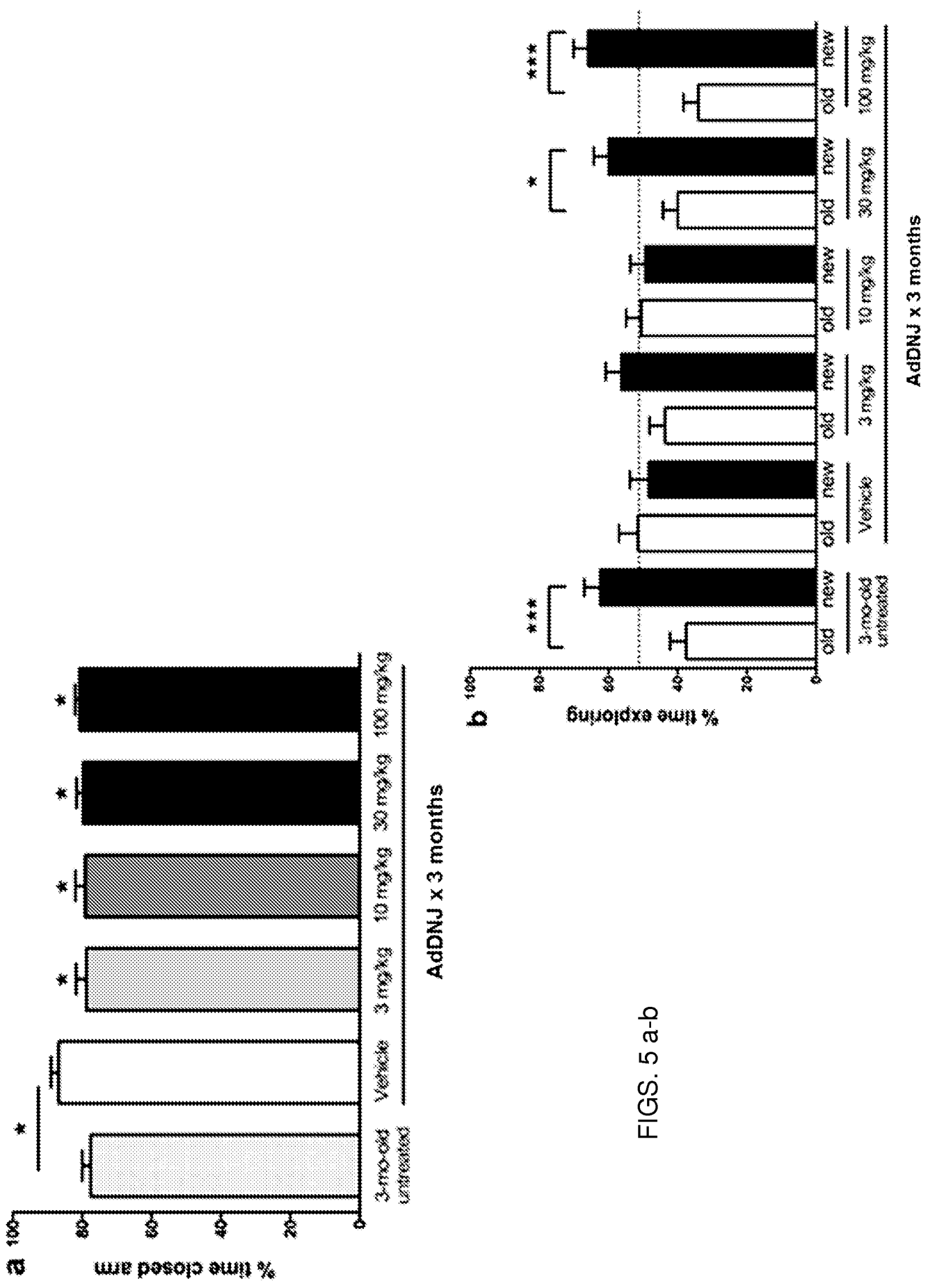

C
Total Hex
4-MU nmol/mg/hr
2500
2000
1500
1000
500
0
3-mo-old untreated
Vehicle
3mg/kg
10mg/kg
30mg/kg
100mg/kg
AdDNJ x 3 months
**
***
***

FIG. 4 c


a
% time closed arm
100
80
60
40
20
0
*
*
*
*
*
3-mo-old untreated
Vehicle
3 mg/kg
10 mg/kg
30 mg/kg
100 mg/kg
AdDNJ x 3 months
b
% time exploring
100
80
60
40
20
0
***
*
***
old
new
old
new
old
new
old
new
old
new
3-mo-old untreated
Vehicle
3 mg/kg
10 mg/kg
30 mg/kg
100 mg/kg
AdDNJ x 3 months

FIGS. 5 a-b

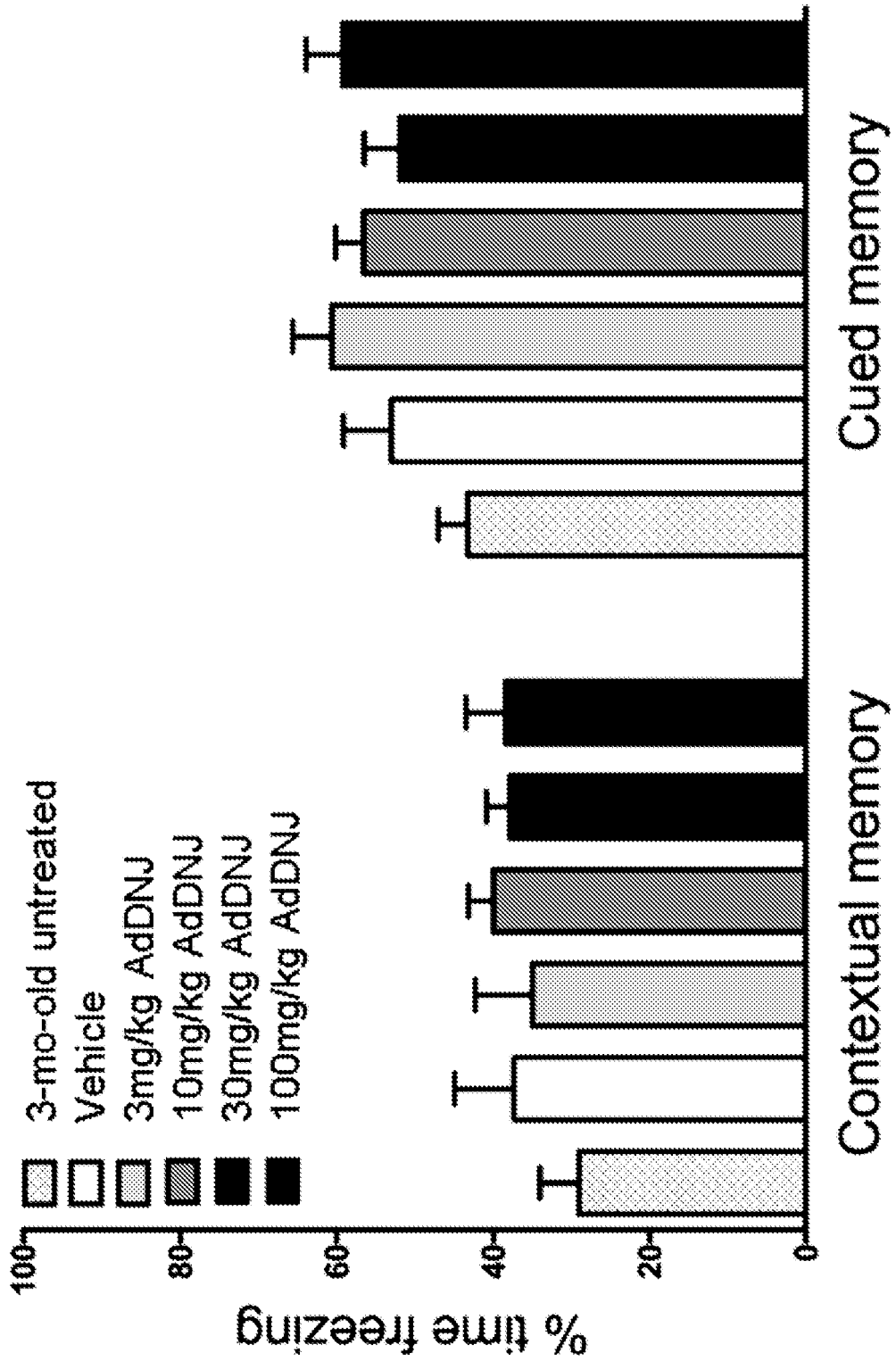
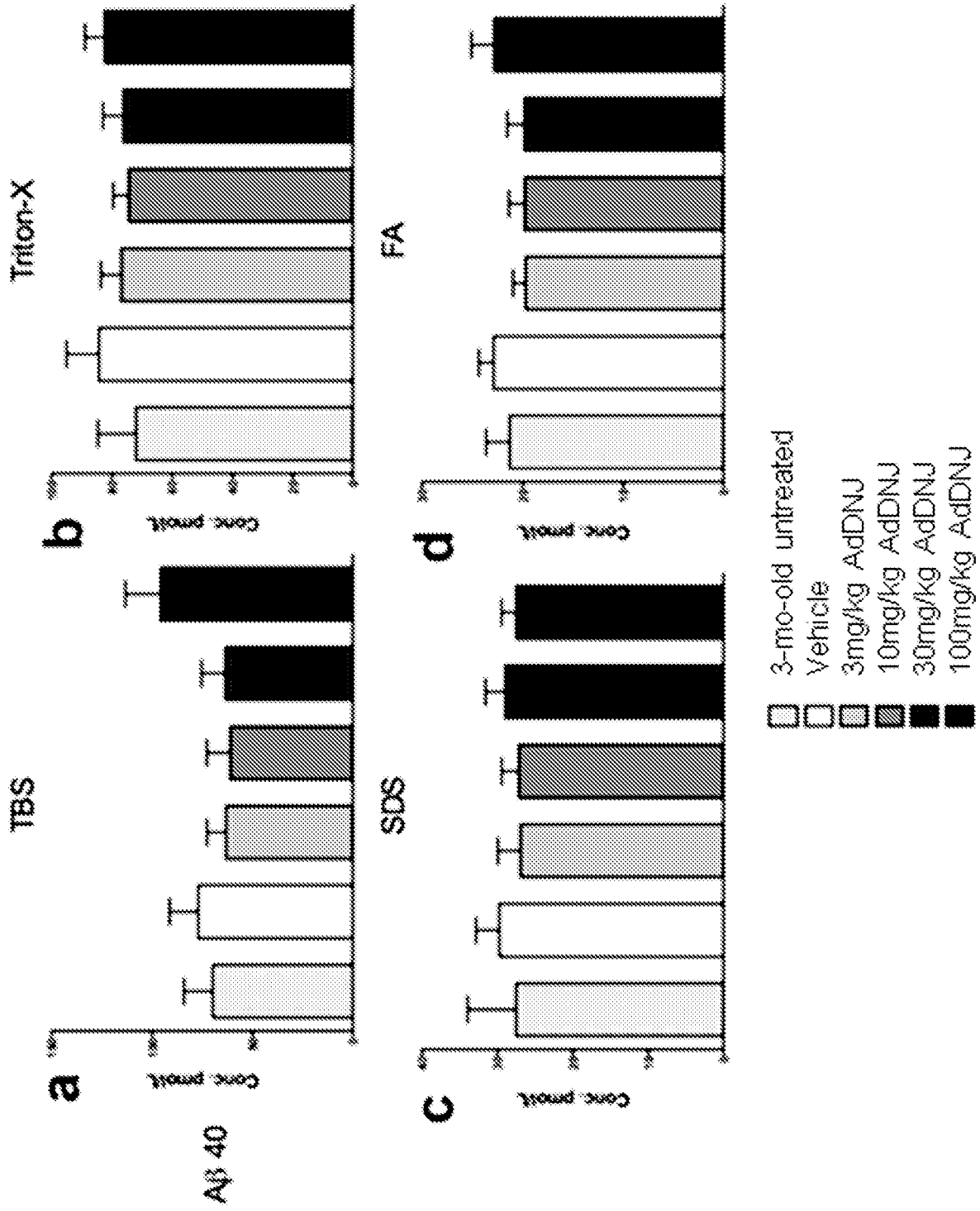
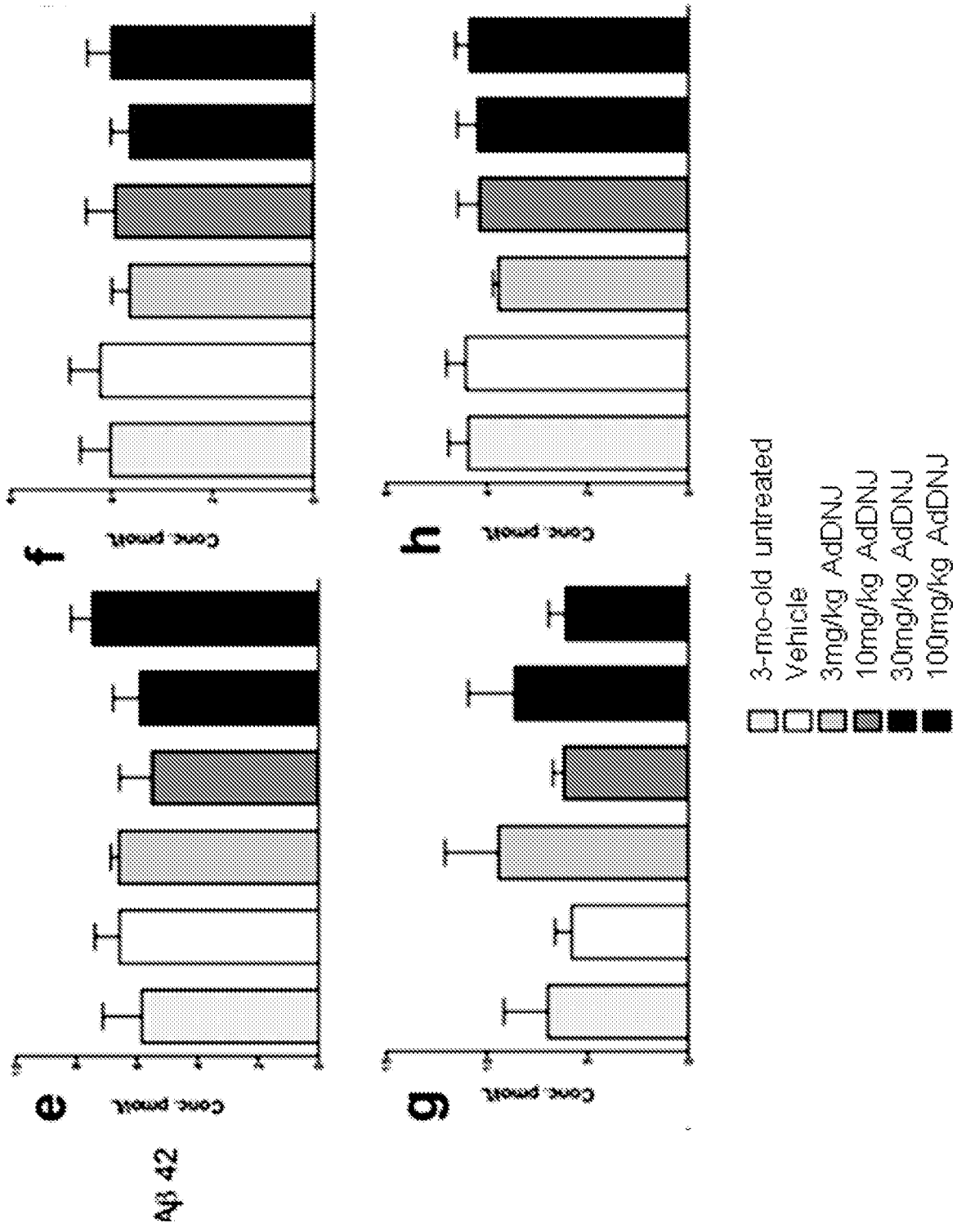

% time freezing
100
80
60
40
20
0
3-mo-old untreated
Vehicle
3mg/kg AdDNJ
10mg/kg AdDNJ
30mg/kg AdDNJ
100mg/kg AdDNJ
Contextual memory
Cued memory

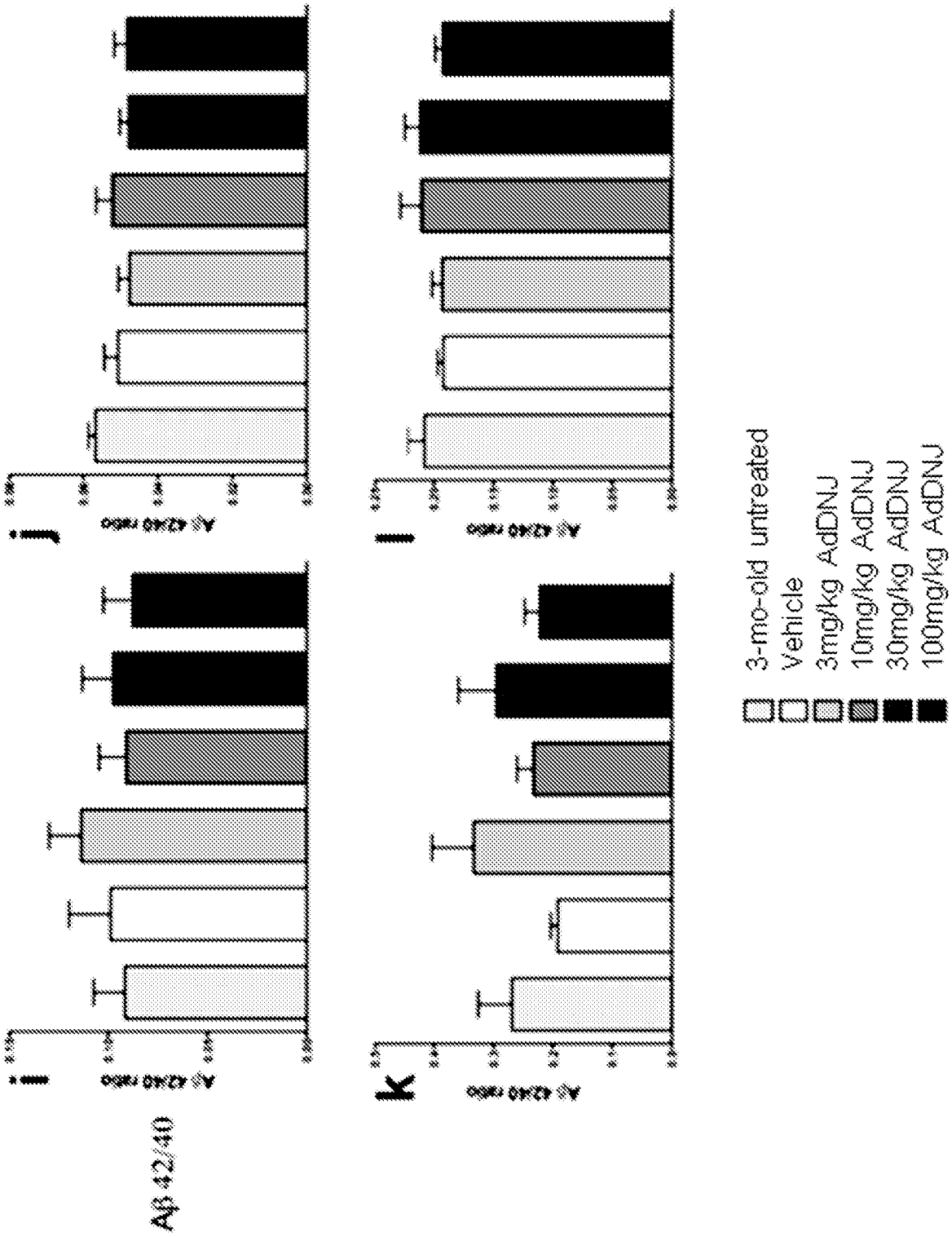
FIG. 6


a
TBS
Aβ 40
b
Triton-X
c
SDS
d
FA
conc pmol/L
3-mo-old untreated
Vehicle
3mg/kg AdDNJ
10mg/kg AdDNJ
30mg/kg AdDNJ
100mg/kg AdDNJ

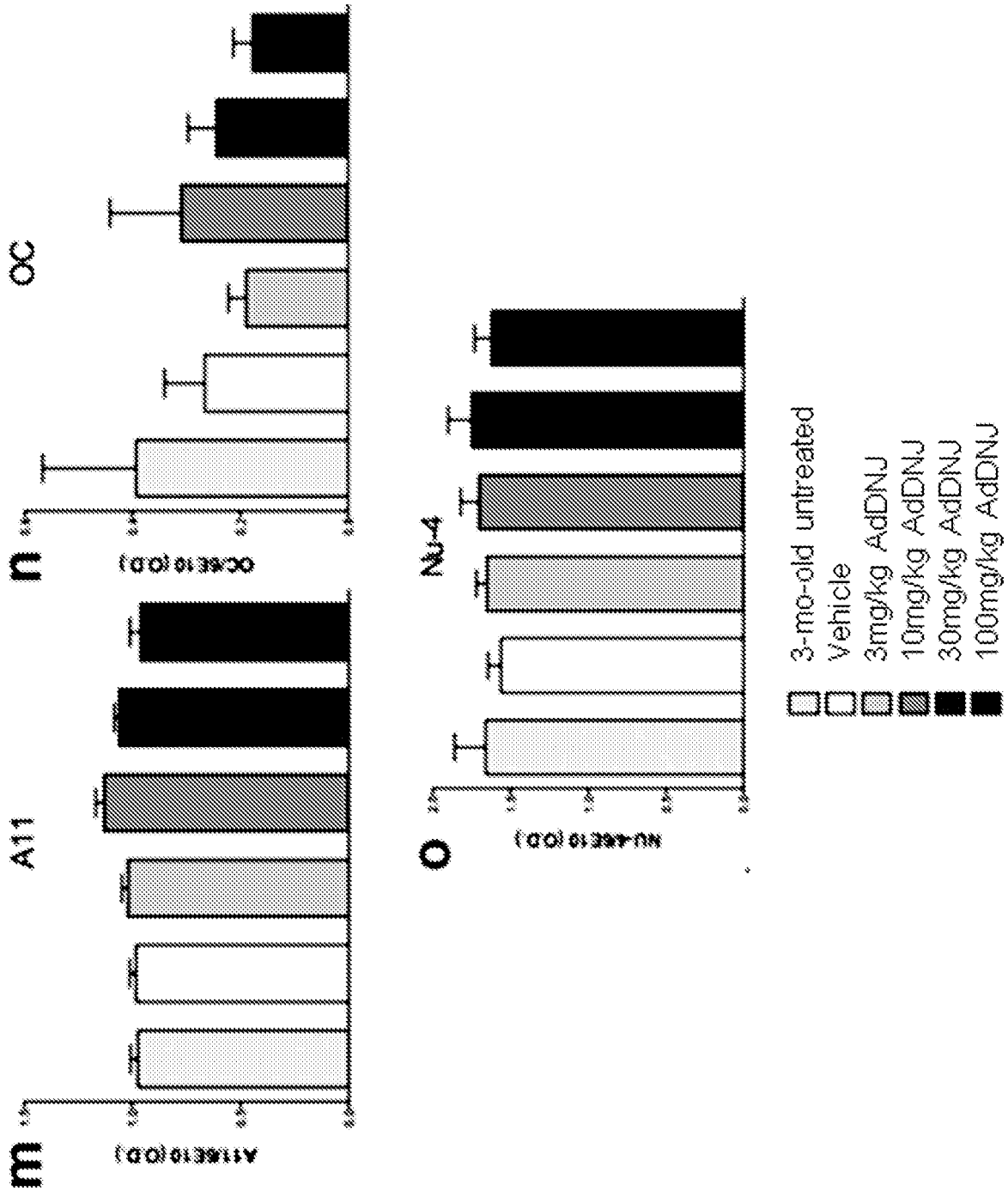
FIGS. 7 a-d


e
f
g
h
Aβ 42
Conc pmol/L
3-mo-old untreated
Vehicle
3mg/kg AdDNJ
10mg/kg AdDNJ
30mg/kg AdDNJ
100mg/kg AdDNJ

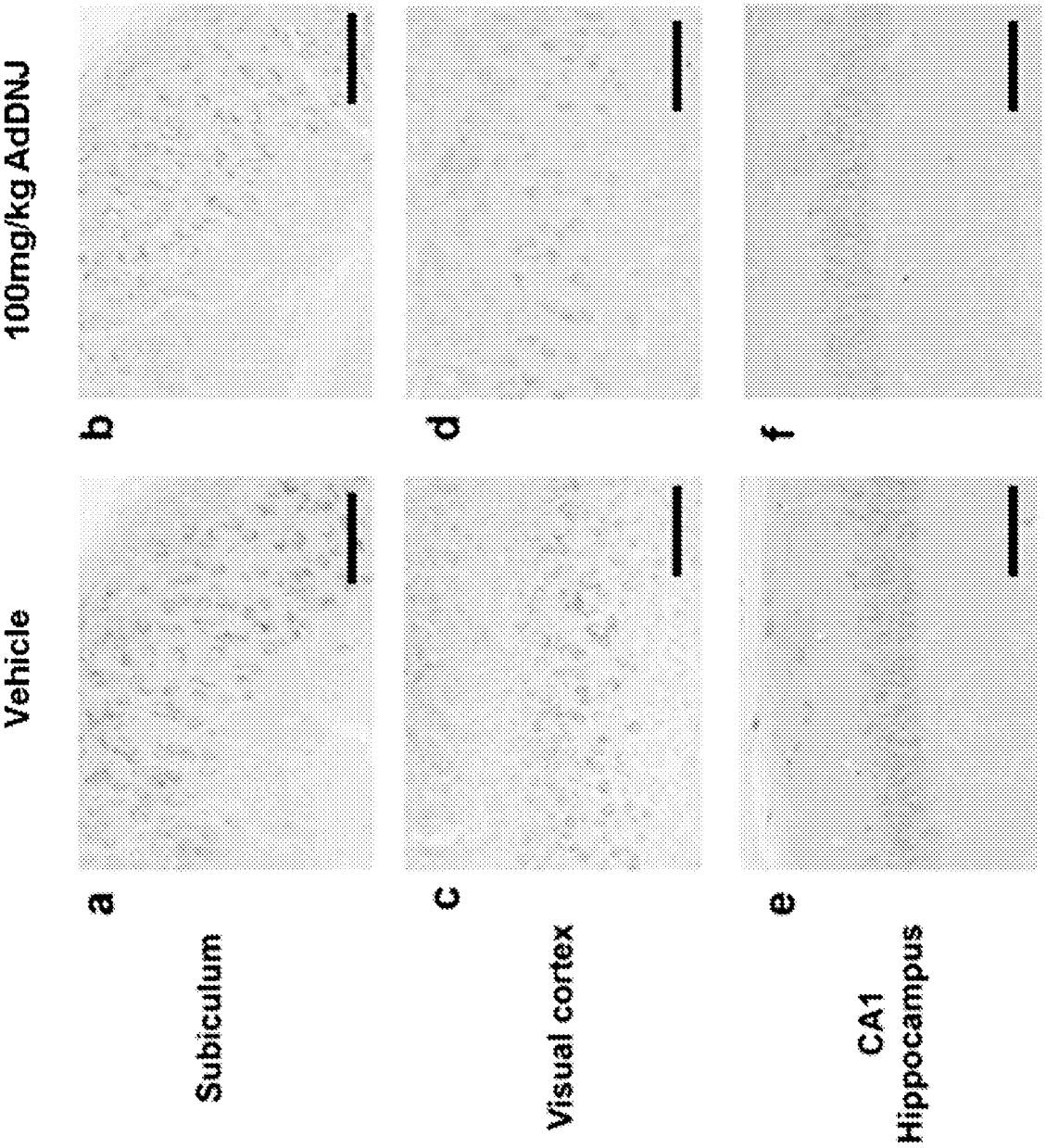
FIGS. 7 e-h


Aβ 42/40
J
K
3-mo-old untreated
Vehicle
3mg/kg AdDNJ
10mg/kg AdDNJ
30mg/kg AdDNJ
100mg/kg AdDNJ

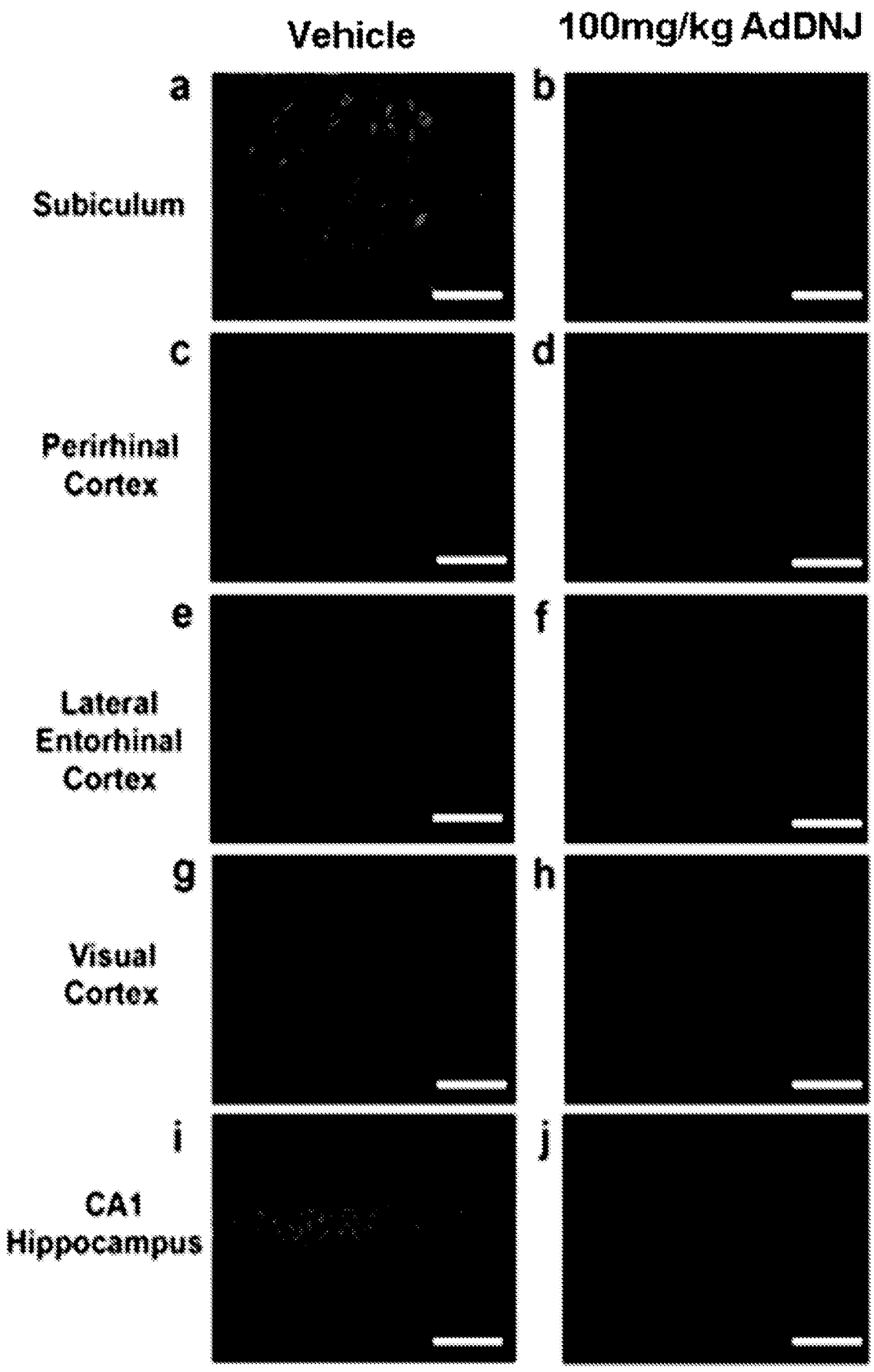
FIGS. 7 i-l


m
A11
A11/ME19 (O.D.)
n
OC
OC/ME19 (O.D.)
o
Nu-4
Nu-4/ME19 (O.D.)
3-mo-old untreated
Vehicle
3mg/kg AdDNJ
10mg/kg AdDNJ
30mg/kg AdDNJ
100mg/kg AdDNJ

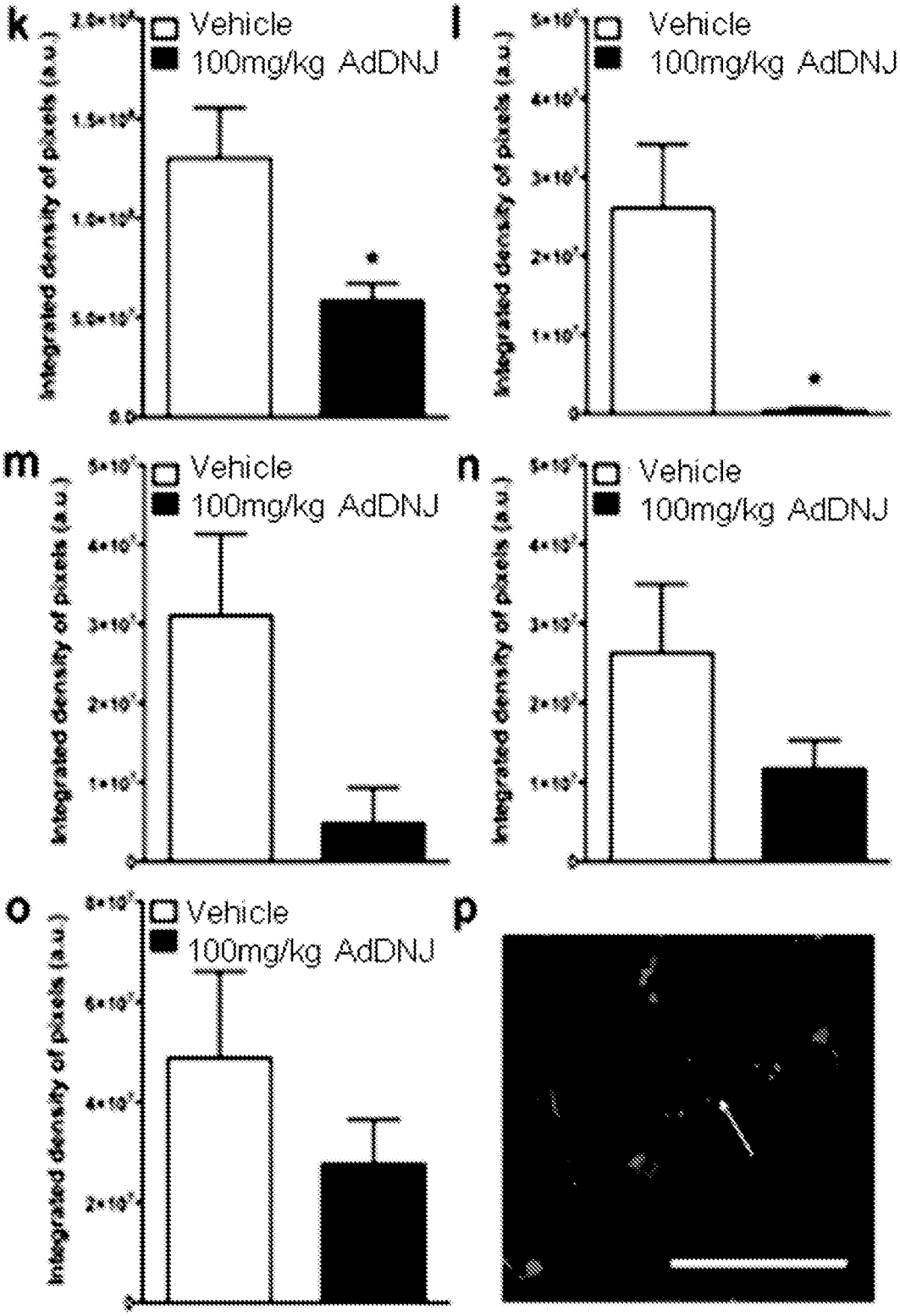
FIGS. 7 m-o


Vehicle
100mg/kg AdDNJ
a
b
Subiculum
c
d
Visual cortex
e
f
CA1
Hippocampus

FIGS. 8 a-f


Vehicle
100mg/kg AdDNJ
a
b
Subiculum
c
d
Perirhinal Cortex
e
f
Lateral Entorhinal Cortex
g
h
Visual Cortex
i
j
CA1 Hippocampus

FIGS. 9 a-j


k
Vehicle
100mg/kg AdDNJ
Integrated density of pixels (a.u.)
l
Vehicle
100mg/kg AdDNJ
Integrated density of pixels (a.u.)
m
Vehicle
100mg/kg AdDNJ
Integrated density of pixels (a.u.)
n
Vehicle
100mg/kg AdDNJ
Integrated density of pixels (a.u.)
o
Vehicle
100mg/kg AdDNJ
Integrated density of pixels (a.u.)
p

FIGS. 9 k-p

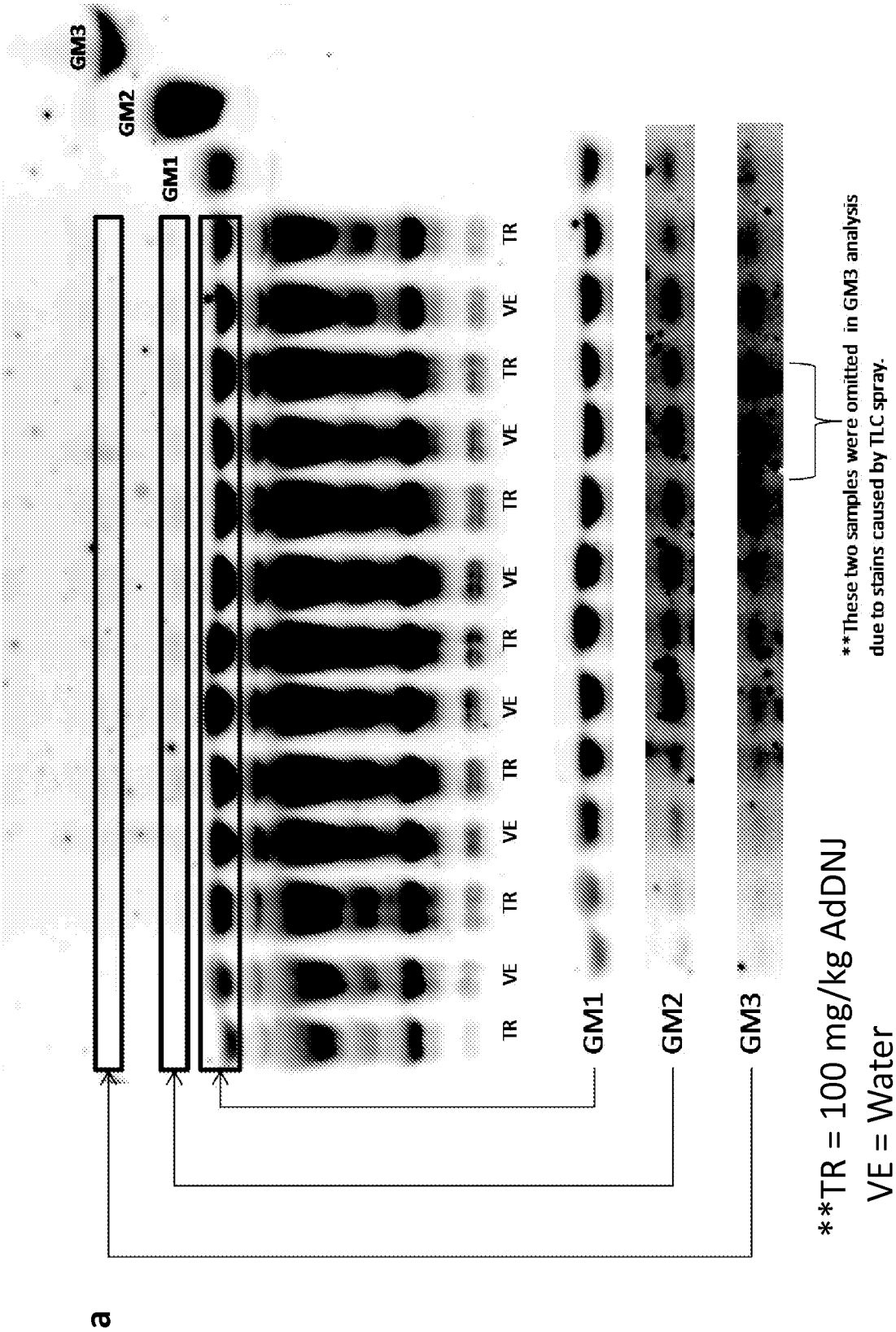
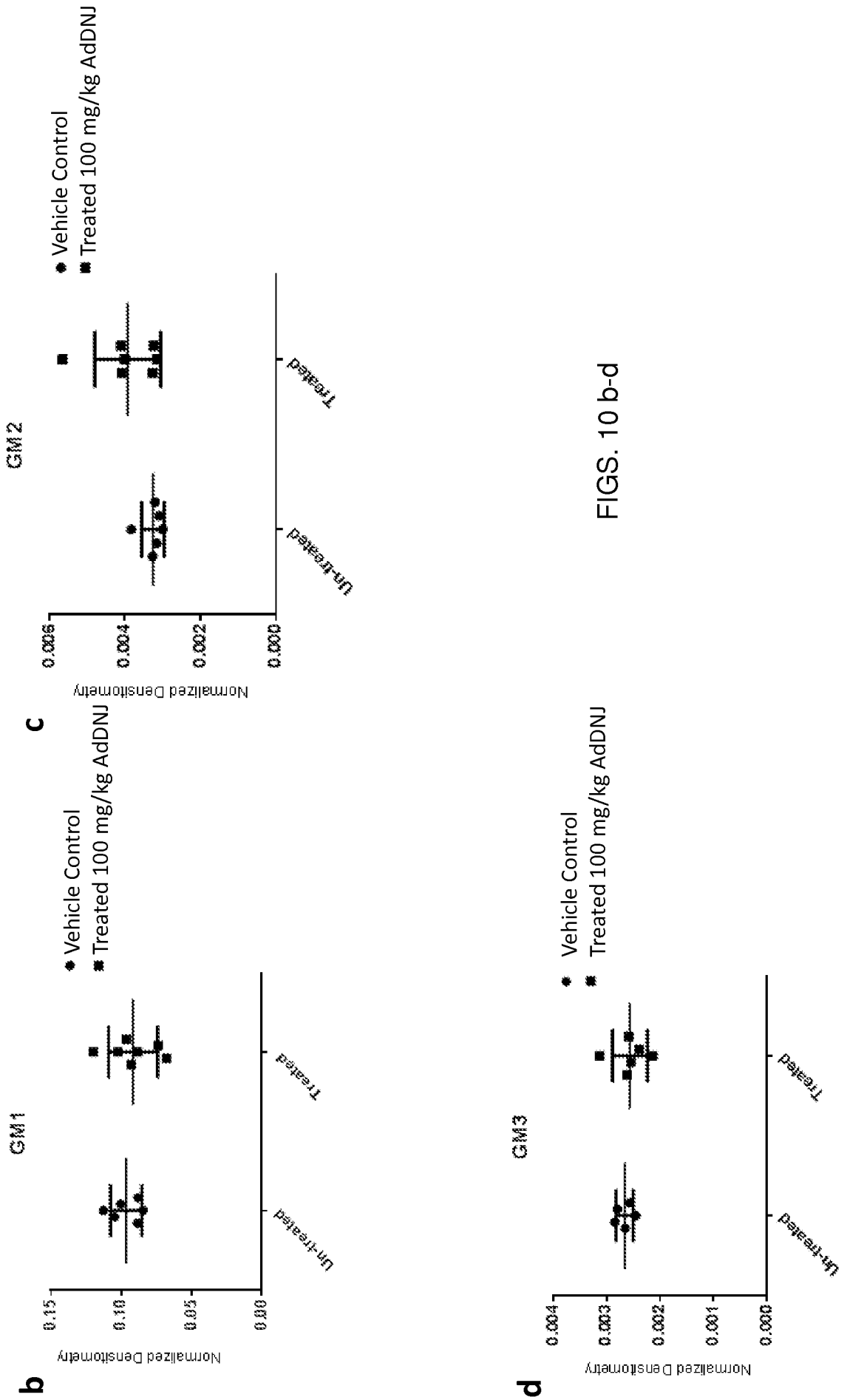

GM3
GM2
GM1
TR VE TR VE TR VE TR VE TR VE TR VE TR VE TR VE TR VE TR
GM1
GM2
GM3
**These two samples were omitted in GM3 analysis due to stains caused by TLC spray.
**TR = 100 mg/kg AdDNJ
VE = Water
a

FIG. 10 a


b
GM1
Vehicle Control
Treated 100 mg/kg AdDNJ
Normalized Densitometry
0.15
0.10
0.05
0.00
Un-treated
Treated
c
GM2
Vehicle Control
Treated 100 mg/kg AdDNJ
Normalized Densitometry
0.006
0.004
0.002
0.000
Un-treated
Treated
d
GM3
Vehicle Control
Treated 100 mg/kg AdDNJ
Normalized Densitometry
0.004
0.003
0.002
0.001
0.000
Un-treated
Treated

FIGS. 10 b-d