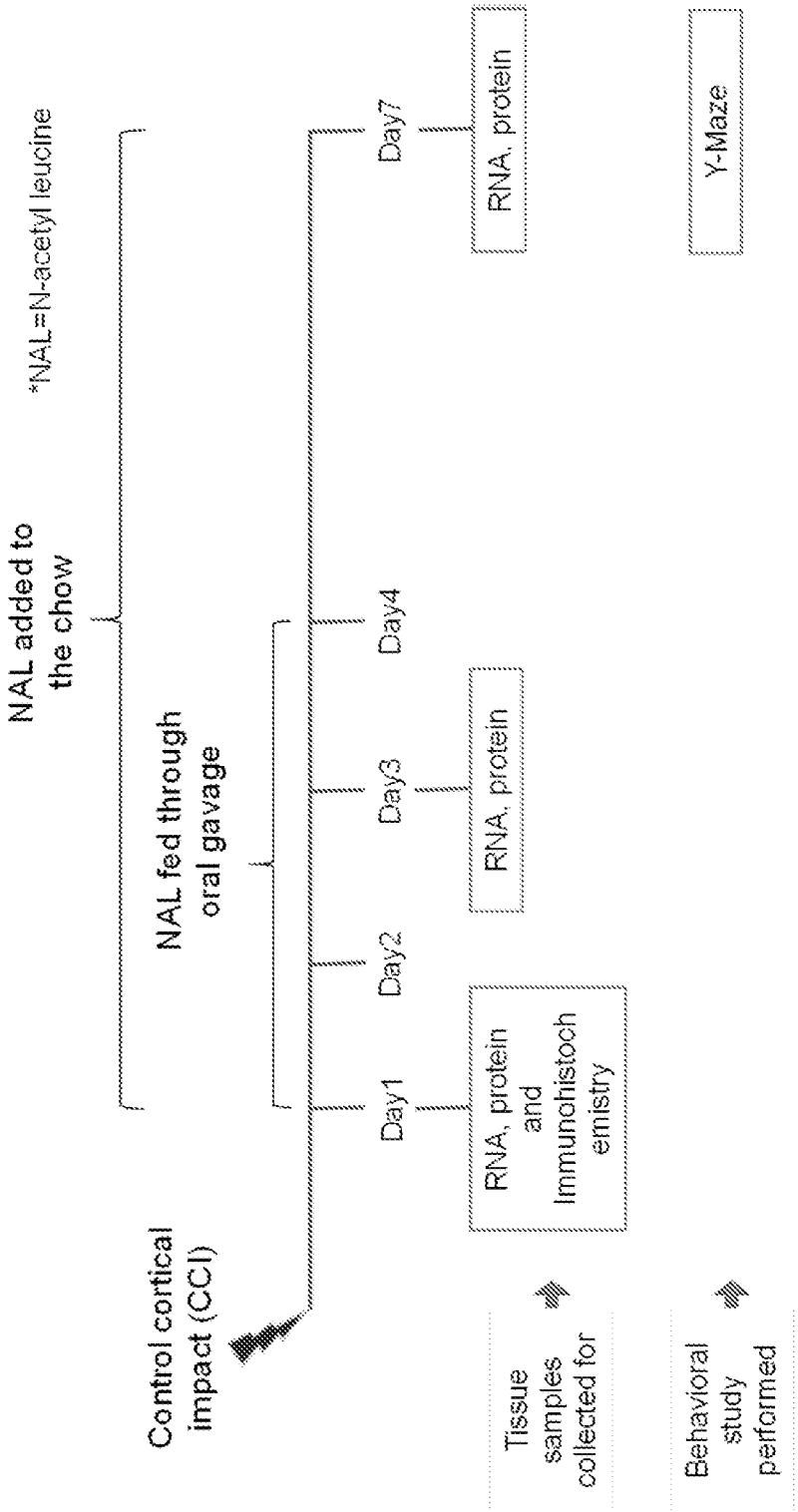

*NAL=N-acetyl leucine
NAL added to the chow
NAL fed through oral gavage
Control cortical impact (CCI)
Day1
Day2
Day3
Day4
Day7
RNA, protein and Immunohistoch emistry
RNA, protein
RNA, protein
Tissue samples collected for
Behavioral study performed
Y-Maze

Fig. 1

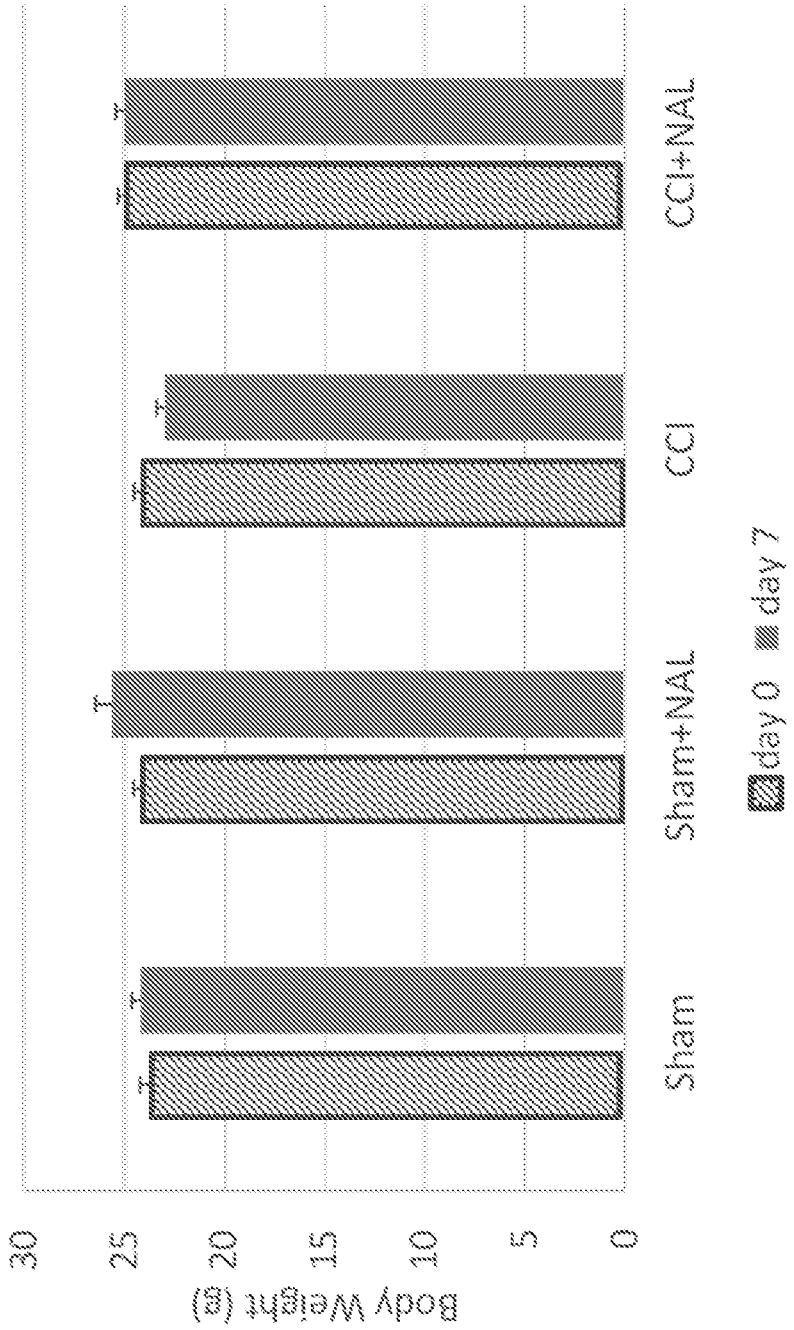

Body Weight (g)
30
25
20
15
10
5
0
Sham
Sham+NAL
CCI
CCI+NAL
day 0
day 7

Fig. 2

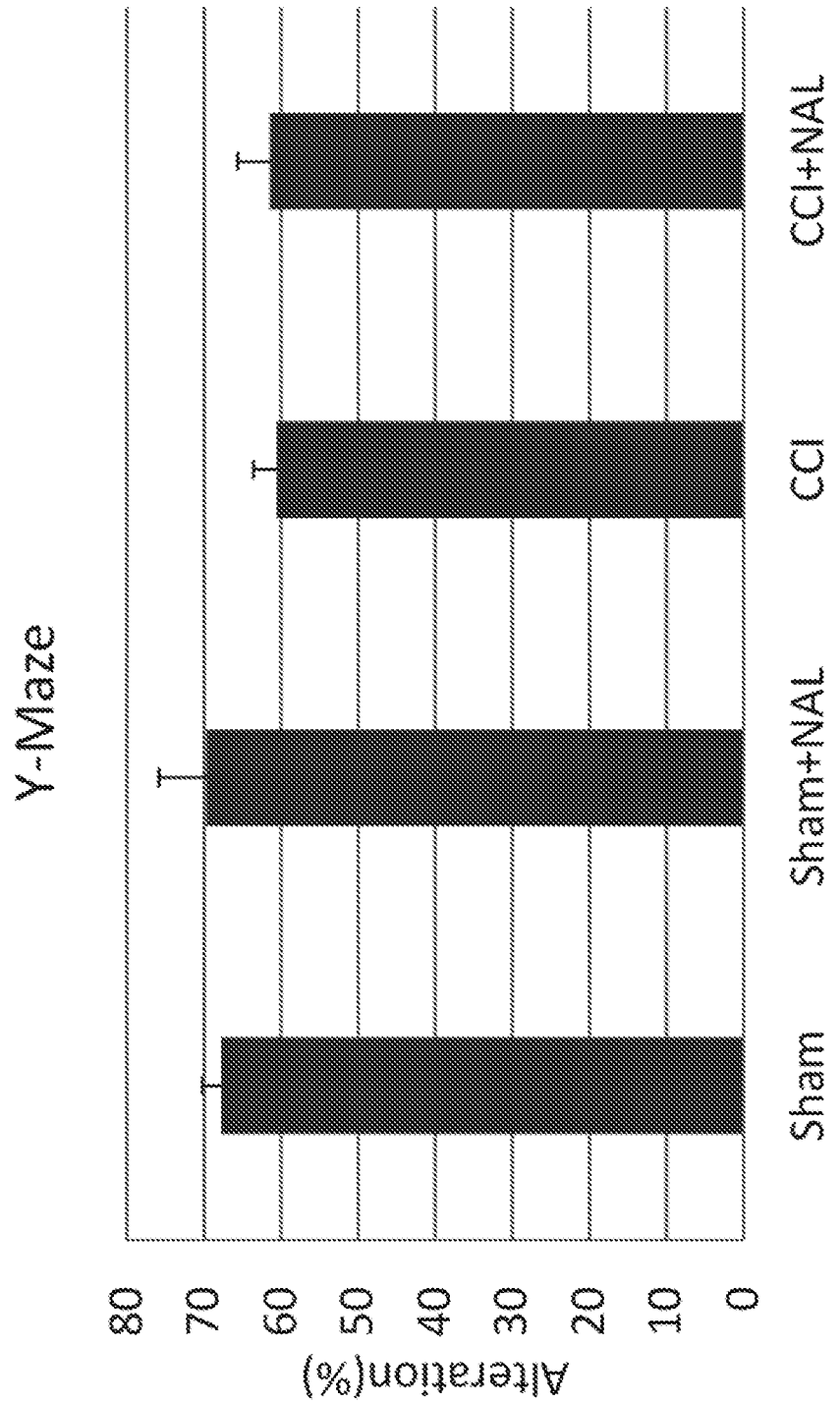

Y-Maze
Alteration(%)
80
70
60
50
40
30
20
10
0
Sham
Sham+NAL
CCI
CCI+NAL

Fig. 3

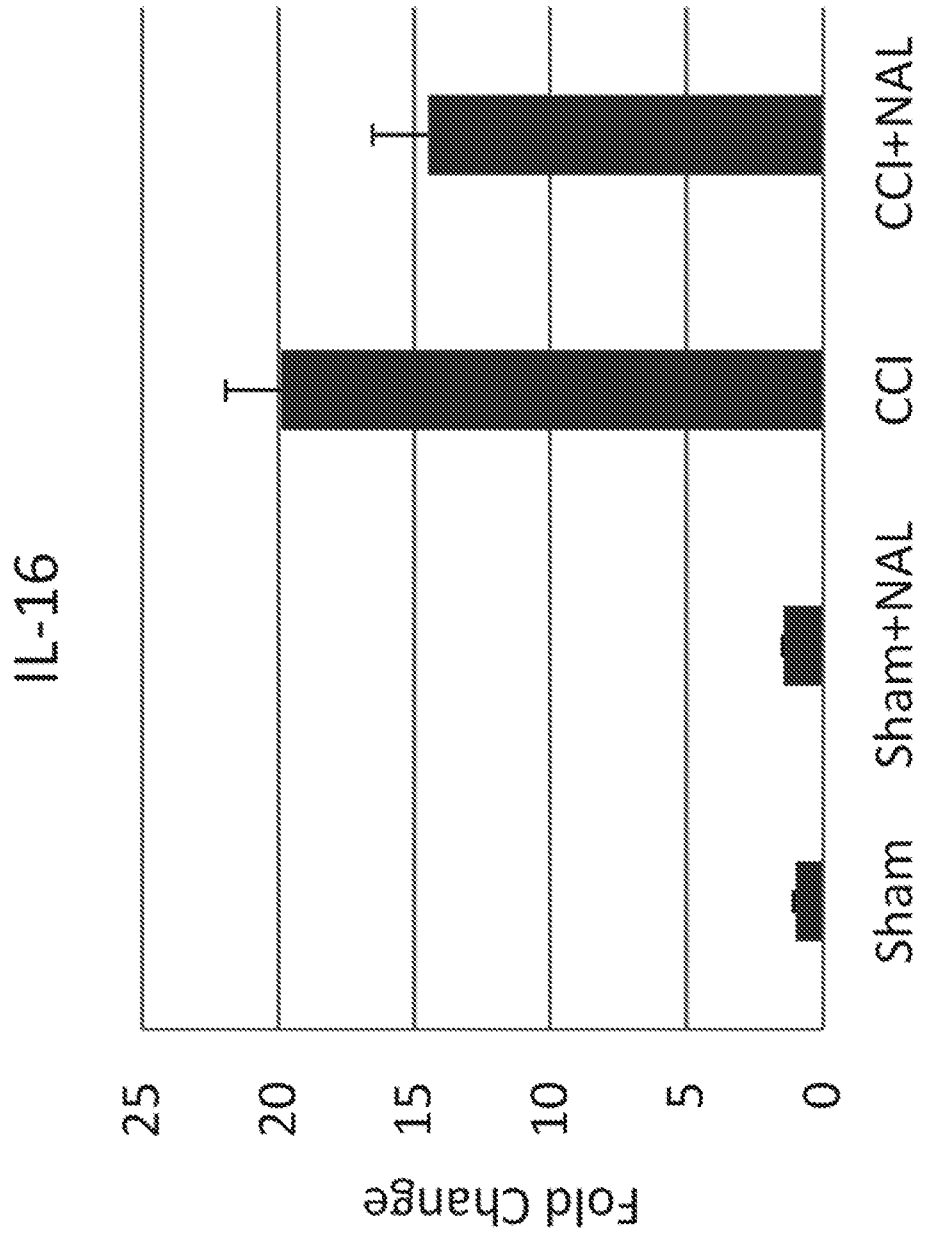


Fig. 4

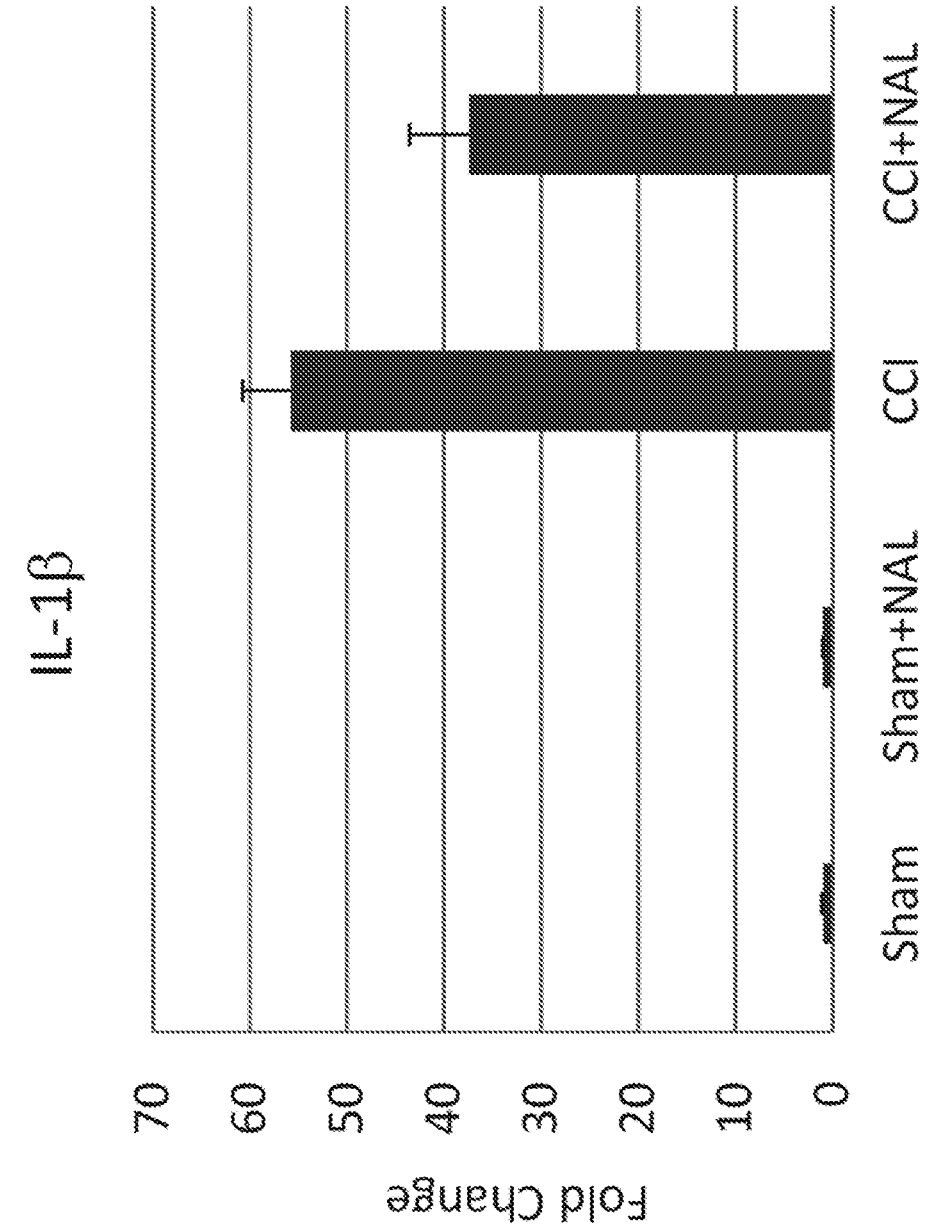


Fig. 5

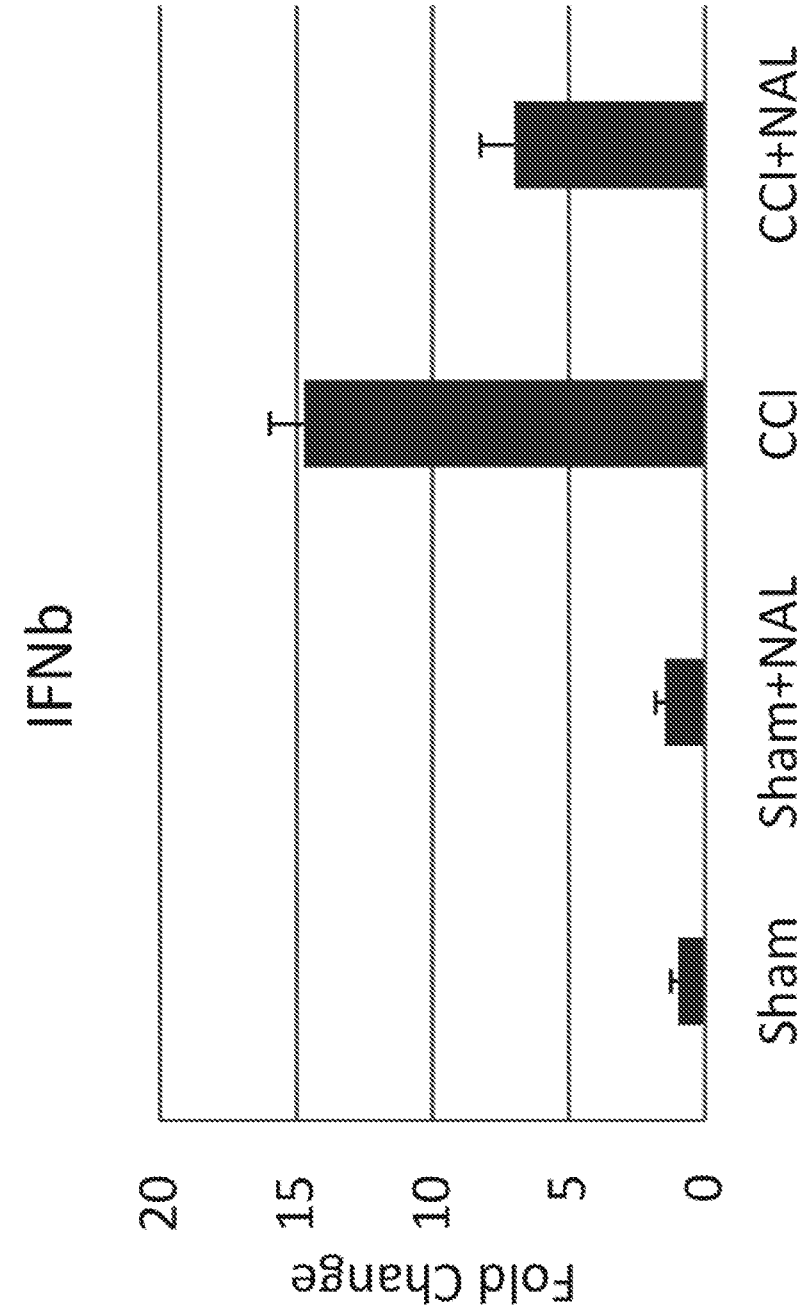


Fig. 6

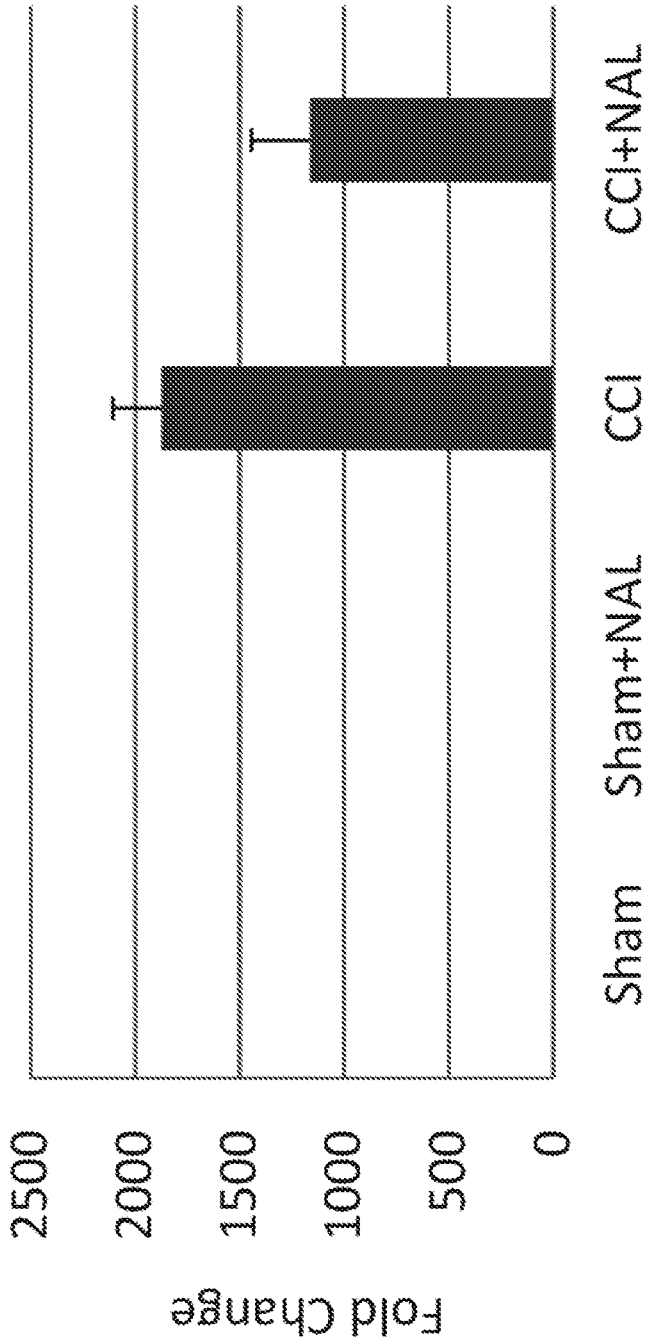

Arg1
Fold Change
2500
2000
1500
1000
500
0
Sham
Sham+NAL
CCI
CCI+NAL

Fig. 7

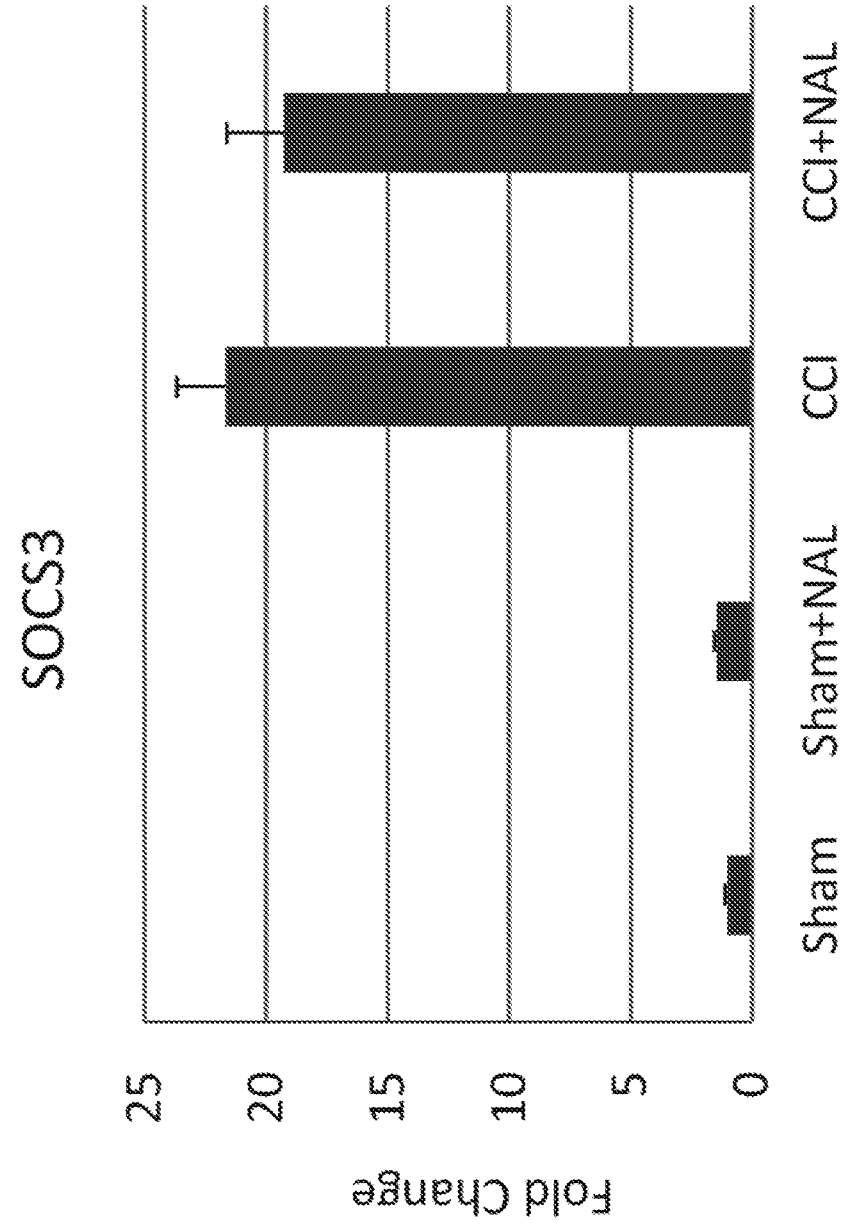


Fig. 8

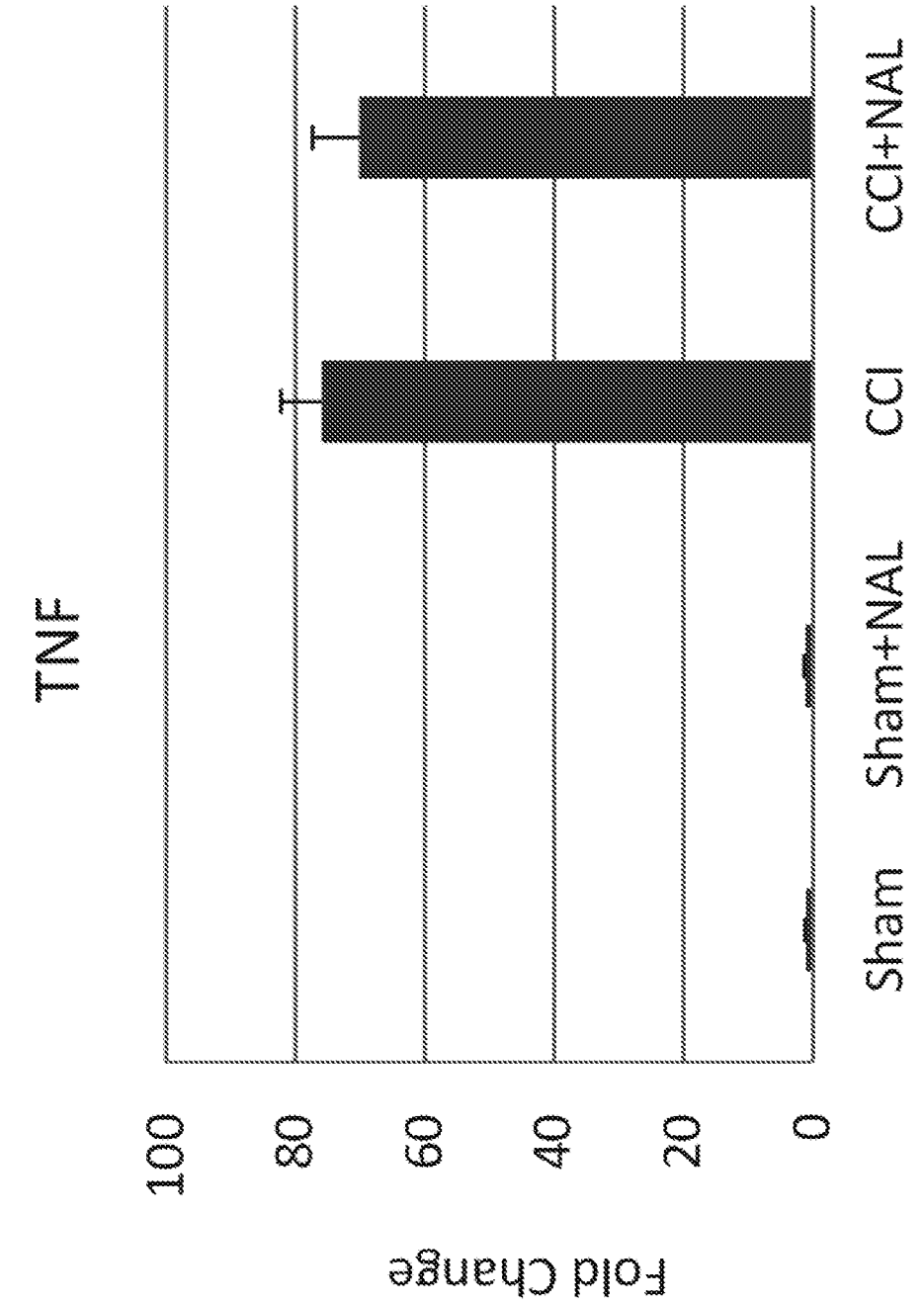


Fig. 9

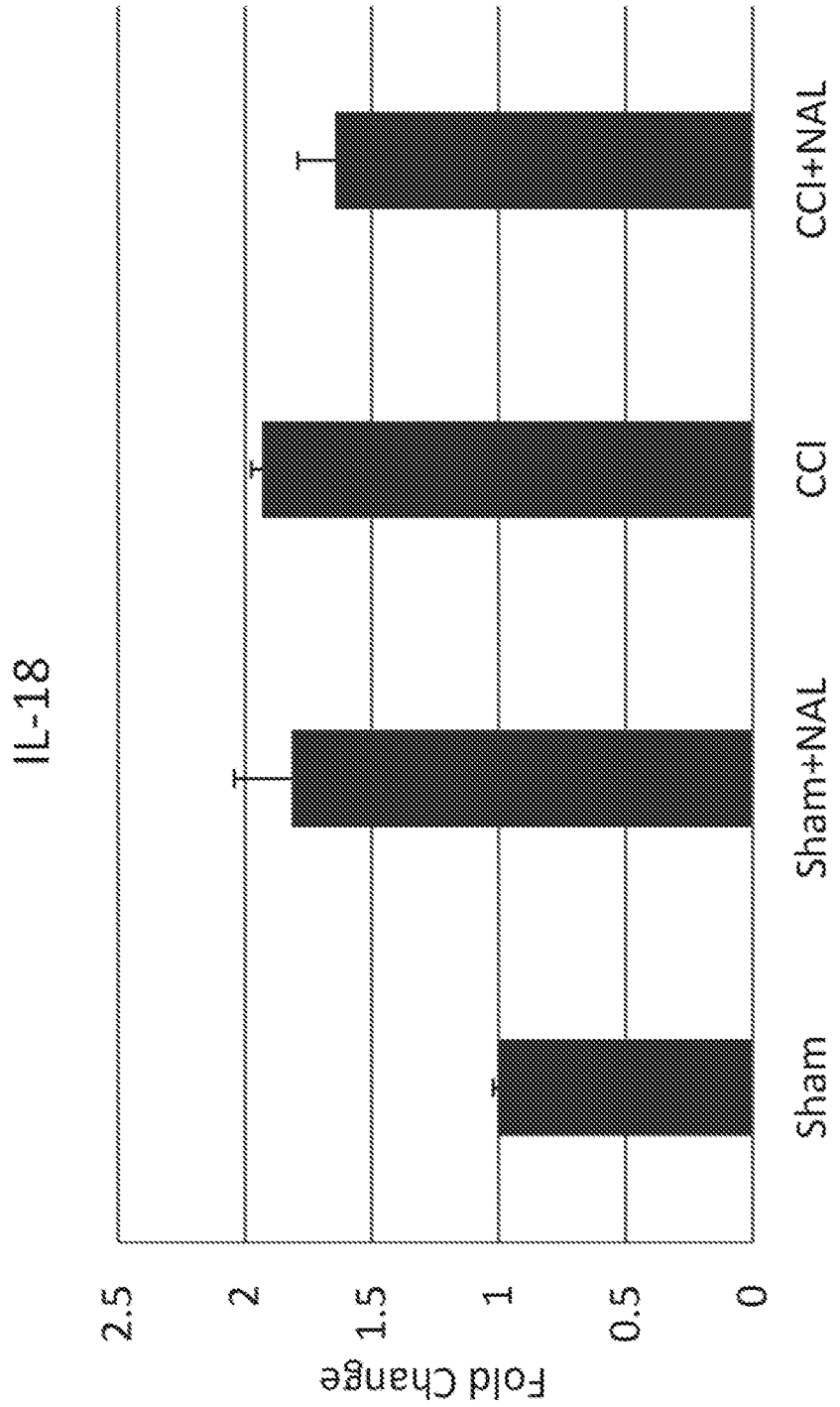


Fig. 10

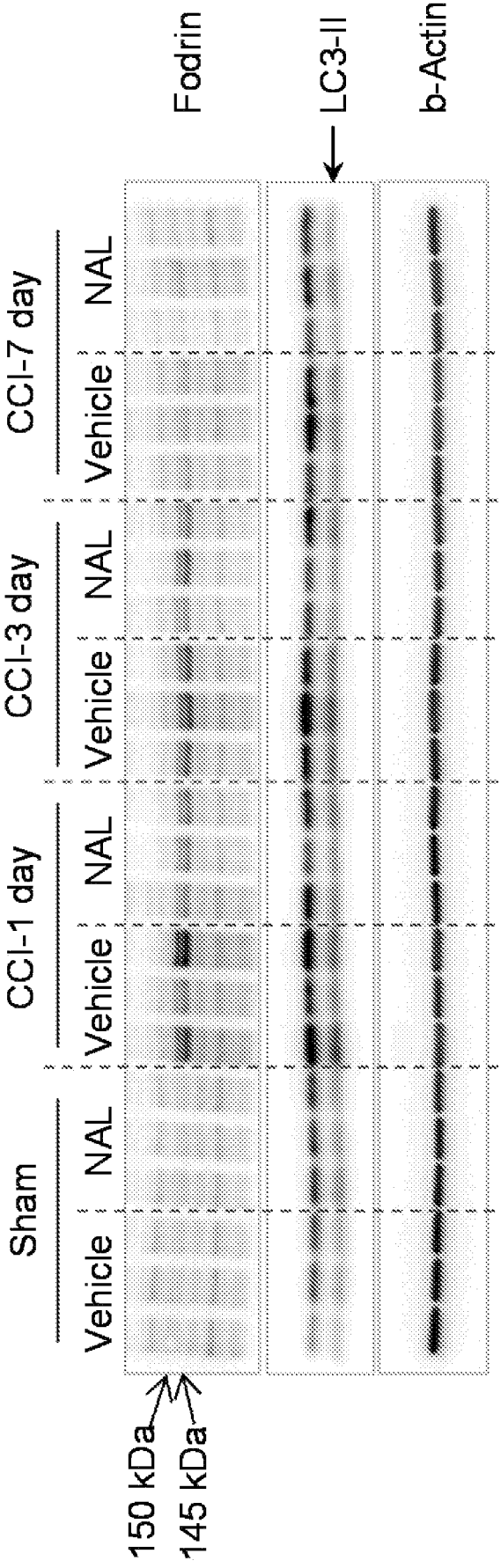

Fodrin
LC3-II
b-Actin
Sham
CCI-1 day
CCI-3 day
CCI-7 day
Vehicle
NAL
Vehicle
NAL
Vehicle
NAL
Vehicle
NAL
150 kDa
145 kDa

Fig. 11

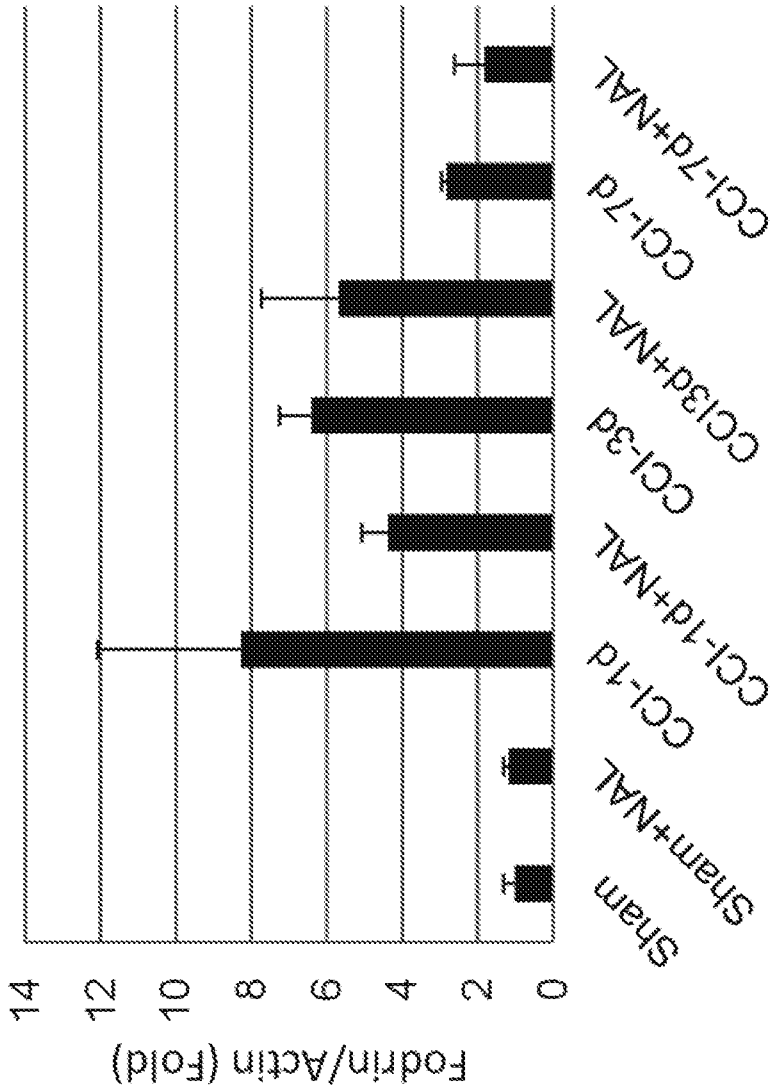

Fodrin/Actin (Fold)
0
2
4
6
8
10
12
14
Sham
Sham+NAL
CCl-1d
CCl-1d+NAL
CCl-3d
CCl3d+NAL
CCl-7d
CCl-7d+NAL

Fig. 12

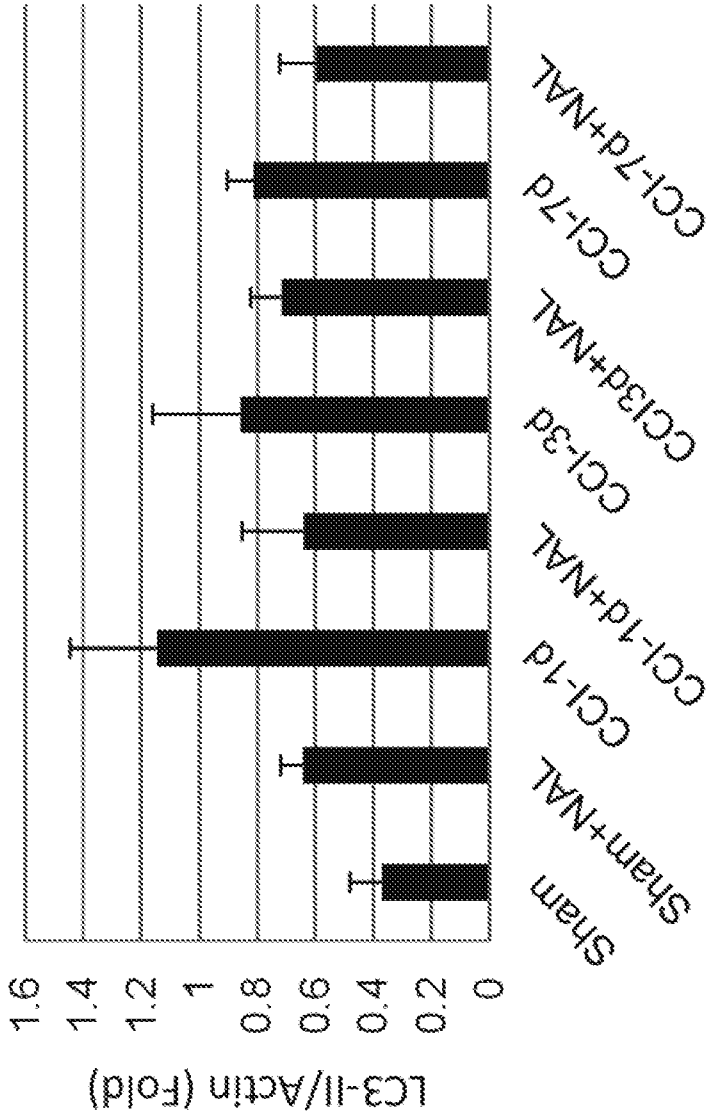

LC3-II/Actin (Fold)
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
Sham
Sham+NAL
CCl-7d
CCl-7d+NAL
CCl-1d
CCl-1d+NAL
CCl-3d
CCl3d+NAL
CCl-7d
CCl-7d+NAL

Fig. 13

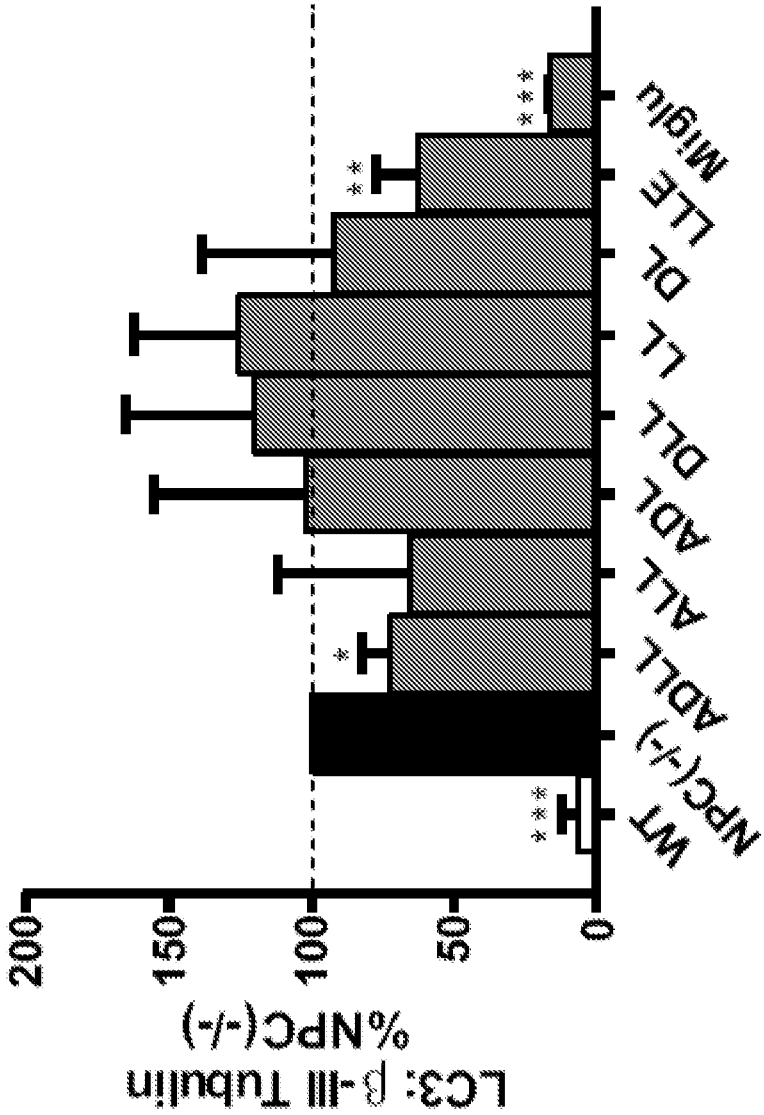

LC3: β-III Tubulin
%NPC(-/-)
200
150
100
50
0
WT
NPC(-/-)
ADLL
ALL
ADL
DLL
LL
DL
LLE
Miglu
*
**
***
**
***

Fig. 14

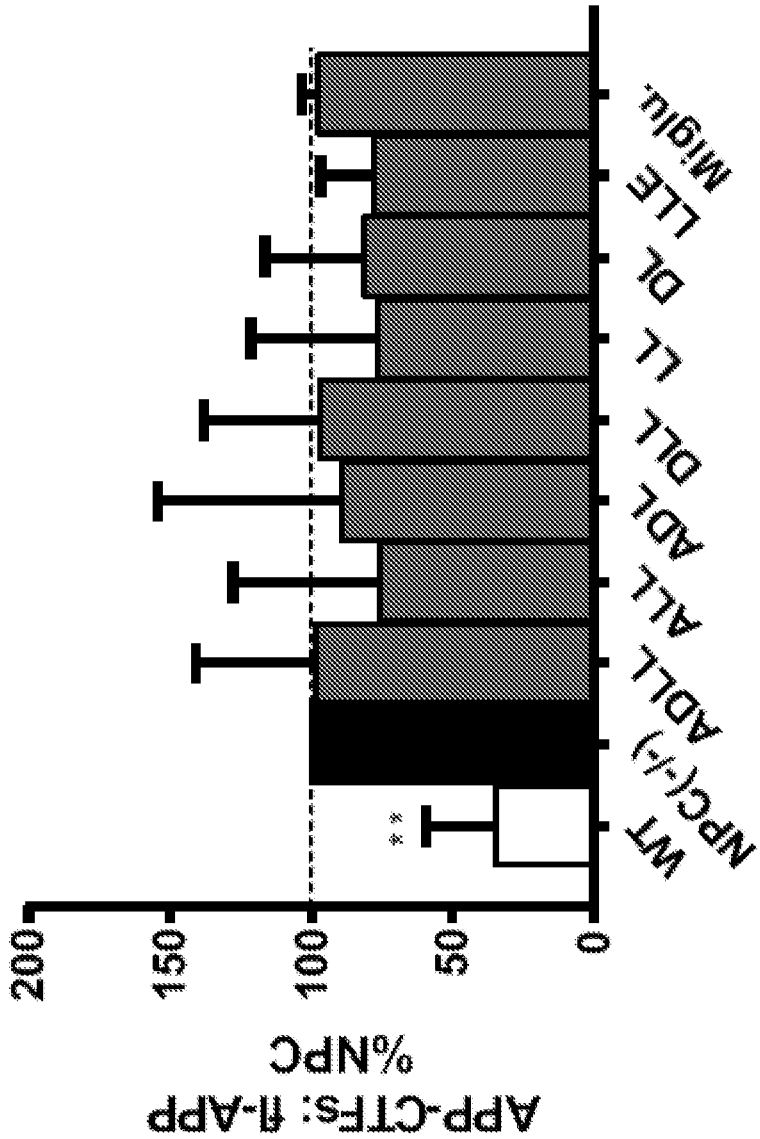

APP-CTFs: fl-APP
%NPC
200
150
100
50
0
**
WT
NPC(-/-)
ADLL
ALL
ADL
DLL
LL
DL
LLE
Miglu.

Fig. 15

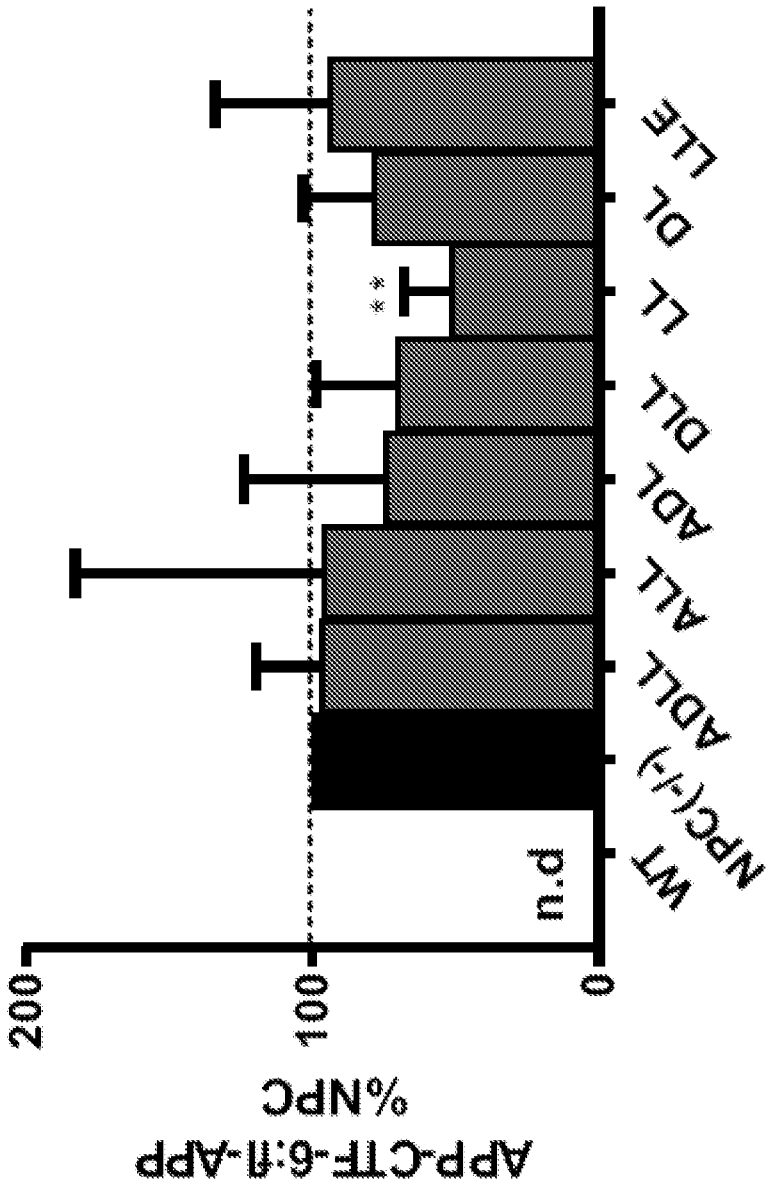


Fig. 16

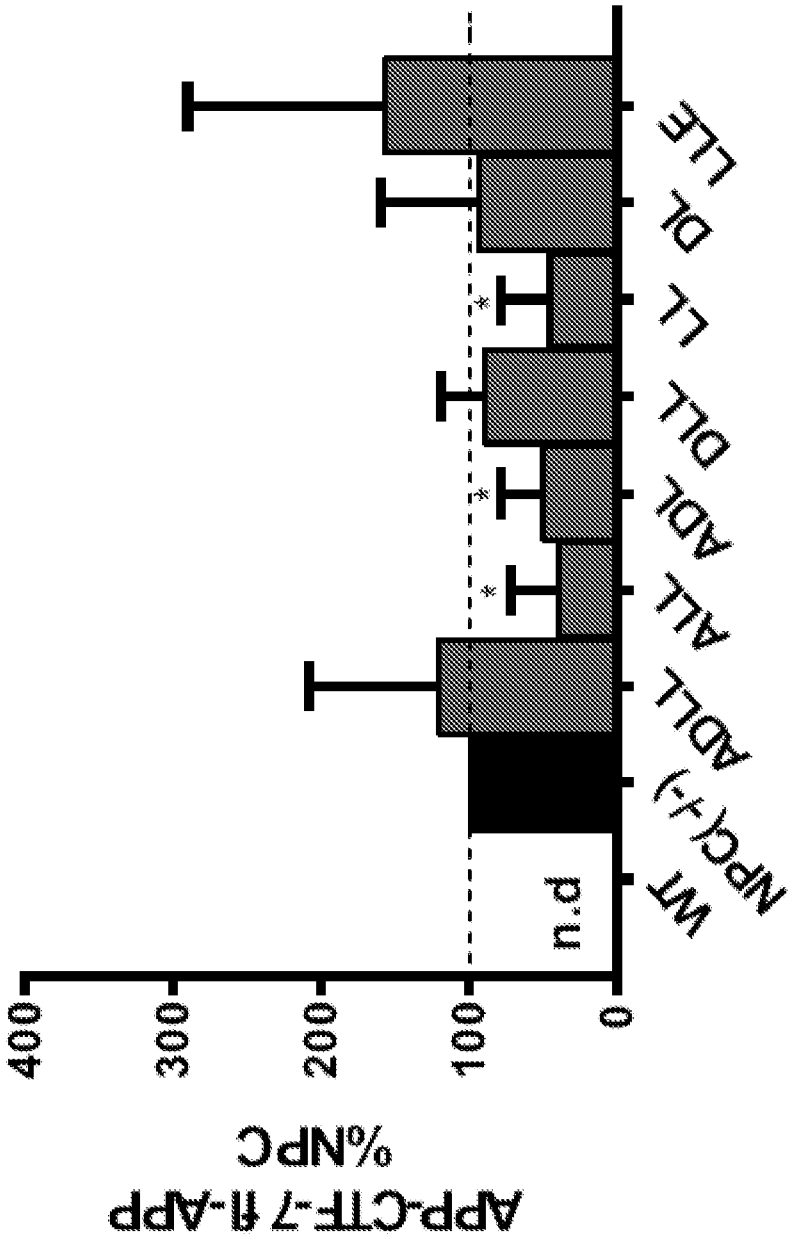

APP-CTF-γ fl-APP
%NPC
400
300
200
100
0
n.d
WT
NPC(-/-)
ADLL
ALL
ADL
DLL
LL
DL
LLE
*
*
*

Fig. 17

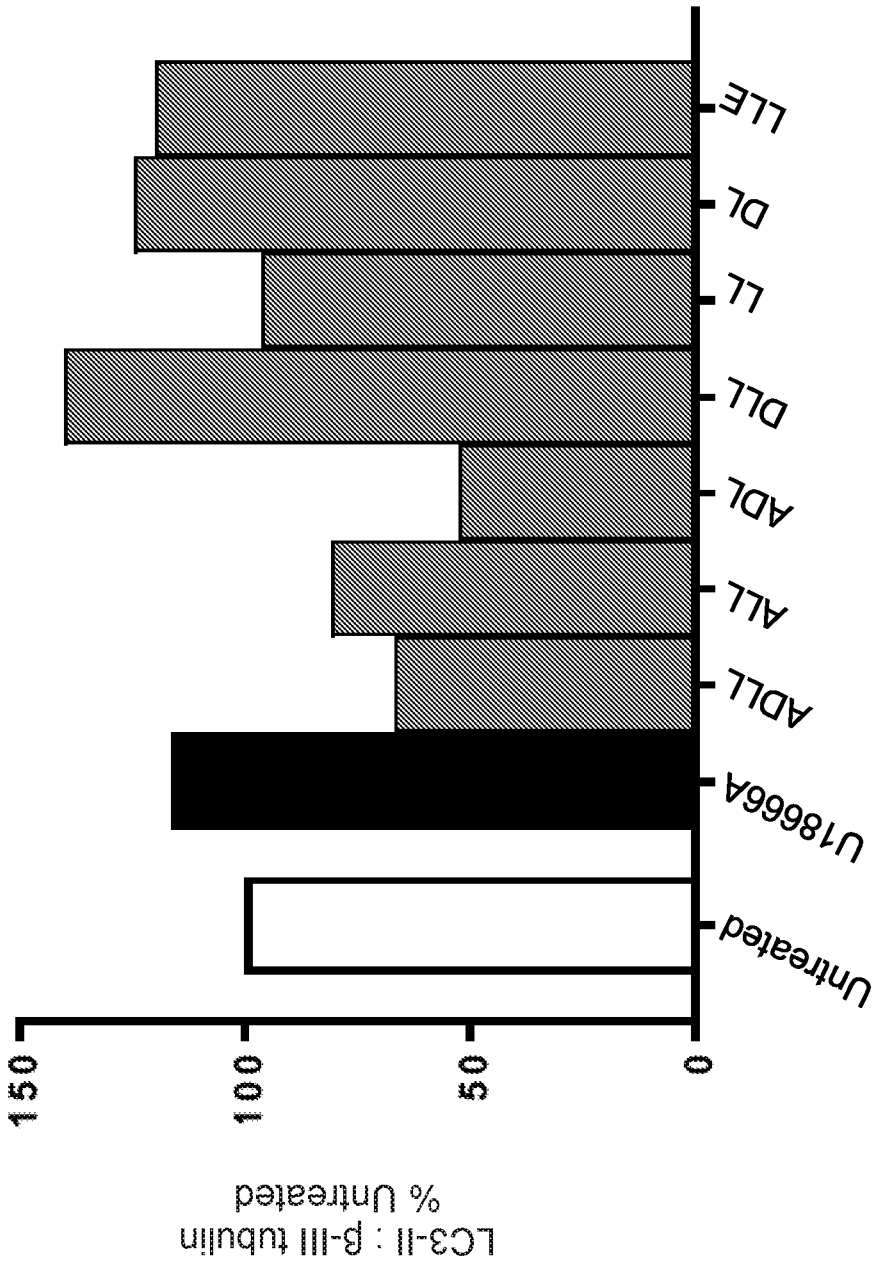

LC3-II : β-III tubulin
% Untreated
150
100
50
0
Untreated
U18666A
ADLL
ALL
ADL
DLL
LL
DL
LLE

Fig. 18

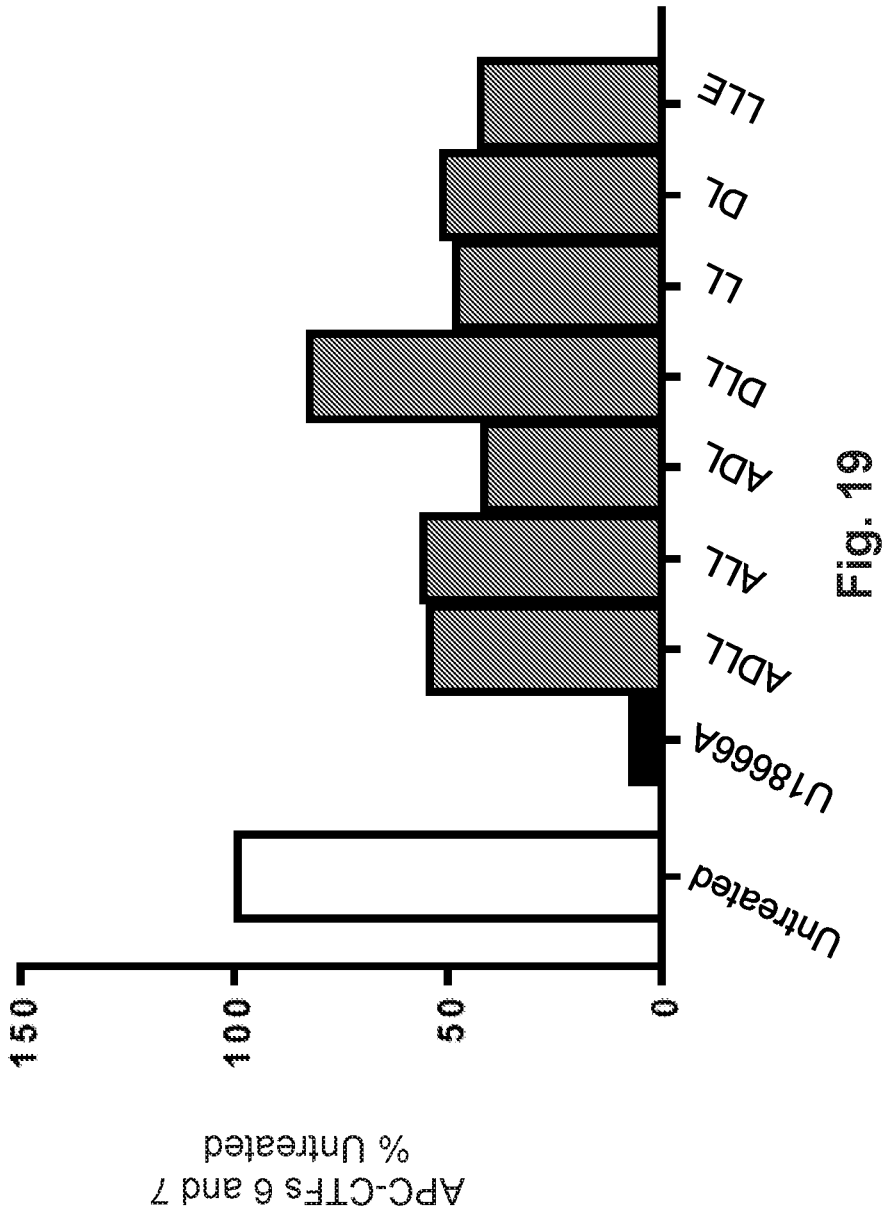

APC-CTFs 6 and 7
% Untreated
150
100
50
0
Untreated
U18666A
ADLL
ALL
ADL
DLL
LL
DL
LLE

Fig. 19

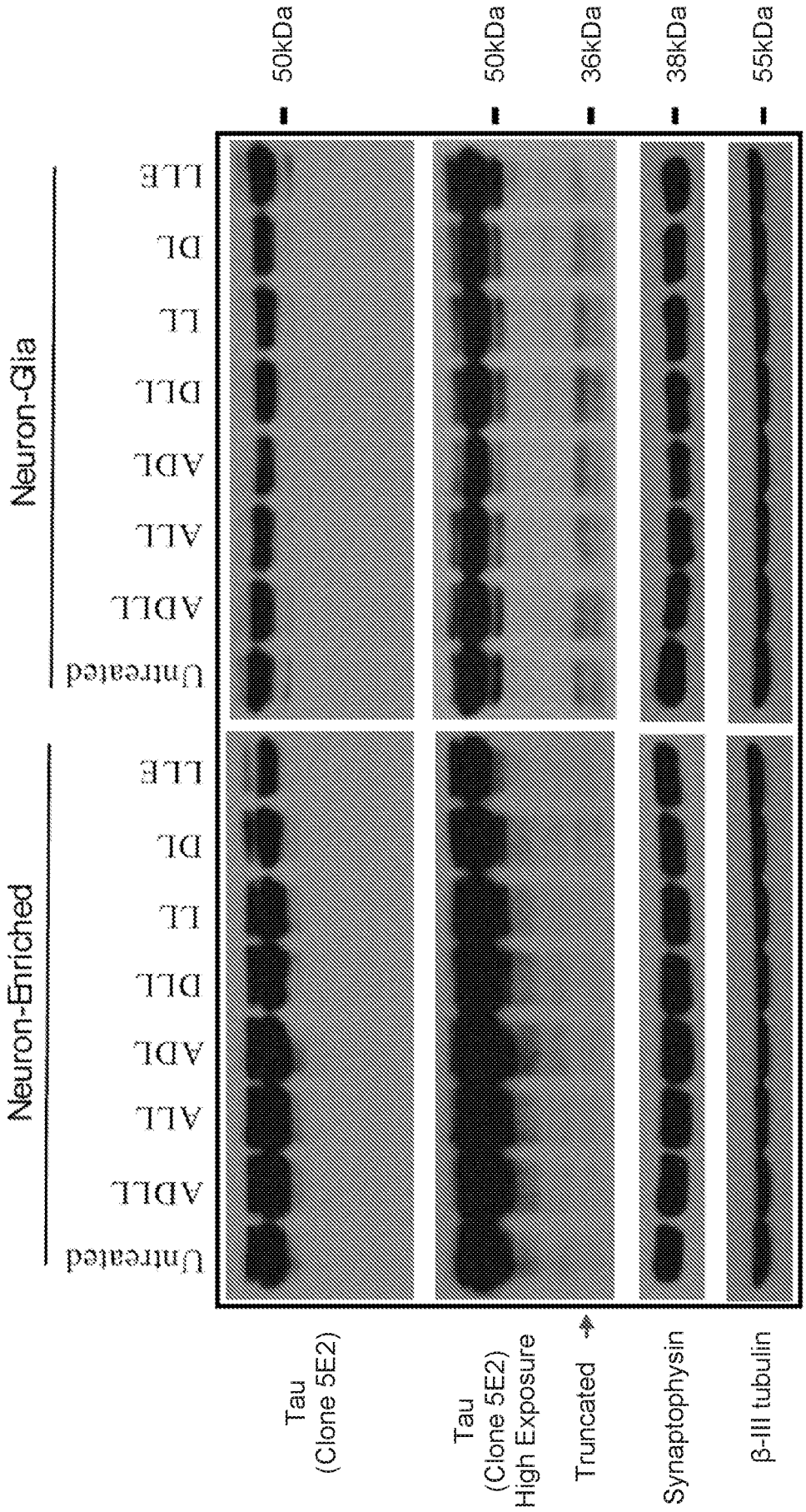

50kDa
50kDa
36kDa
38kDa
55kDa
Neuron-Enriched
Neuron-Glia
Untreated
ADLL
ALL
ADL
DLL
LL
DL
LLE
Tau (Clone 5E2)
Tau (Clone 5E2) High Exposure
Truncated
Synaptophysin
β-III tubulin

Fig. 20

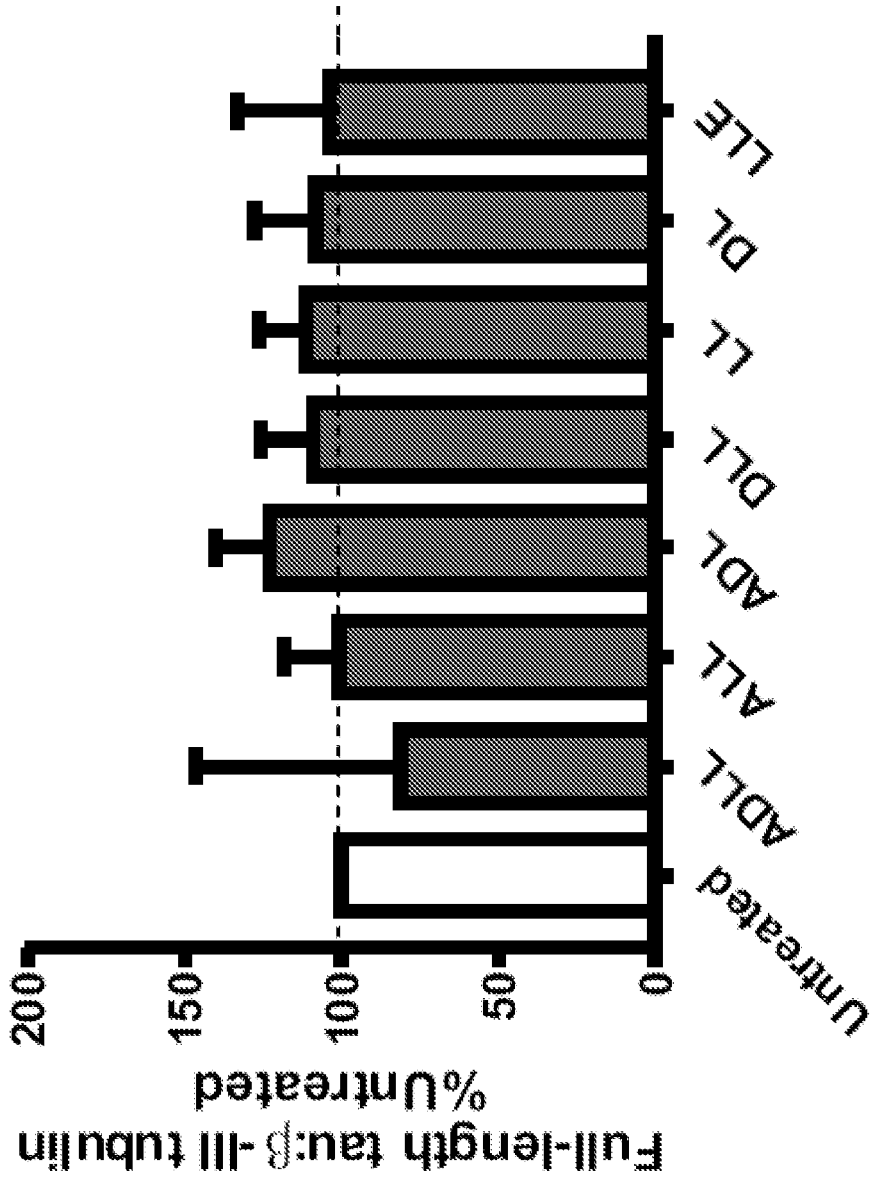

Full-length tau:β-III tubulin
%Untreated
200
150
100
50
0
Untreated
ADLL
ALL
ADL
DLL
LL
DL
LLE

Fig. 21

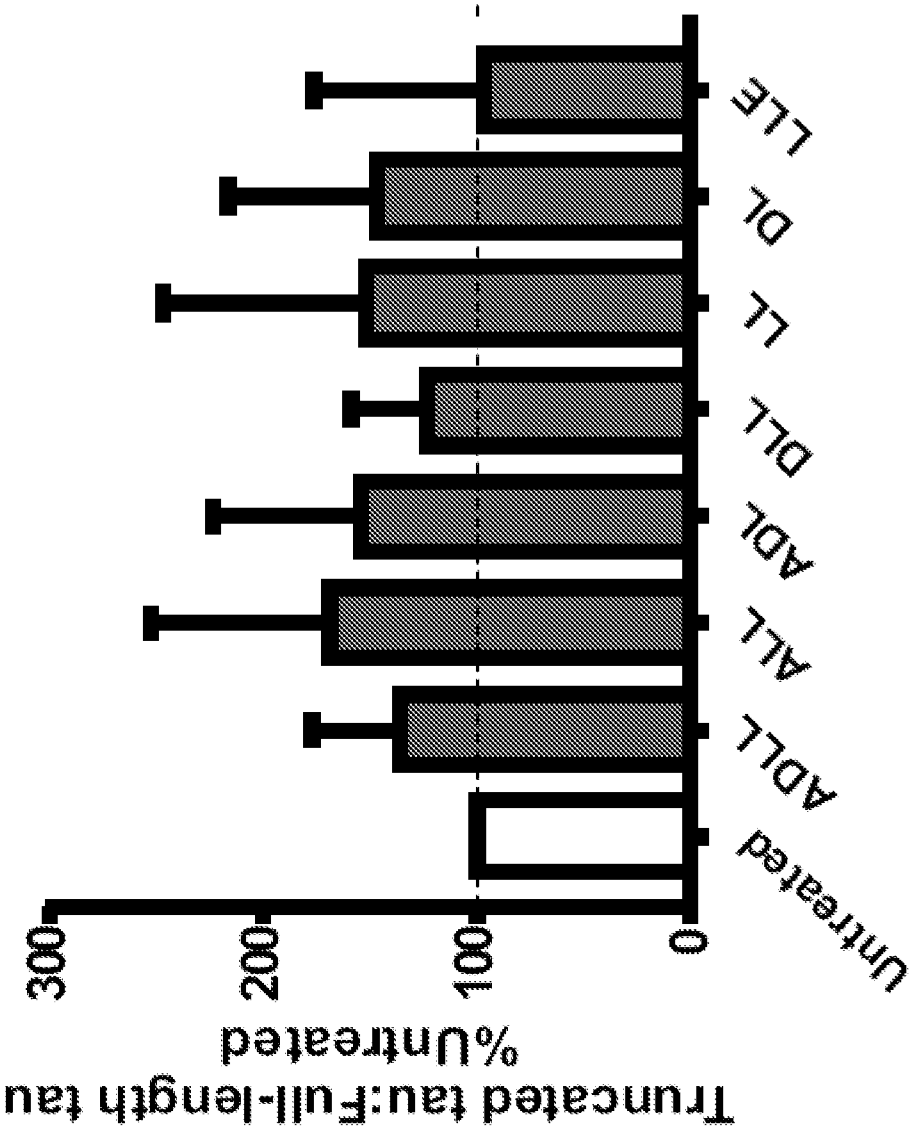

Truncated tau:Full-length tau
%Untreated
300
200
100
0
Untreated
ADLL
ALL
ADL
DLL
LL
DL
LLE

Fig. 22

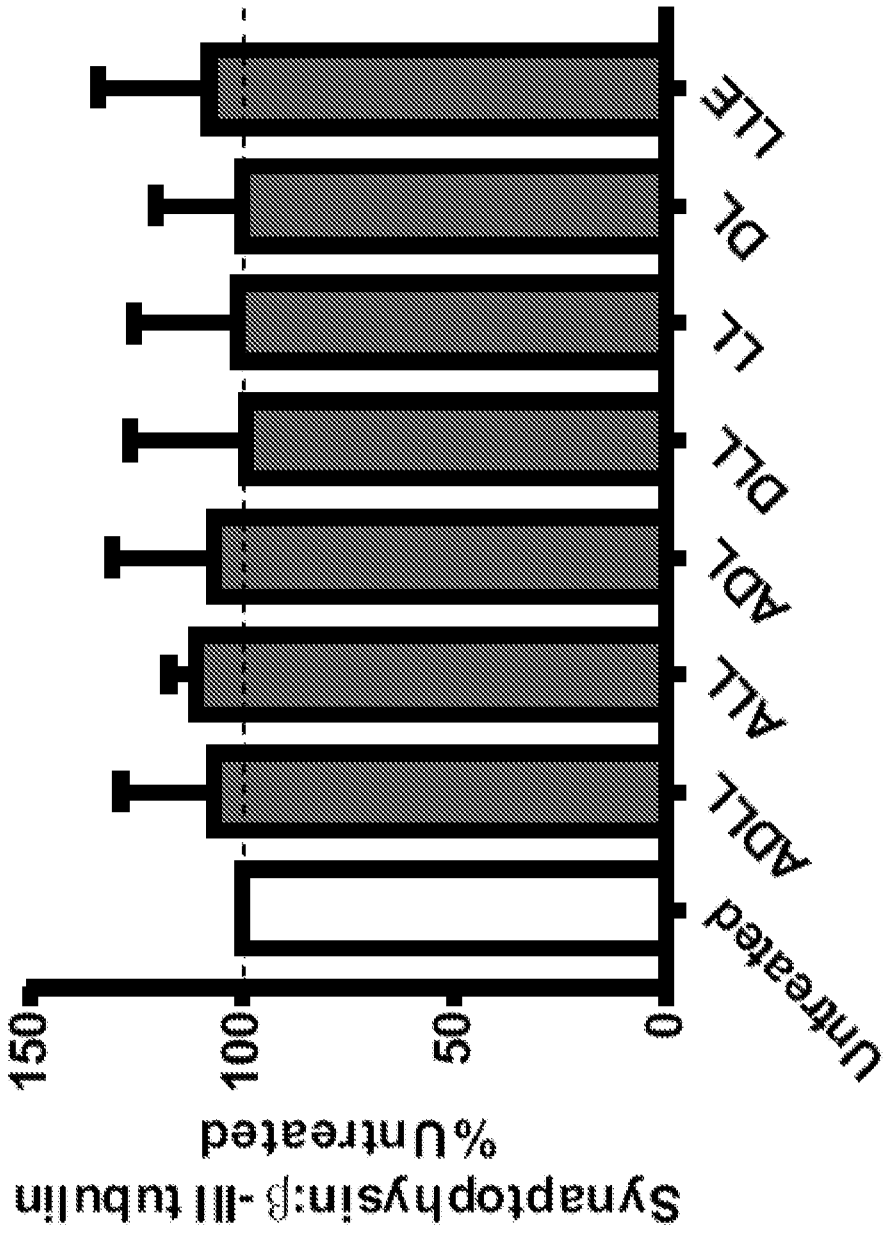

Synaptophysin:β-III tubulin
% Untreated
150
100
50
0
Untreated
ADLL
ALL
ADL
DLL
LL
DL
LLE

Fig. 23

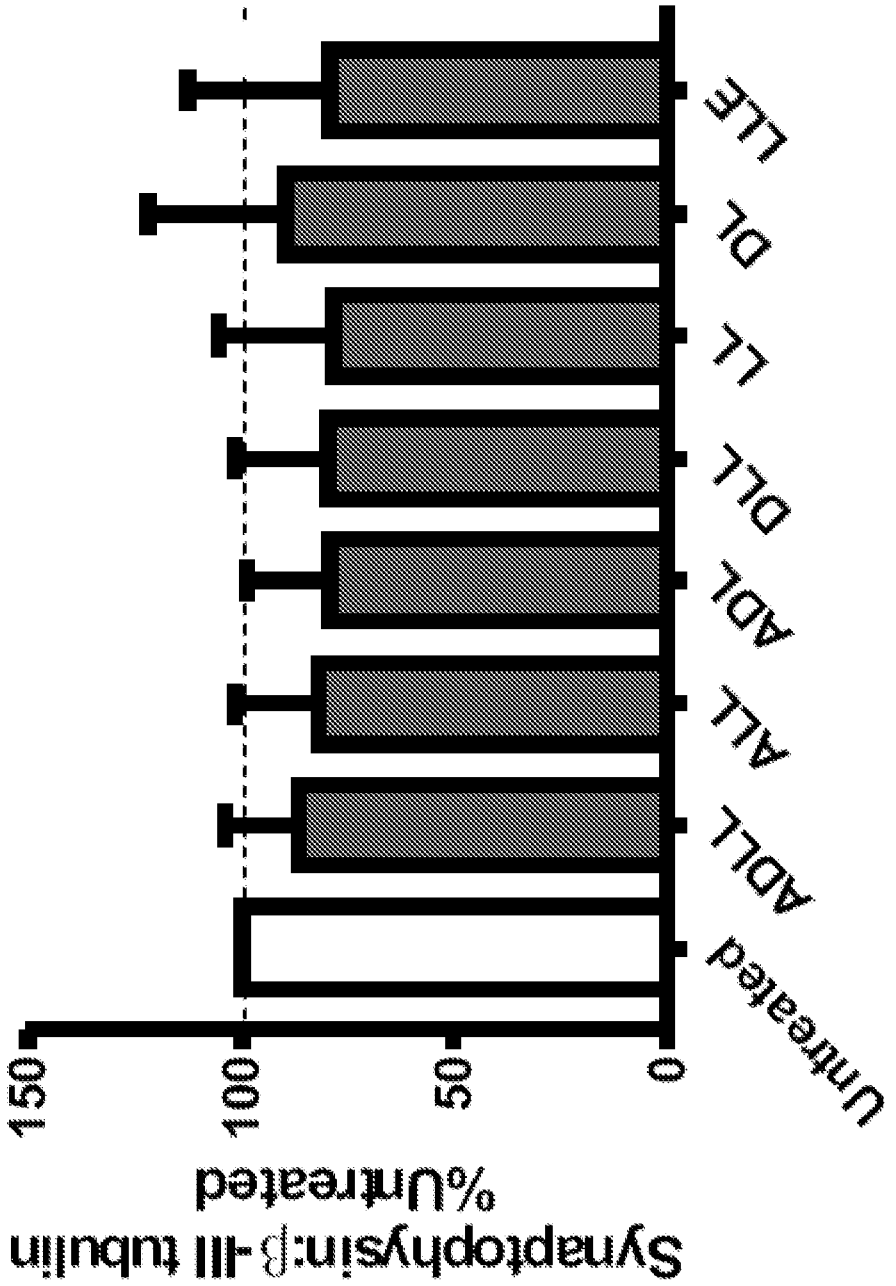

Synaptophysin:β-III tubulin
%Untreated
150
100
50
0
Untreated
ADLL
ALL
ADL
DLL
LL
DL
LLE

Fig. 24

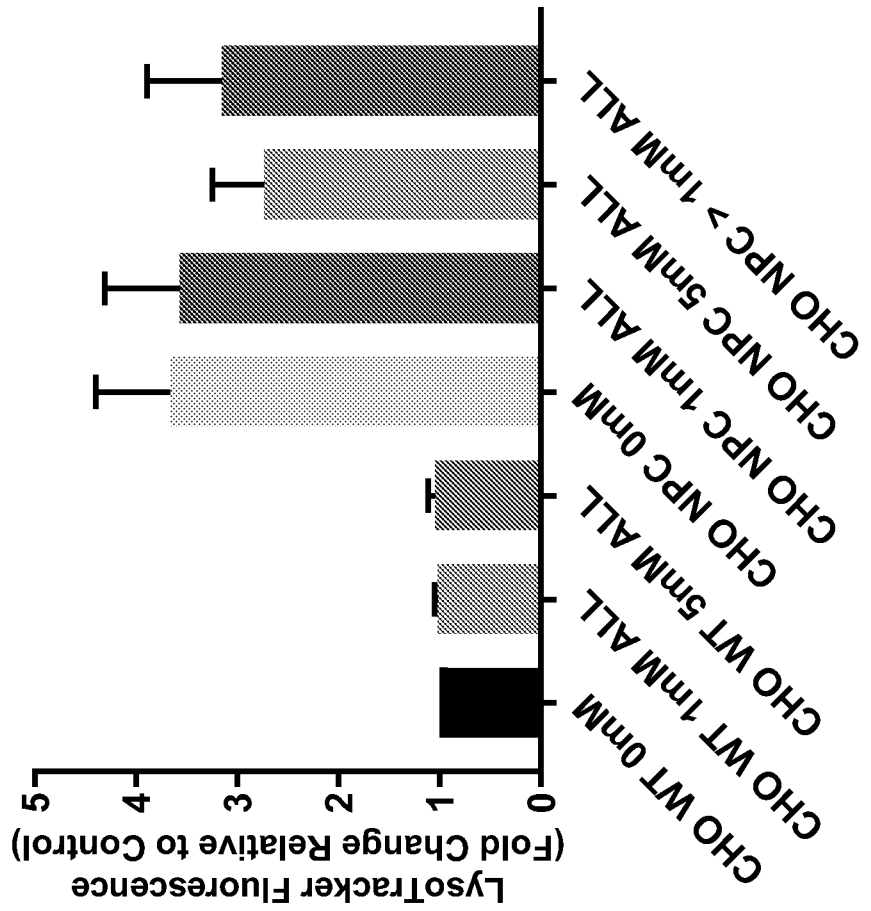

LysoTracker Fluorescence
(Fold Change Relative to Control)
0
1
2
3
4
5
CHO WT 0mM
CHO WT 1mM ALL
CHO WT 5mM ALL
CHO NPC 0mM
CHO NPC 1mM ALL
CHO NPC 5mM ALL
CHO NPC > 1mM ALL

Fig. 25

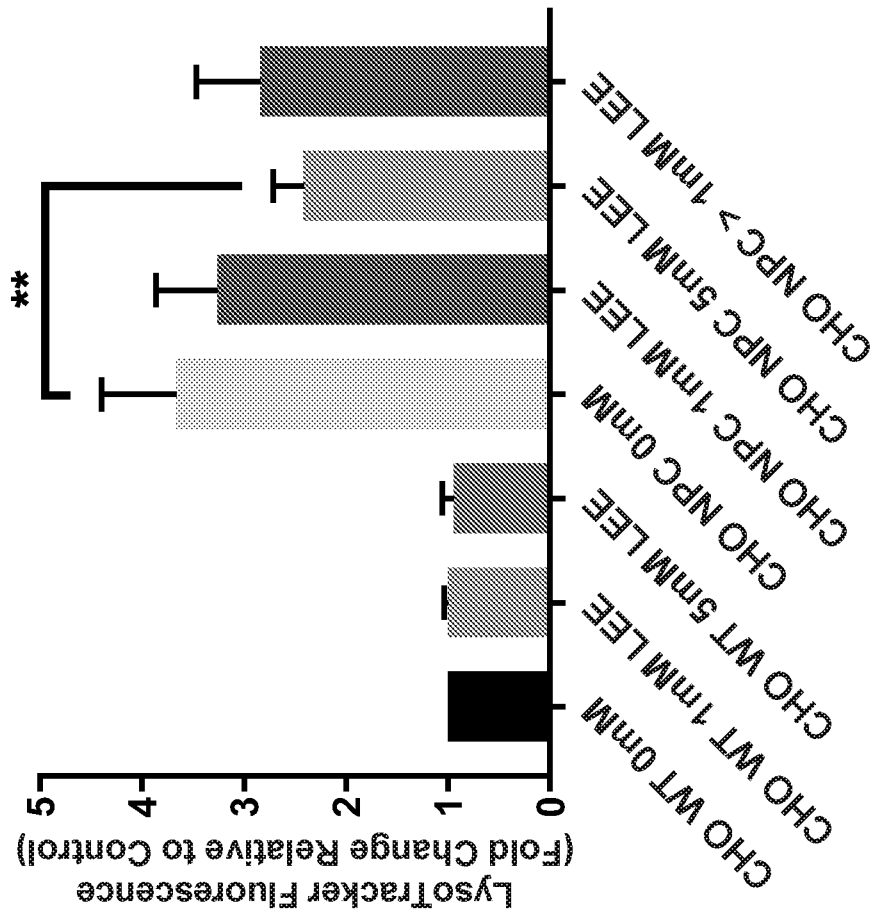

LysoTracker Fluorescence
(Fold Change Relative to Control)
0
1
2
3
4
5
**
CHO WT 0mM
CHO WT 1mM LEE
CHO WT 5mM LEE
CHO NPC 0mM
CHO NPC 1mM LEE
CHO NPC 5mM LEE
CHO NPC > 1mM LEE

Fig. 26

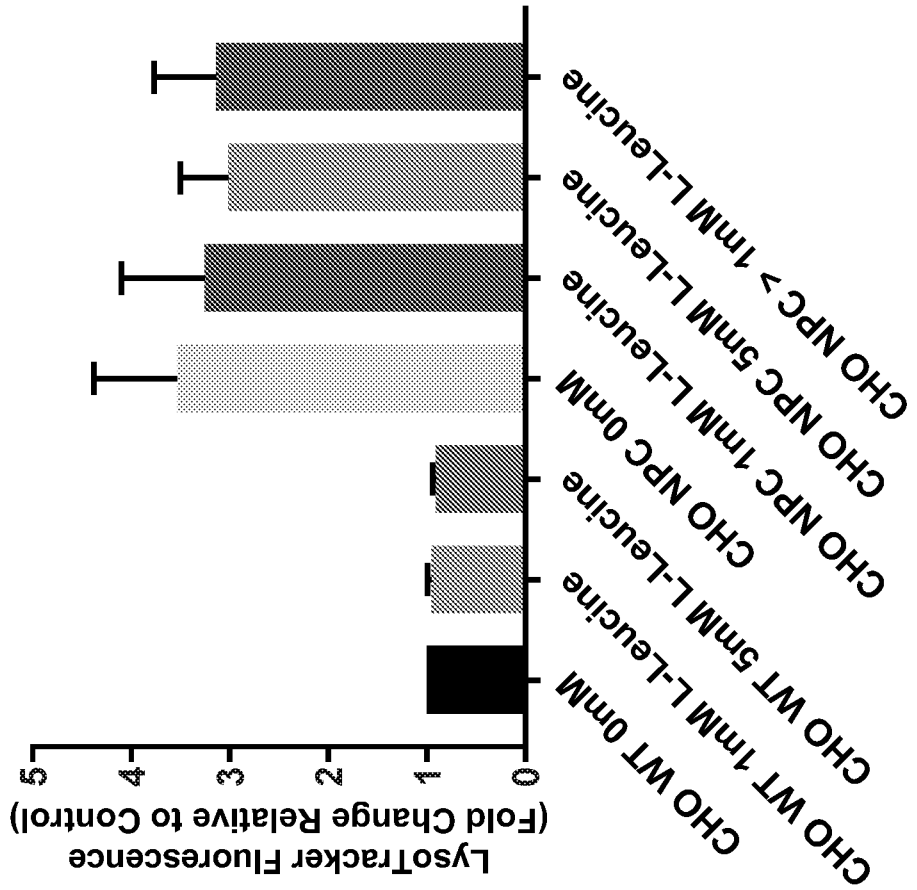

LysoTracker Fluorescence
(Fold Change Relative to Control)
0
1
2
3
4
5
CHO WT 0mM
CHO WT 1mM L-Leucine
CHO WT 5mM L-Leucine
CHO NPC 0mM
CHO NPC 1mM L-Leucine
CHO NPC 5mM L-Leucine
CHO NPC > 1mM L-Leucine

Fig. 27

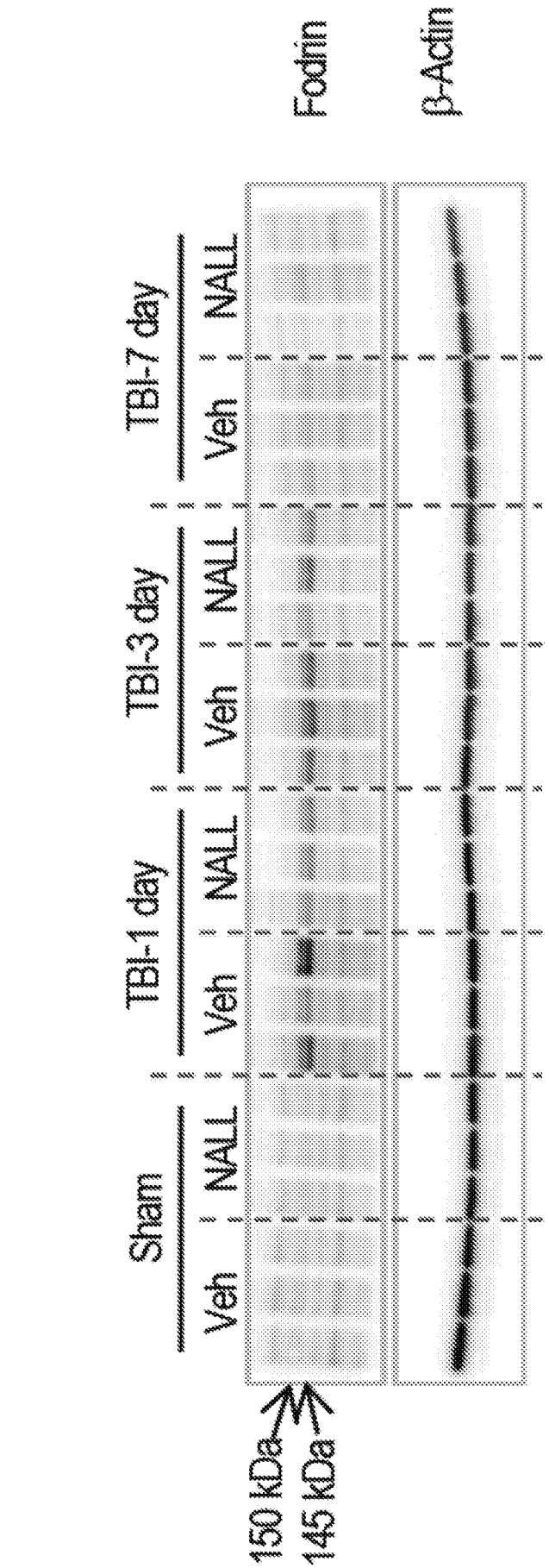

Sham
TBI-1 day
TBI-3 day
TBI-7 day
Veh
NALL
Veh
NALL
Veh
NALL
Veh
NALL
Fodrin
β-Actin
150 kDa
145 kDa

Fig. 28

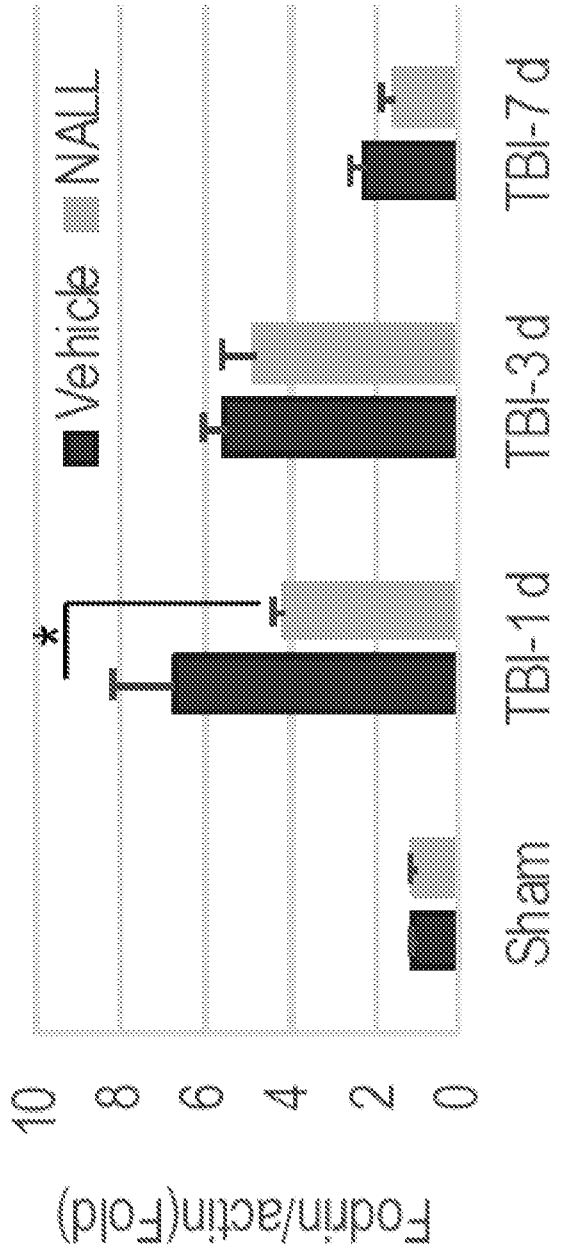

Vehicle
NALL
Sham
TBI-1 d
TBI-3 d
TBI-7 d
*
Fodrin/actin(Fold)
10
8
6
4
2
0

Fig. 29

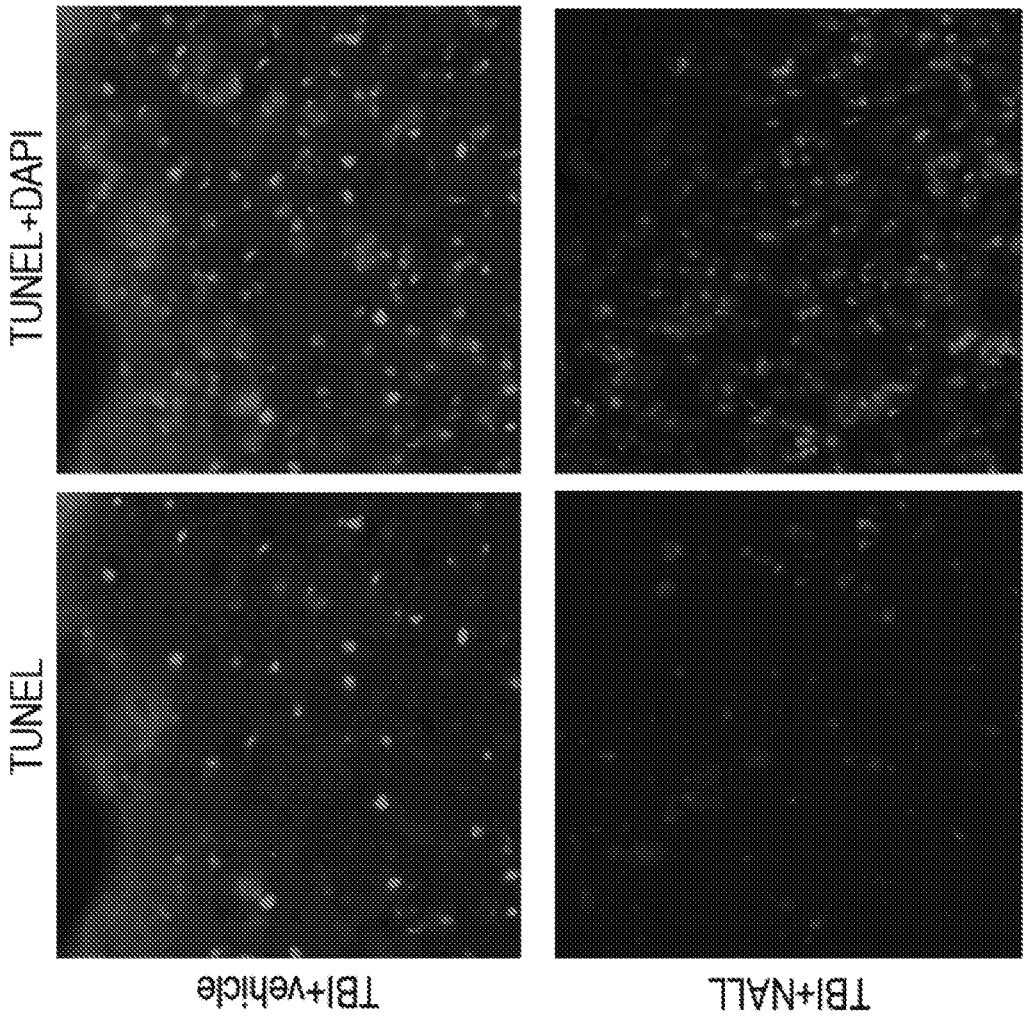


Fig. 30

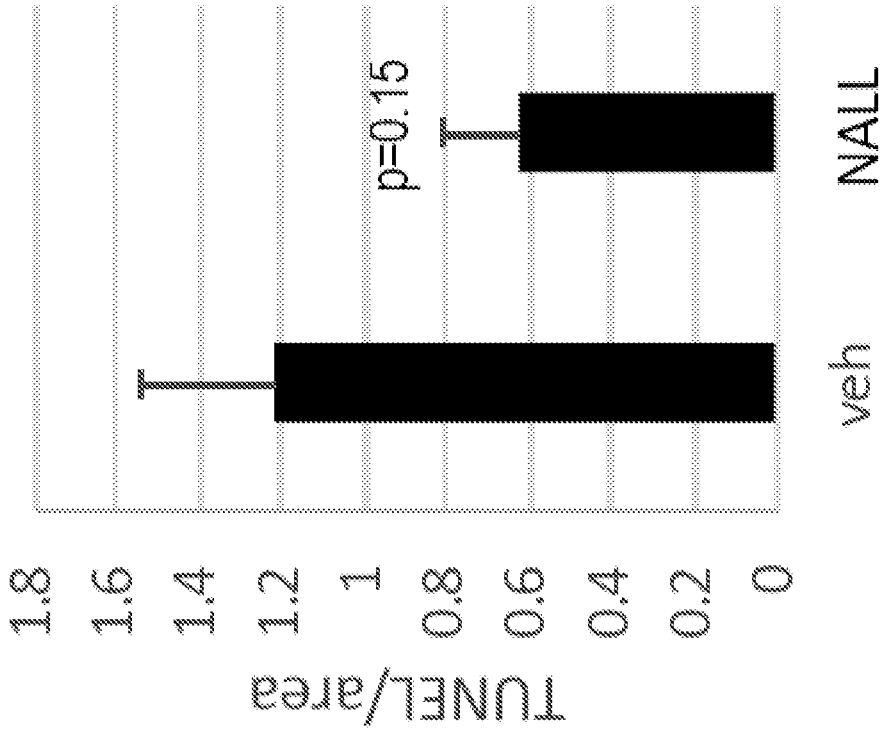


Fig. 31

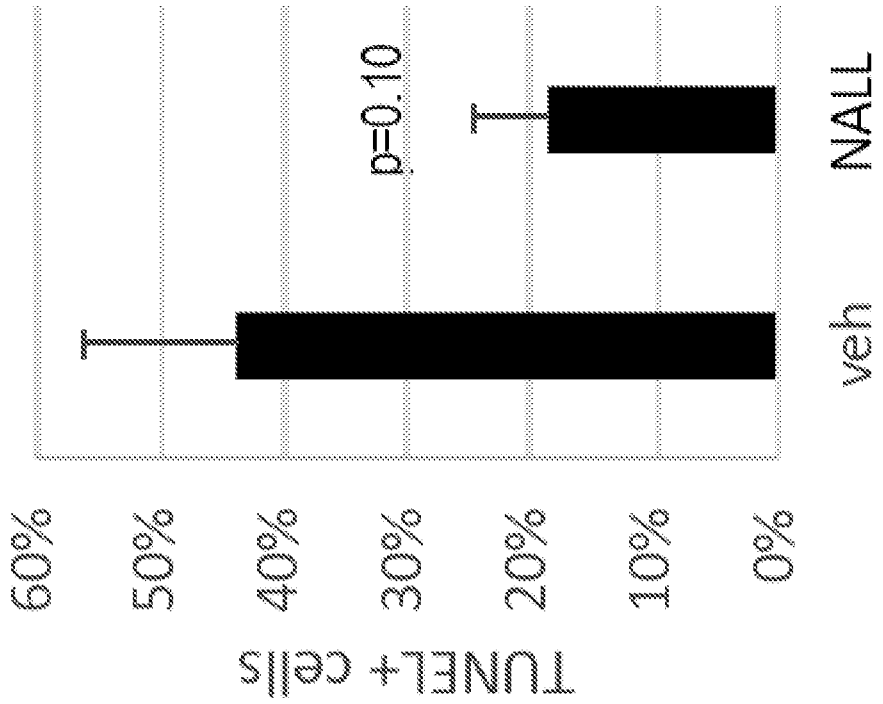


Fig. 32

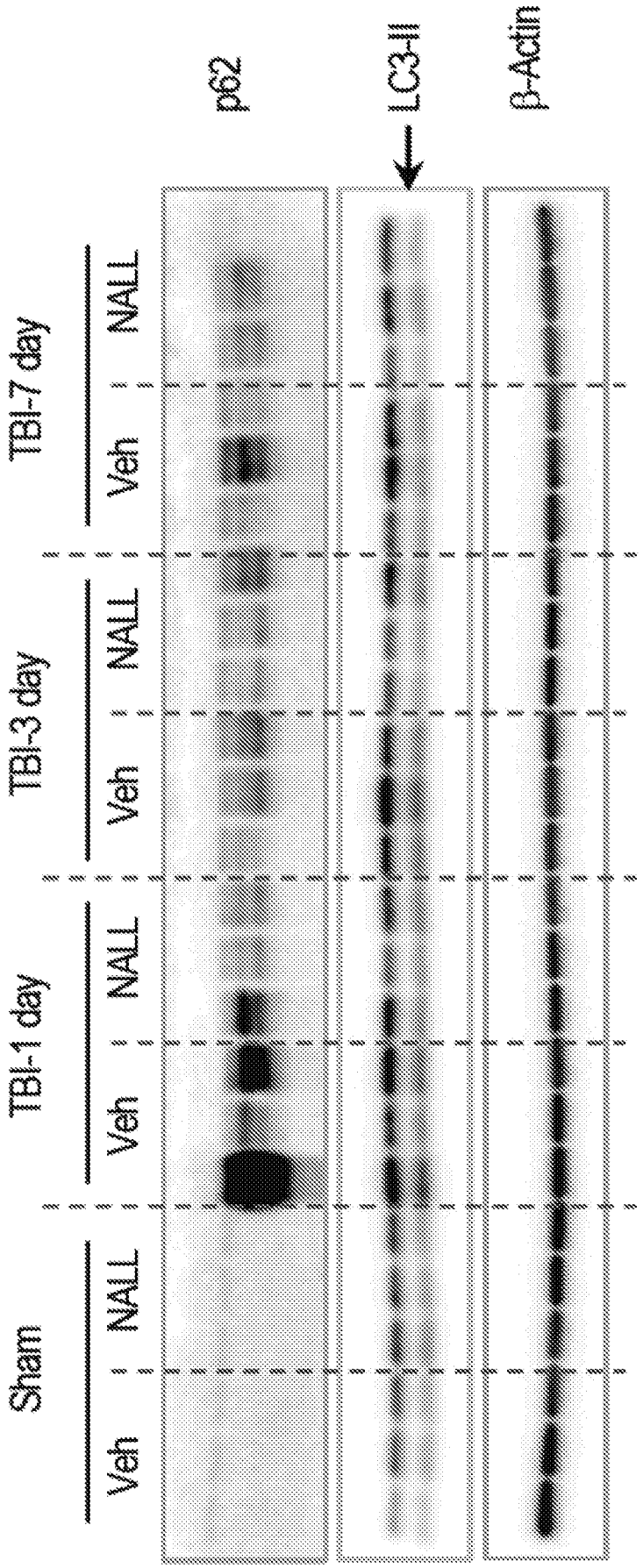

p62
LC3-II
β-Actin
Sham
TBI-1 day
TBI-3 day
TBI-7 day
Veh
NALL
Veh
NALL
Veh
NALL
Veh
NALL

Fig. 33

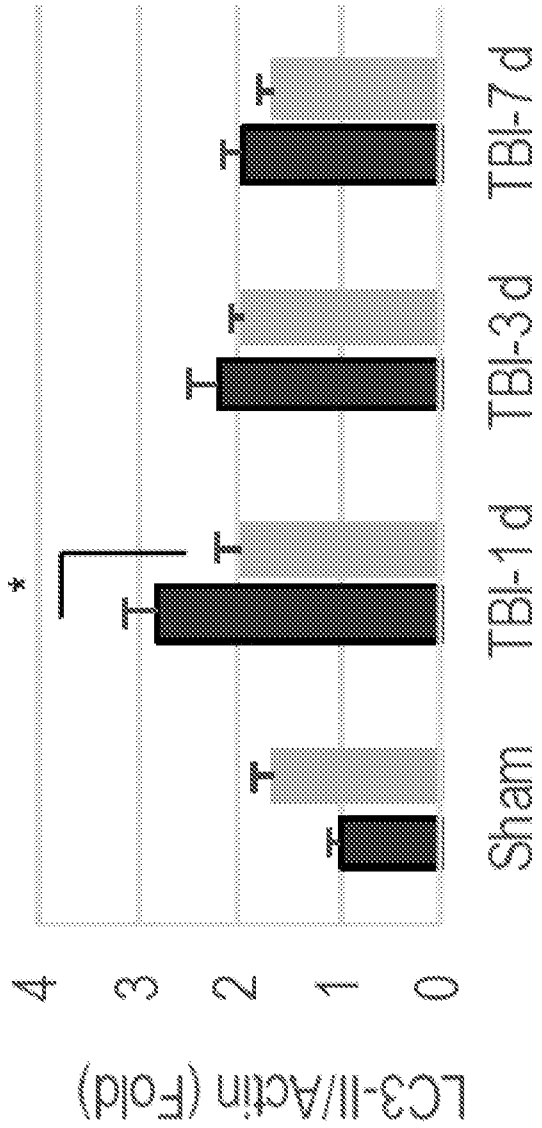


Fig. 34

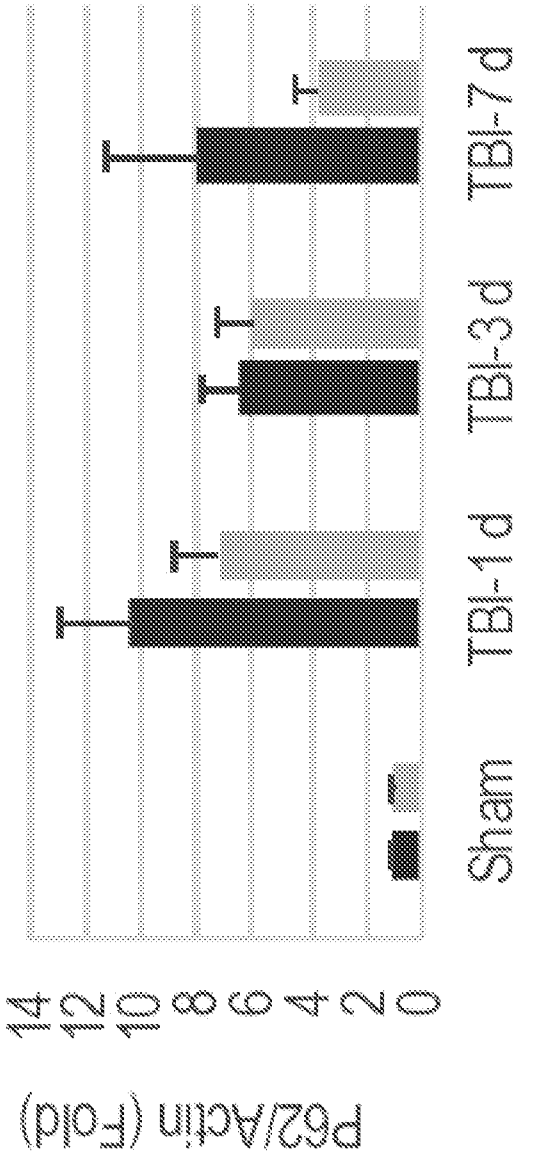

P62/Actin (Fold)
0
2
4
6
8
10
12
14
Sham
TBI-1 d
TBI-3 d
TBI-7 d
Vehicle
NALL

Fig. 35

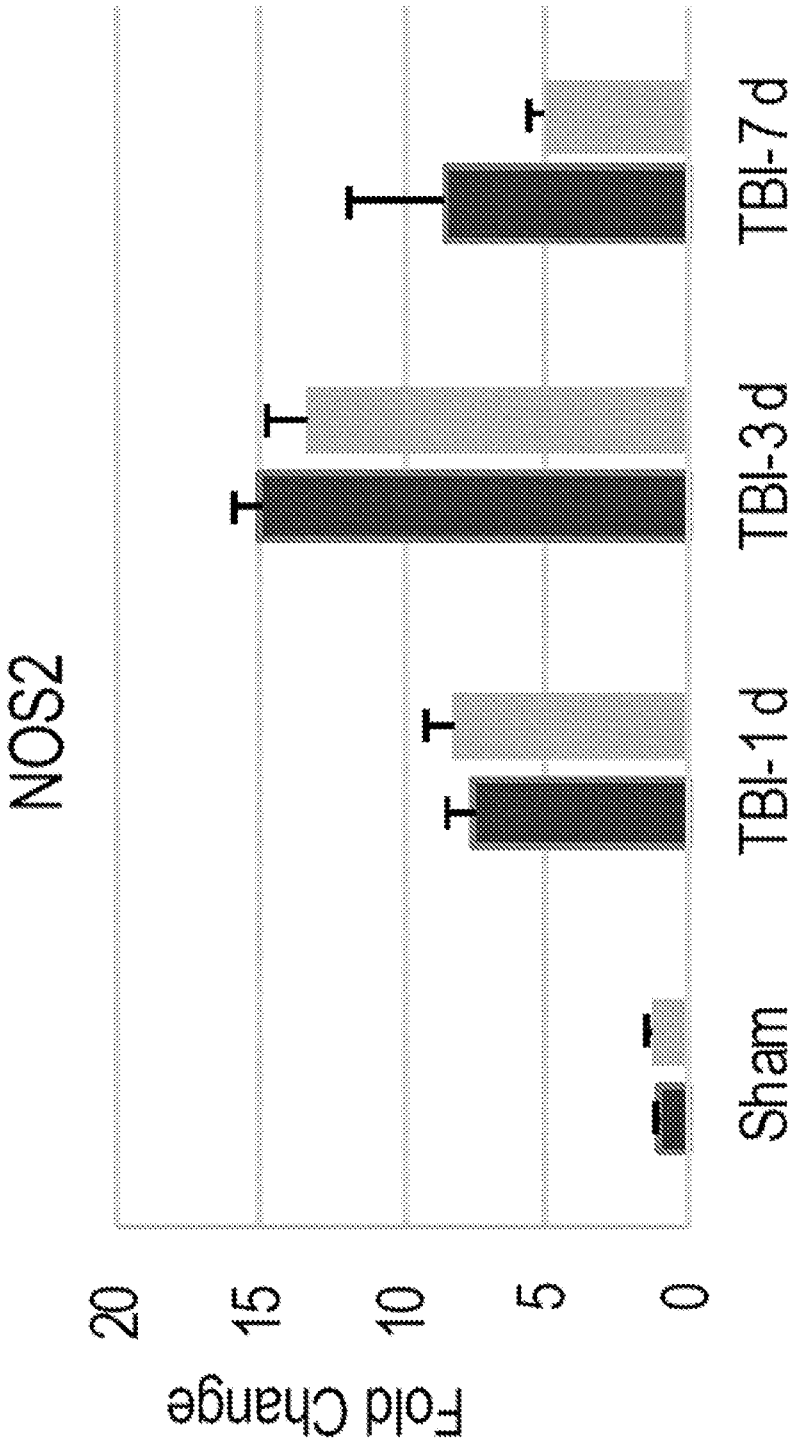

NOS2
Fold Change
20
15
10
5
0
Sham
TBI-1 d
TBI-3 d
TBI-7 d
Vehicle
NALL

Fig. 36

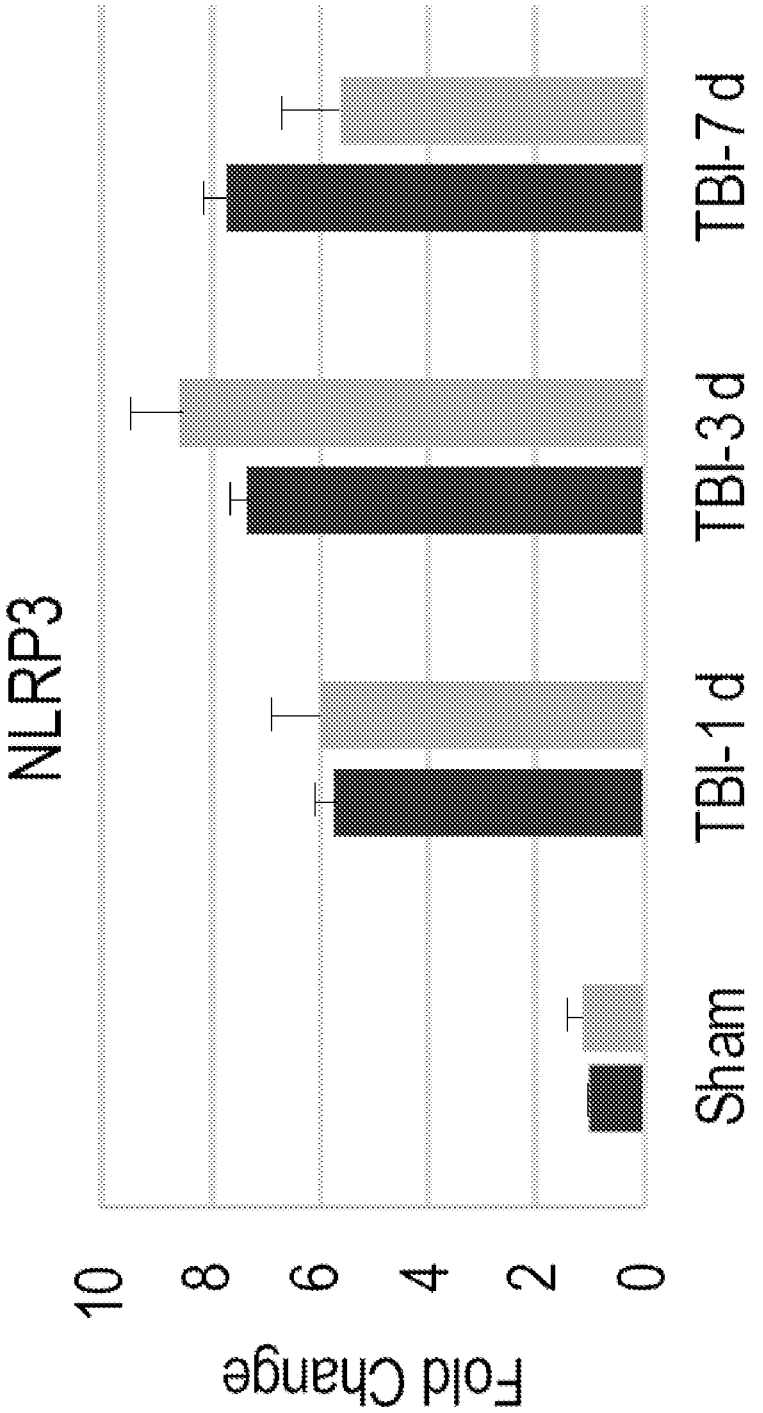

NLRP3
Fold Change
10
8
6
4
2
0
Sham
TBI-1 d
TBI-3 d
TBI-7 d
Vehicle
NALL

Fig. 37

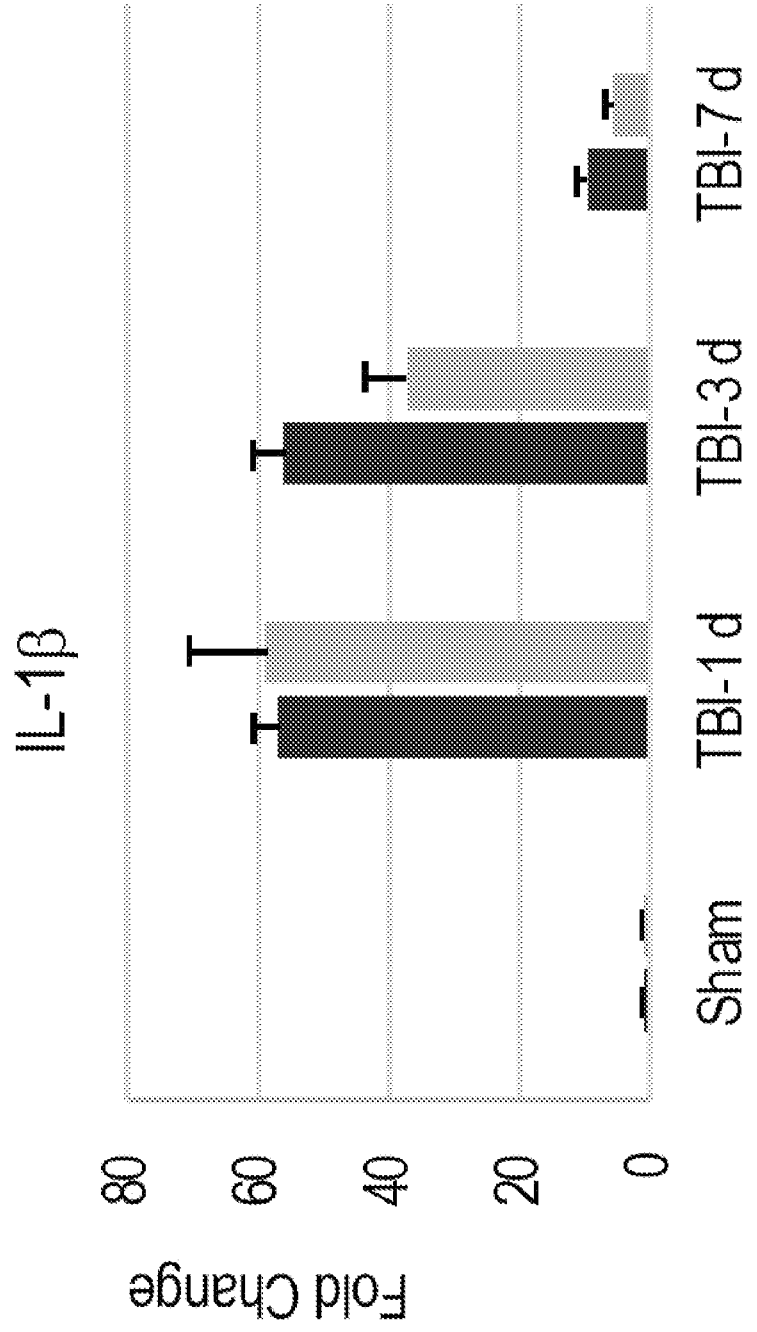

IL-1β
Fold Change
80
60
40
20
0
Sham
TBI-1 d
TBI-3 d
TBI-7 d
Vehicle
NALL

Fig. 38

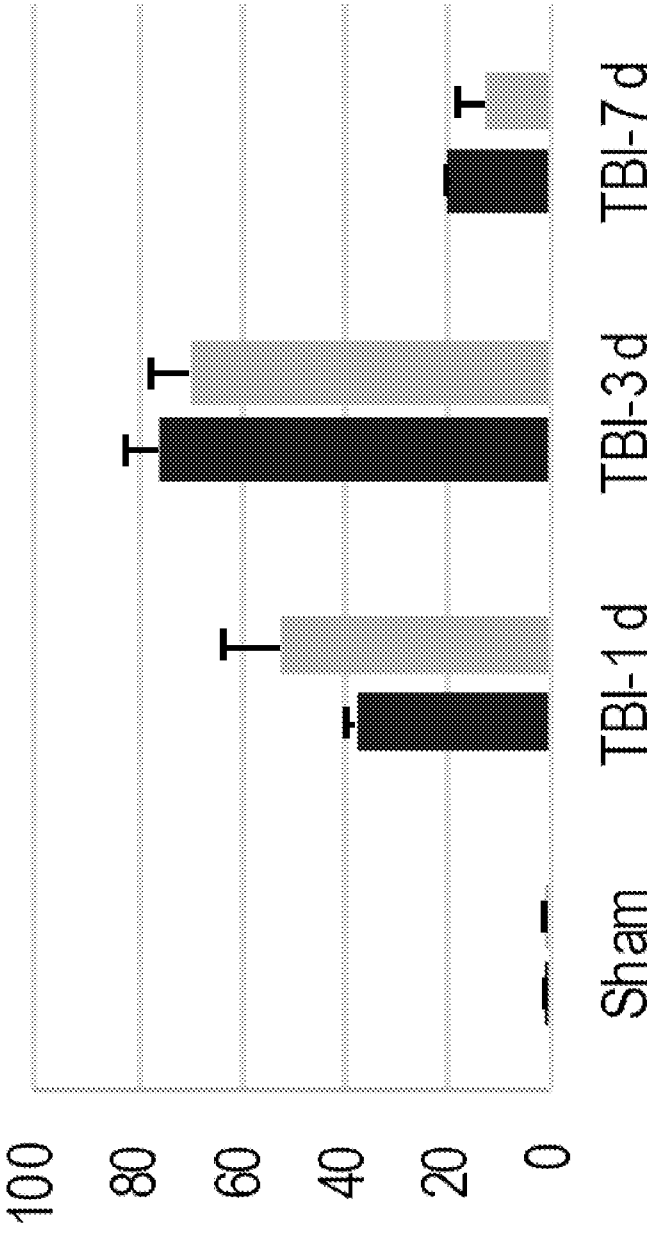


Fig. 39

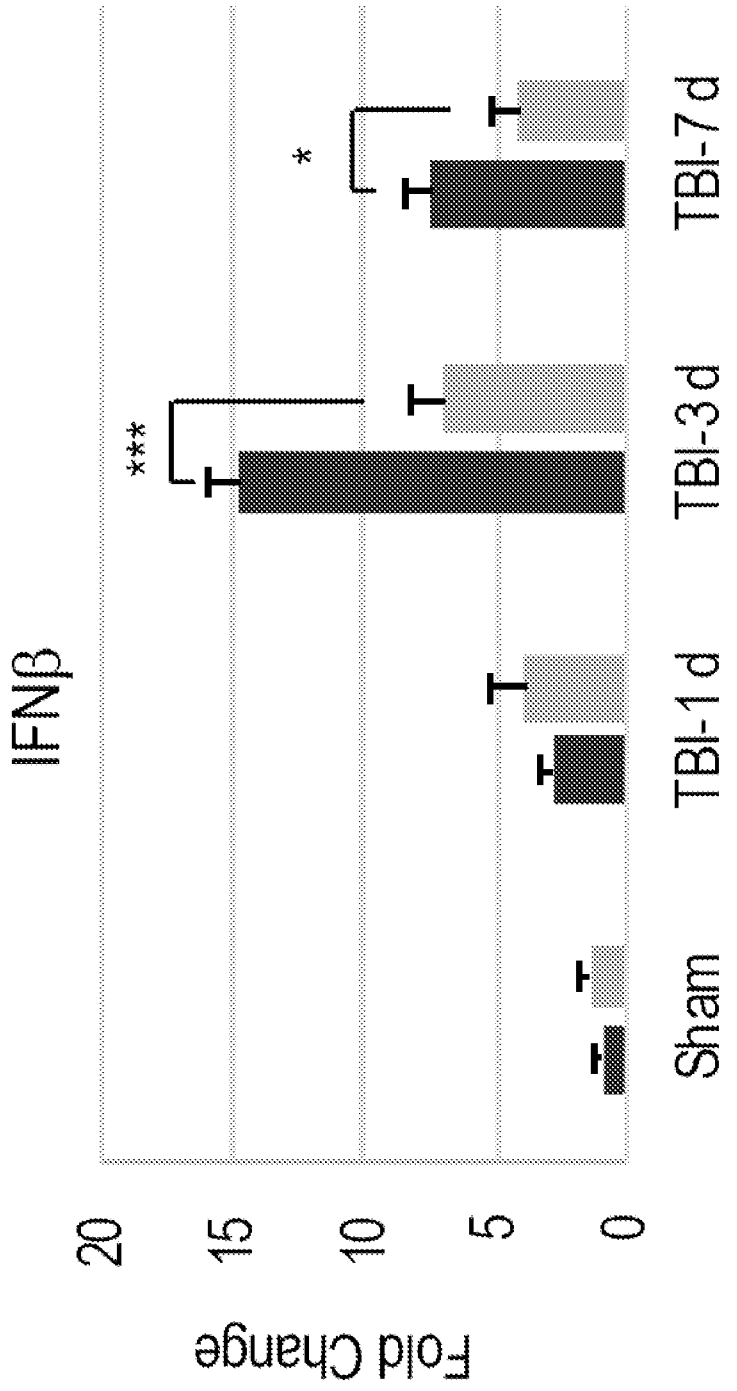

IFNβ
Fold Change
20
15
10
5
0
***
*
Sham
TBI-1 d
TBI-3 d
TBI-7 d
Vehicle
NALL

Fig. 40

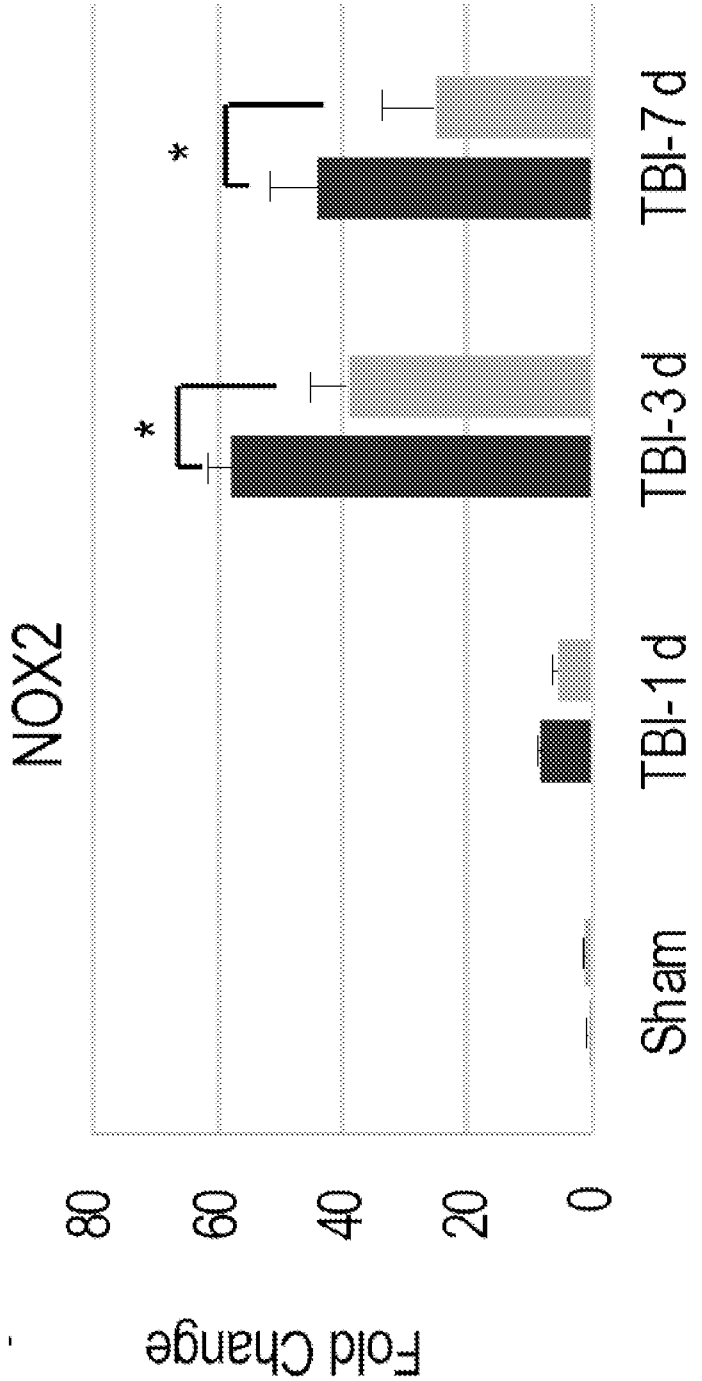

NOX2
Fold Change
80
60
40
20
0
*
*
Sham
TBI-1 d
TBI-3 d
TBI-7 d
Vehicle
NALL

Fig. 41

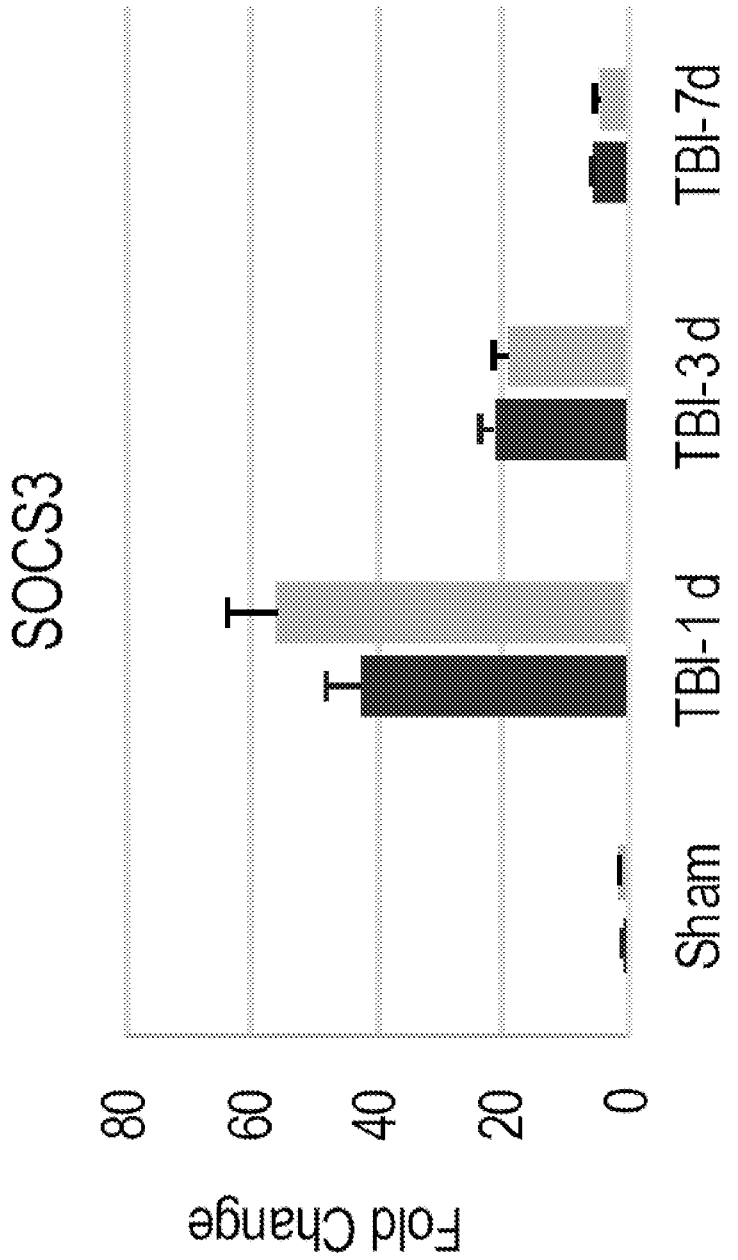

SOCS3
Fold Change
80
60
40
20
0
Sham
TBI-1 d
TBI-3 d
TBI-7d
Vehicle
NALL

Fig. 42

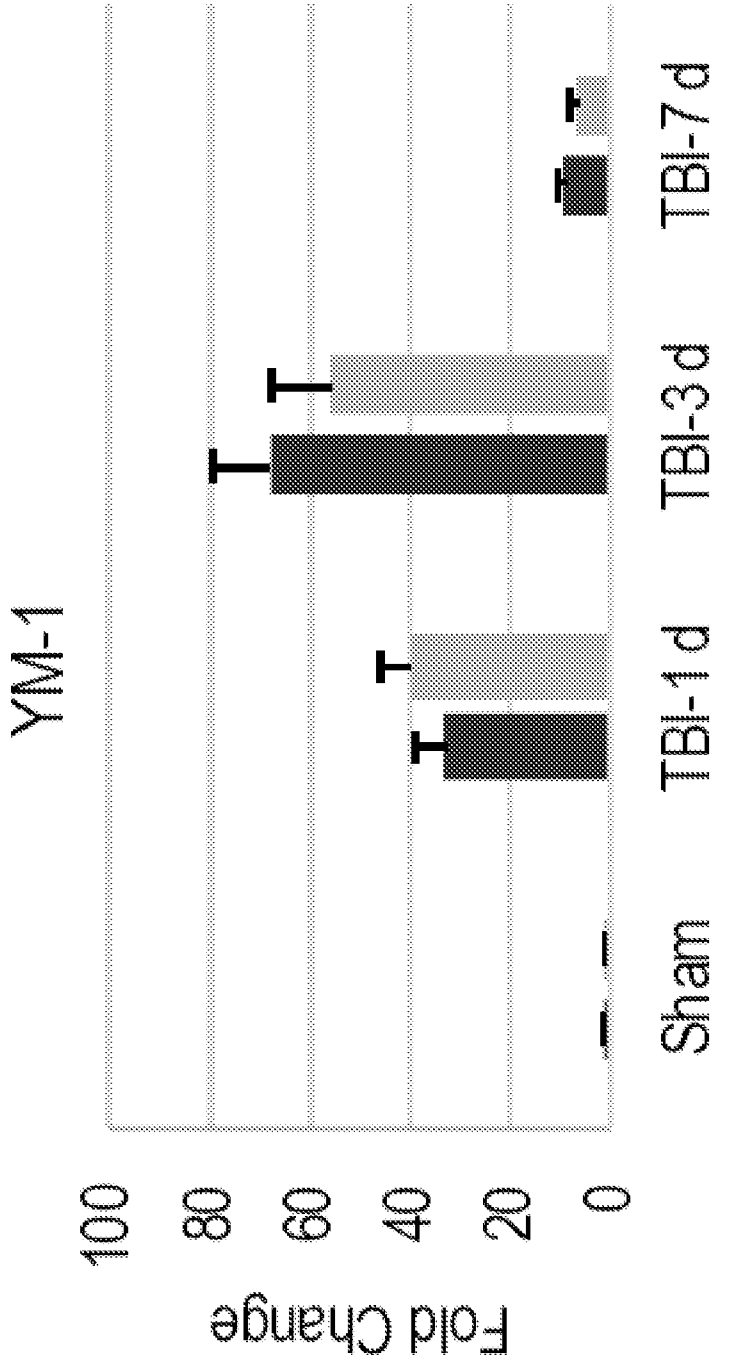

YM-1
Fold Change
100
80
60
40
20
0
Sham
TBI-1 d
TBI-3 d
TBI-7 d
Vehicle
NALL

Fig. 43

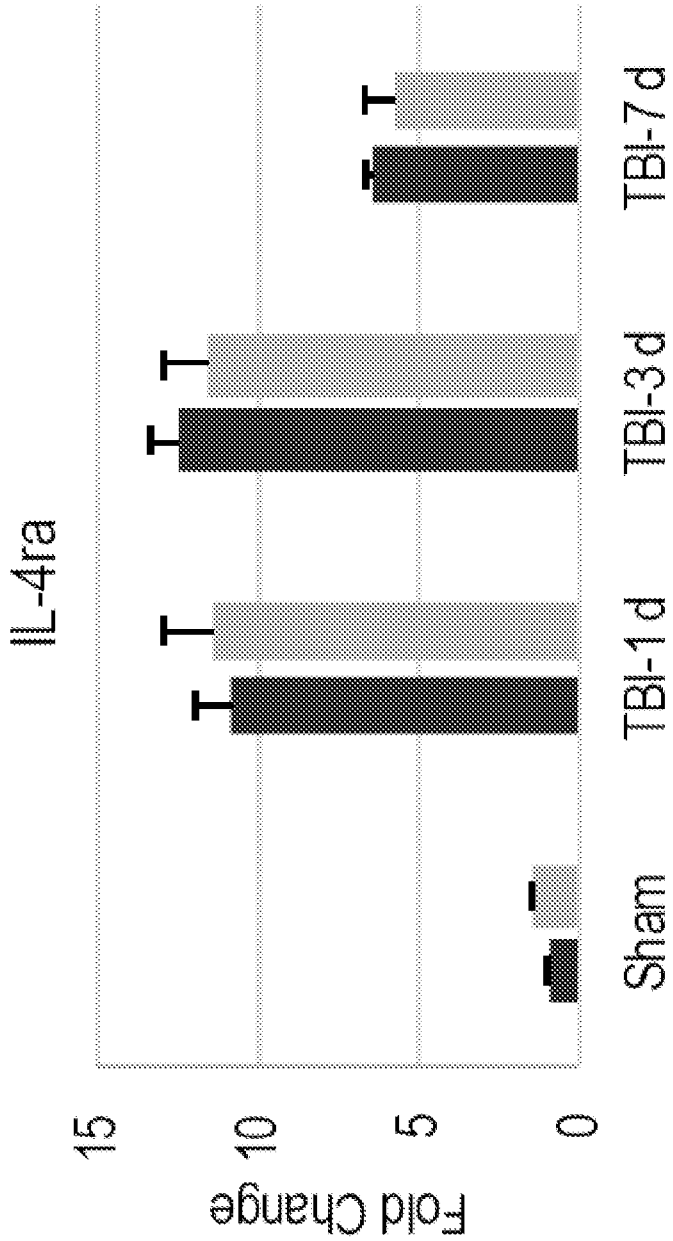

IL-4ra
Fold Change
15
10
5
0
Sham
TBI-1 d
TBI-3 d
TBI-7 d
Vehicle
NALL

Fig. 44

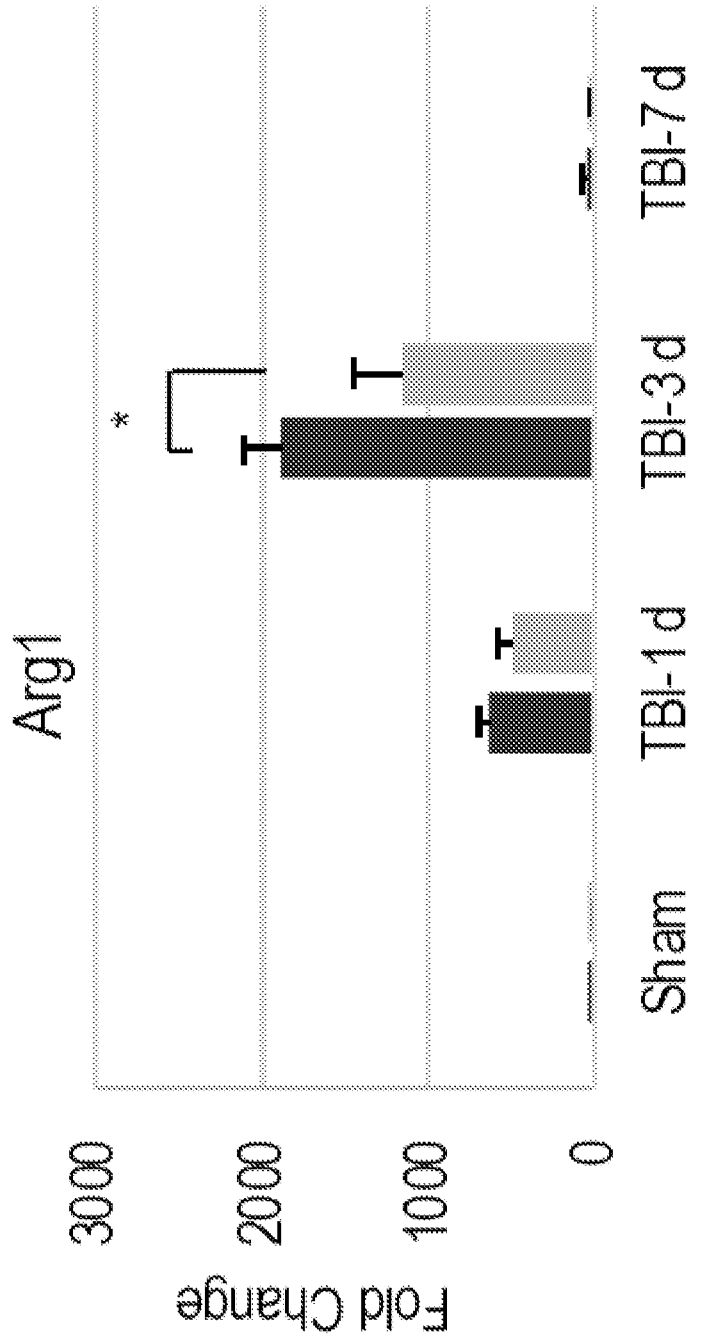

Arg1
Fold Change
3000
2000
1000
0
*
Sham
TBI-1 d
TBI-3 d
TBI-7 d
Vehicle
NALL

Fig. 45

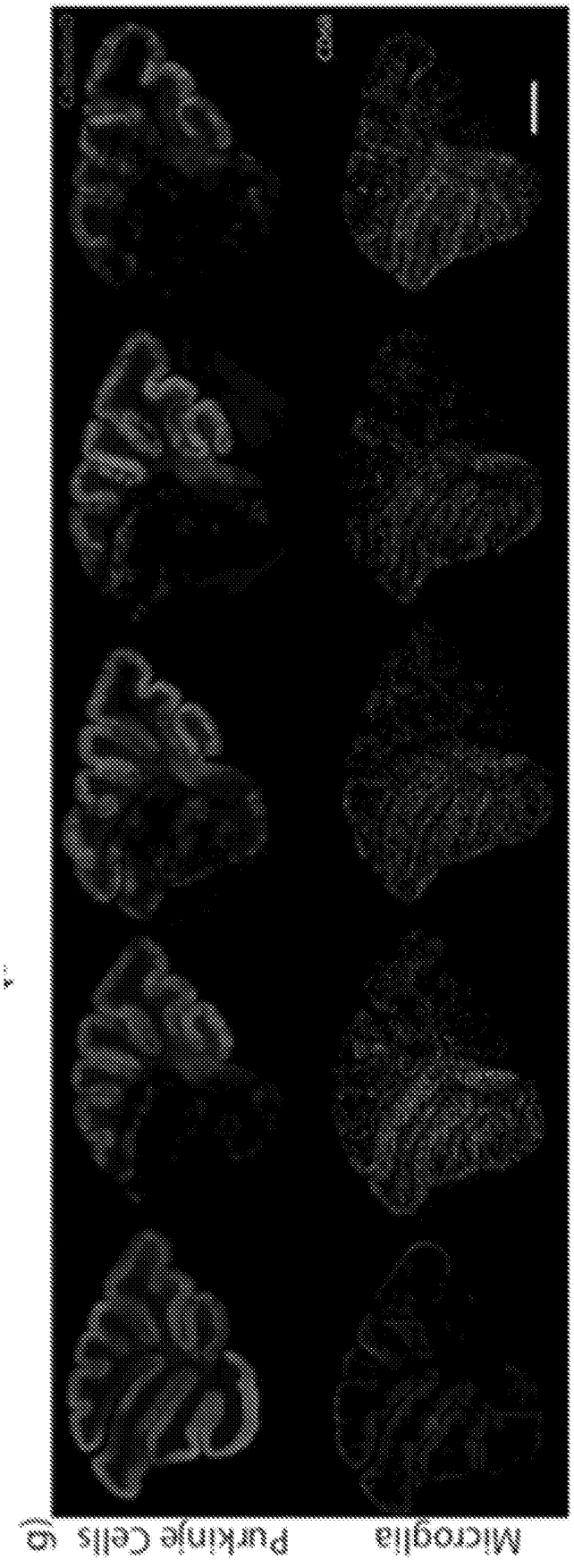

Npc1 +/+ UT
Npc1 -/- UT
Npc1 -/- ADLL
Npc1 -/- ALL
Npc1 -/- ADL
Microglia
Purkinje Cells

Fig. 46

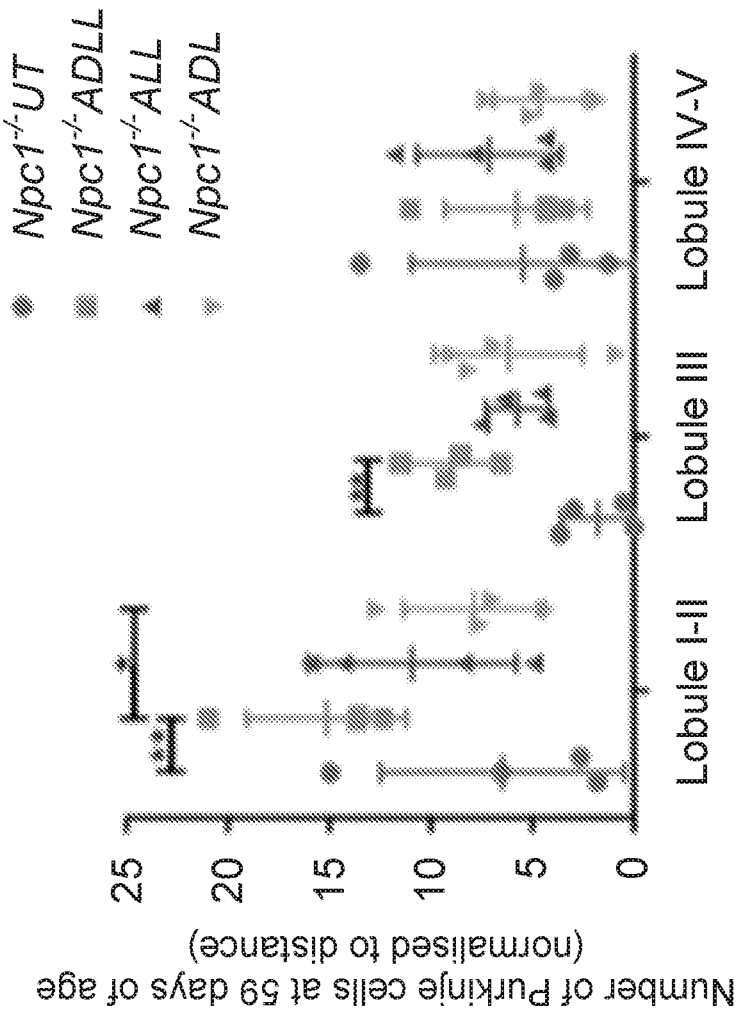

Npc1-/-UT
Npc1-/-ADLL
Npc1-/-ALL
Npc1-/-ADL
Number of Purkinje cells at 59 days of age
(normalised to distance)
25
20
15
10
5
0
Lobule I-II
Lobule III
Lobule IV-V

Fig. 47

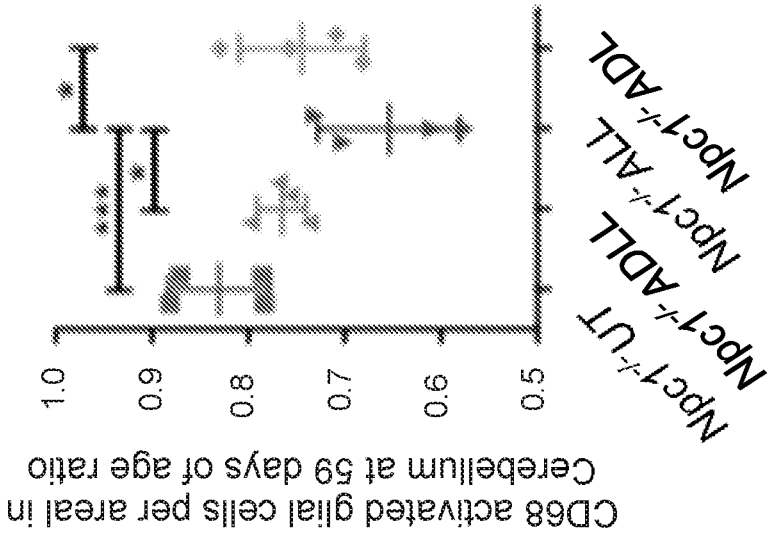

CD68 activated glial cells per areal in Cerebellum at 59 days of age ratio
1.0
0.9
0.8
0.7
0.6
0.5
Npc1-/- UT
Npc1-/- ADLL
Npc1-/- ALL
Npc1-/- ADL

Fig. 48

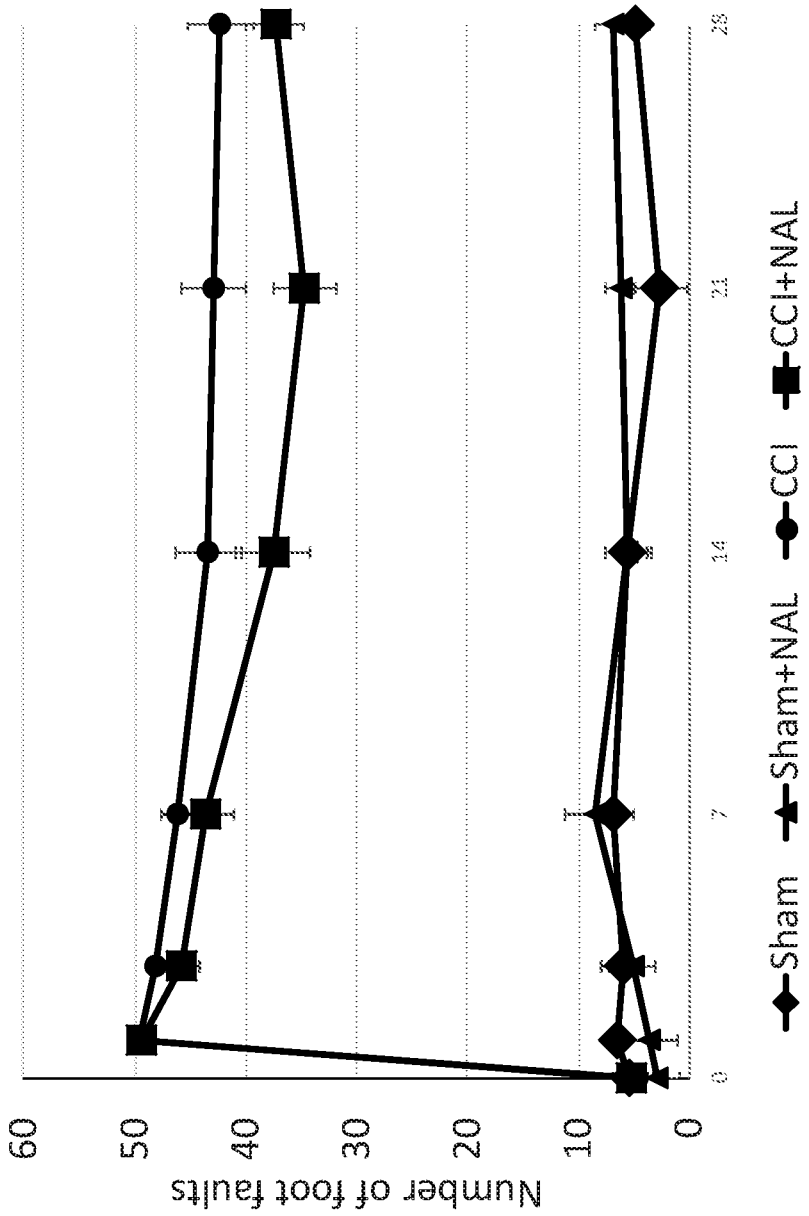

Number of foot faults
60
50
40
30
20
10
0
0
7
14
21
28
Sham
Sham+NAL
CCI
CCI+NAL

Fig. 49

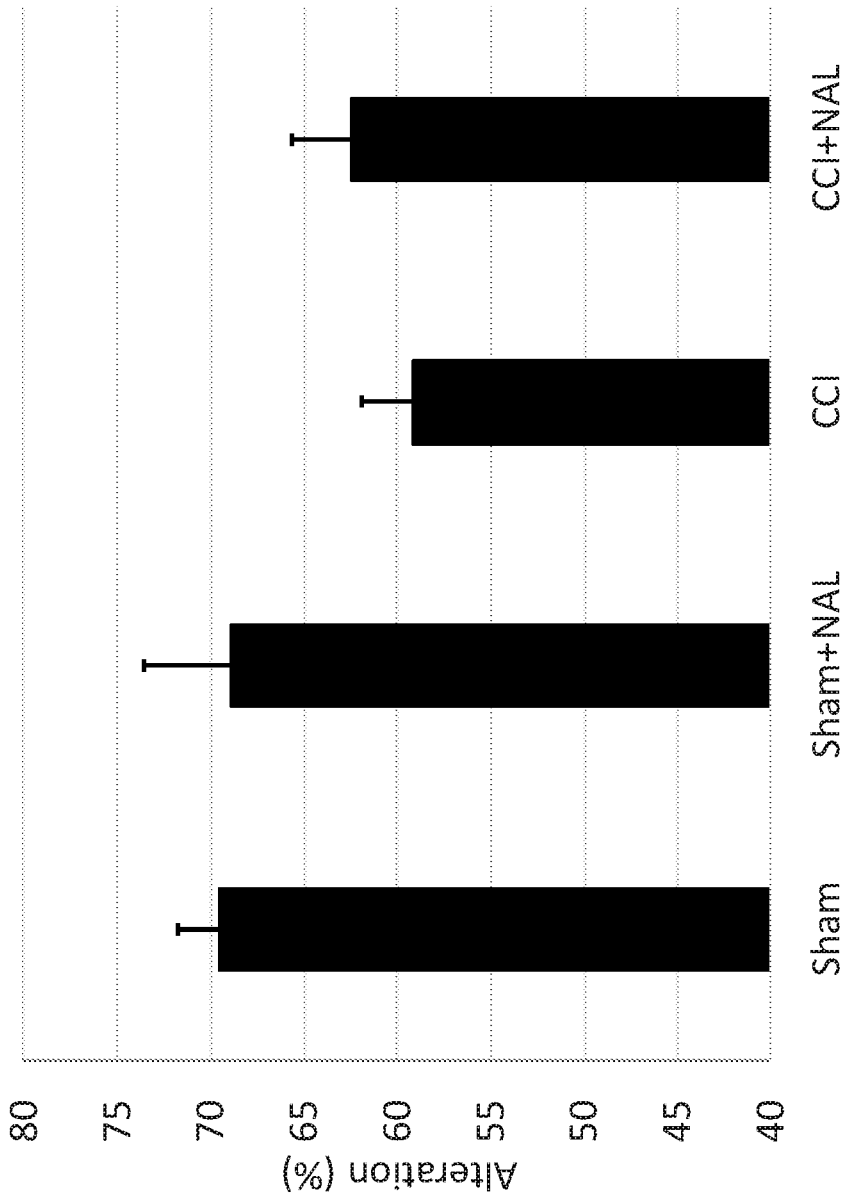


Fig. 50

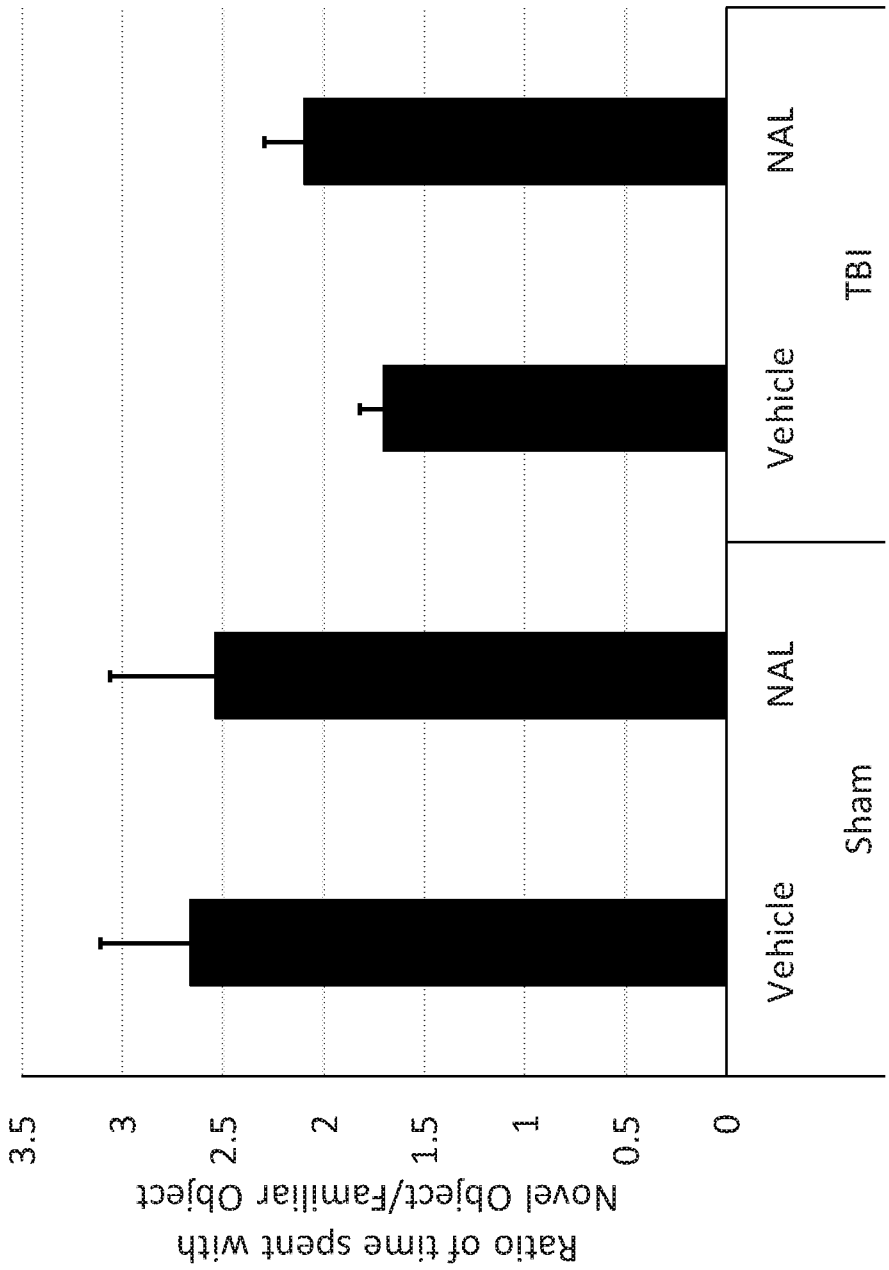

Ratio of time spent with
Novel Object/Familiar Object
3.5
3
2.5
2
1.5
1
0.5
0
Vehicle
NAL
Sham
Vehicle
NAL
TBI

Fig. 51