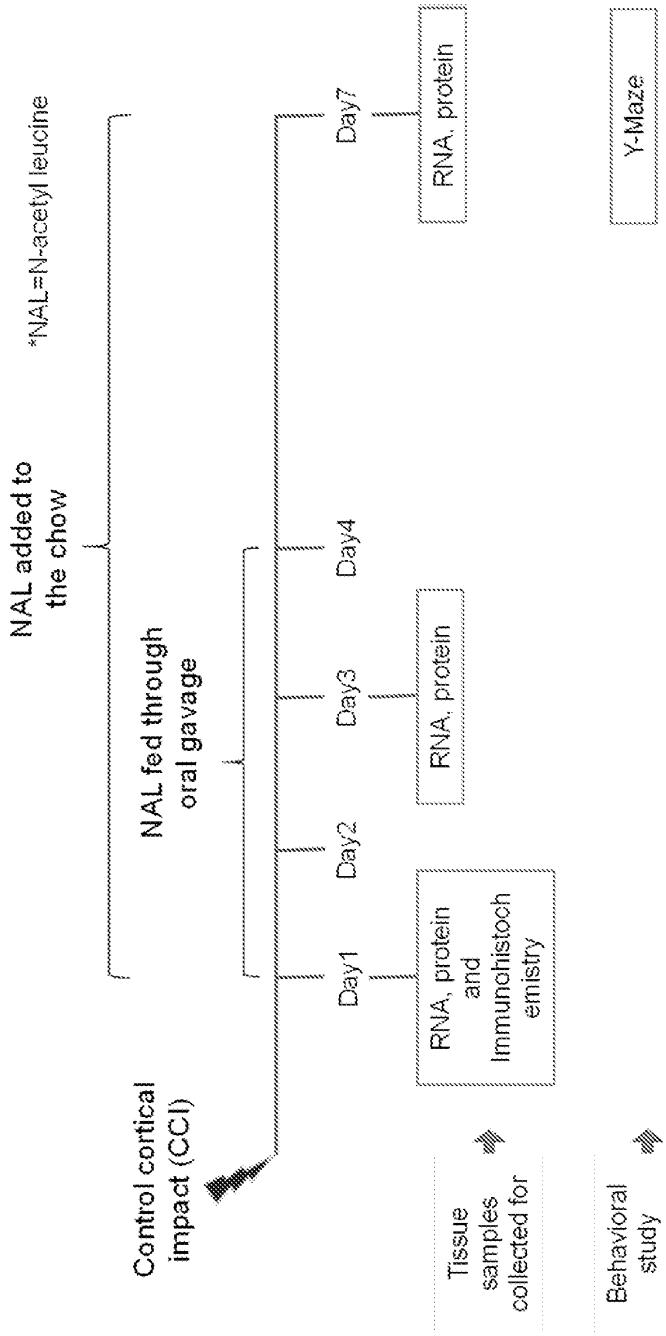

NAL added to the chow
*NAL=N-acetyl leucine
NAL fed through oral gavage
Control cortical impact (CCI)
Day1
Day2
Day3
Day4
Day7
RNA, protein and Immunohistoch emistry
RNA, protein
RNA, protein
Y-Maze
Tissue samples collected for
Behavioral study performed

Fig. 1

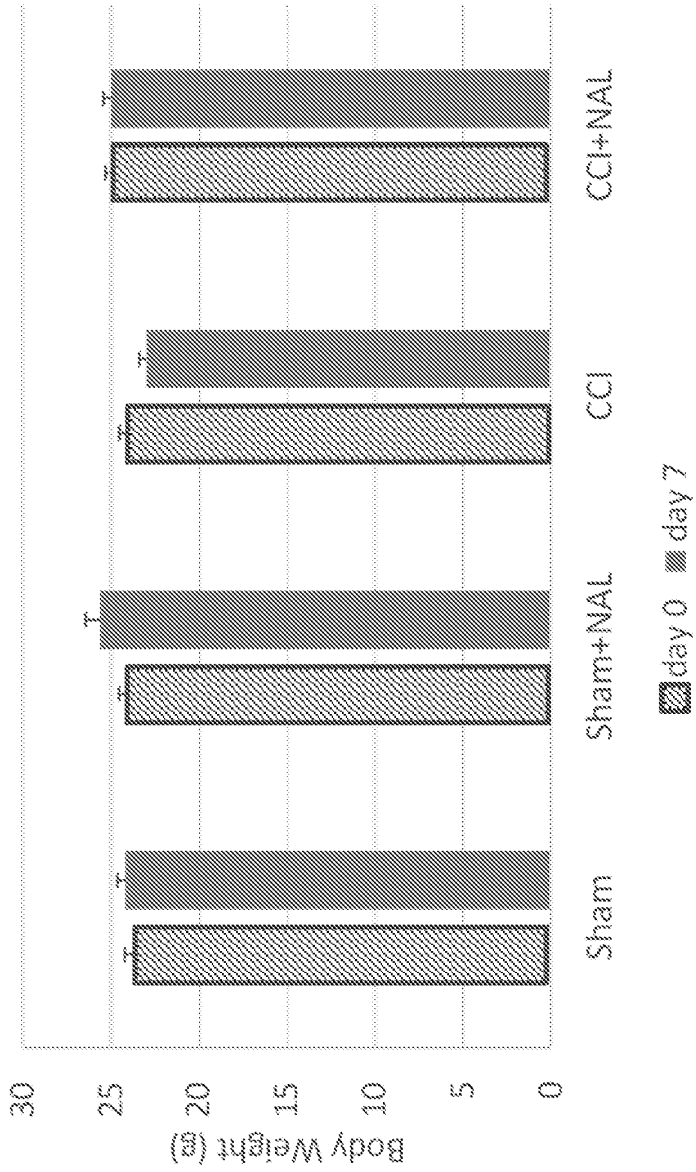

Body Weight (g)
30
25
20
15
10
5
0
Sham
Sham+NAL
CCI
CCI+NAL
day 0
day 7

Fig. 2

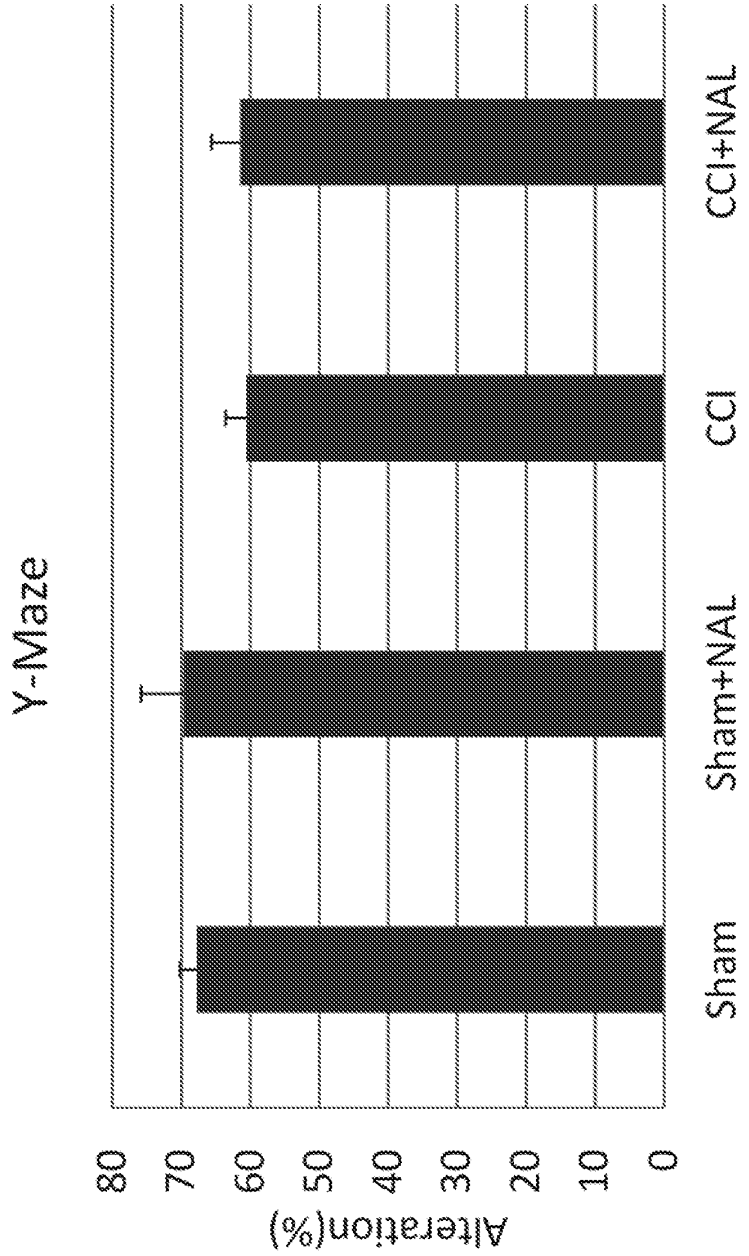

Y-Maze
Alteration(%)
80
70
60
50
40
30
20
10
0
Sham
Sham+NAL
CCI
CCI+NAL

Fig. 3

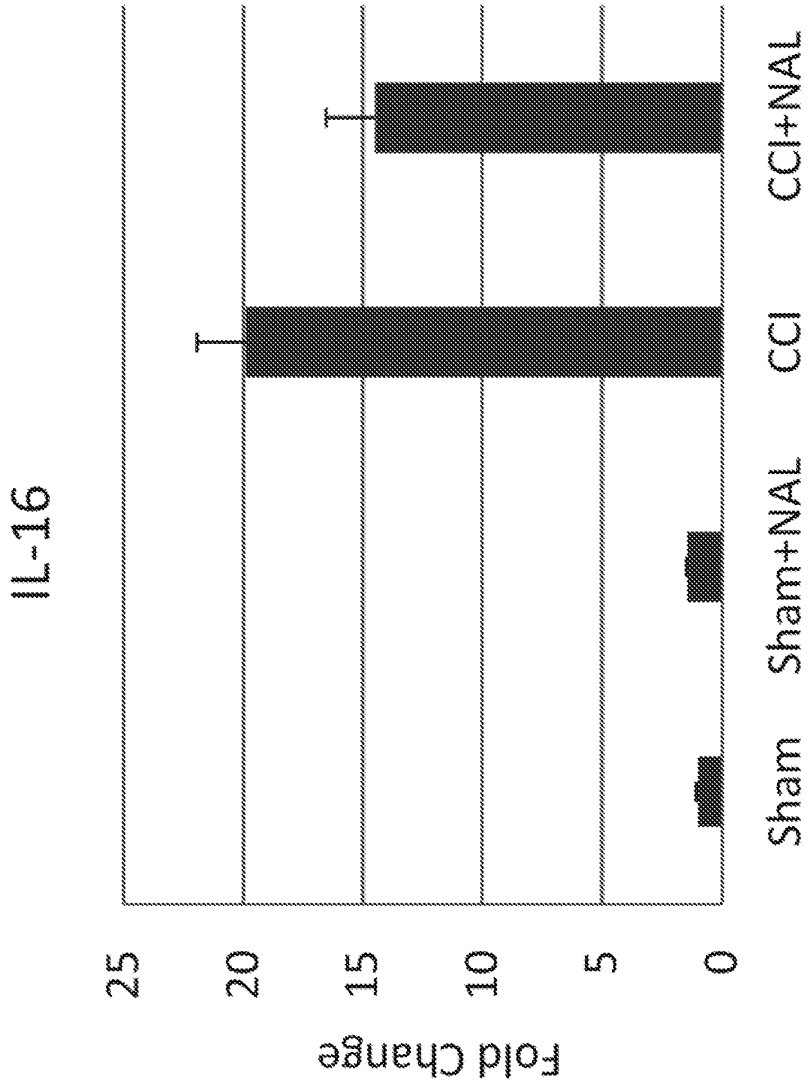


Fig. 4

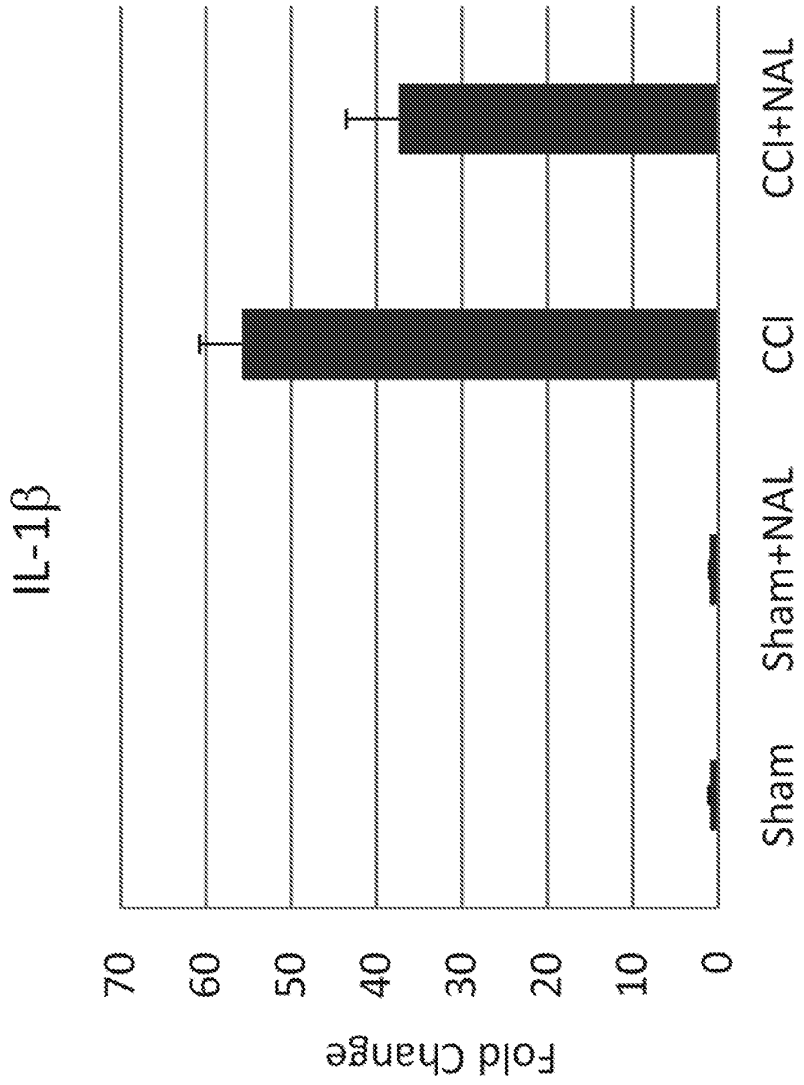


Fig. 5

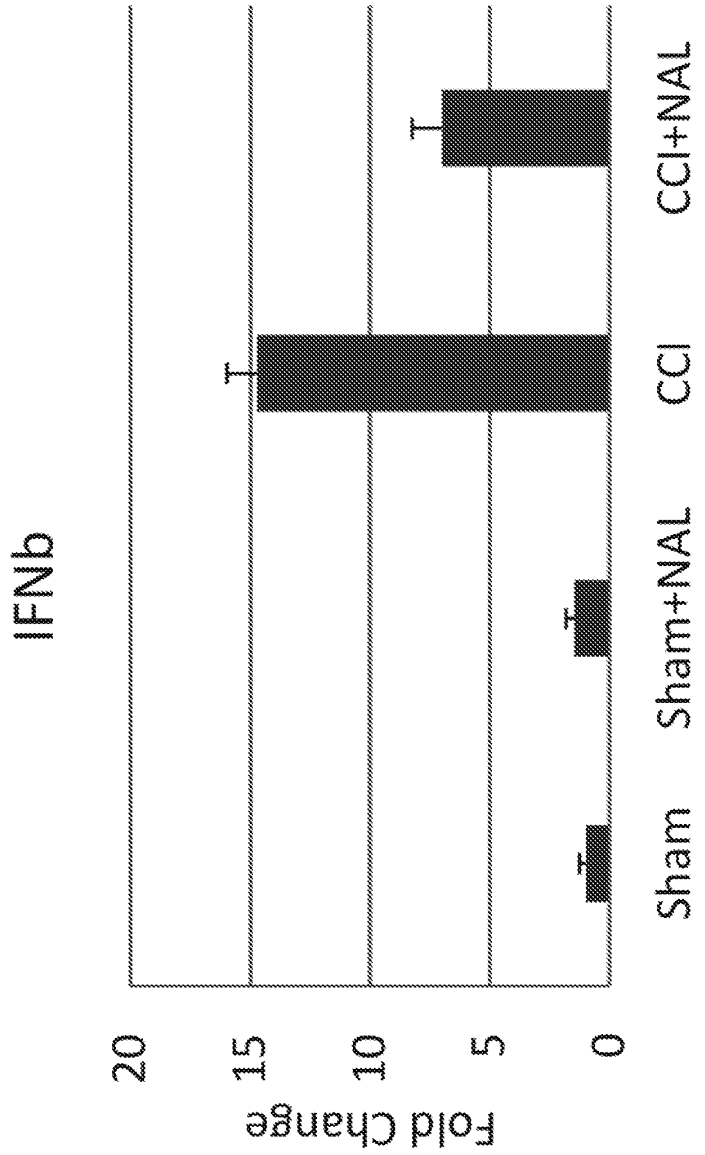


Fig. 6

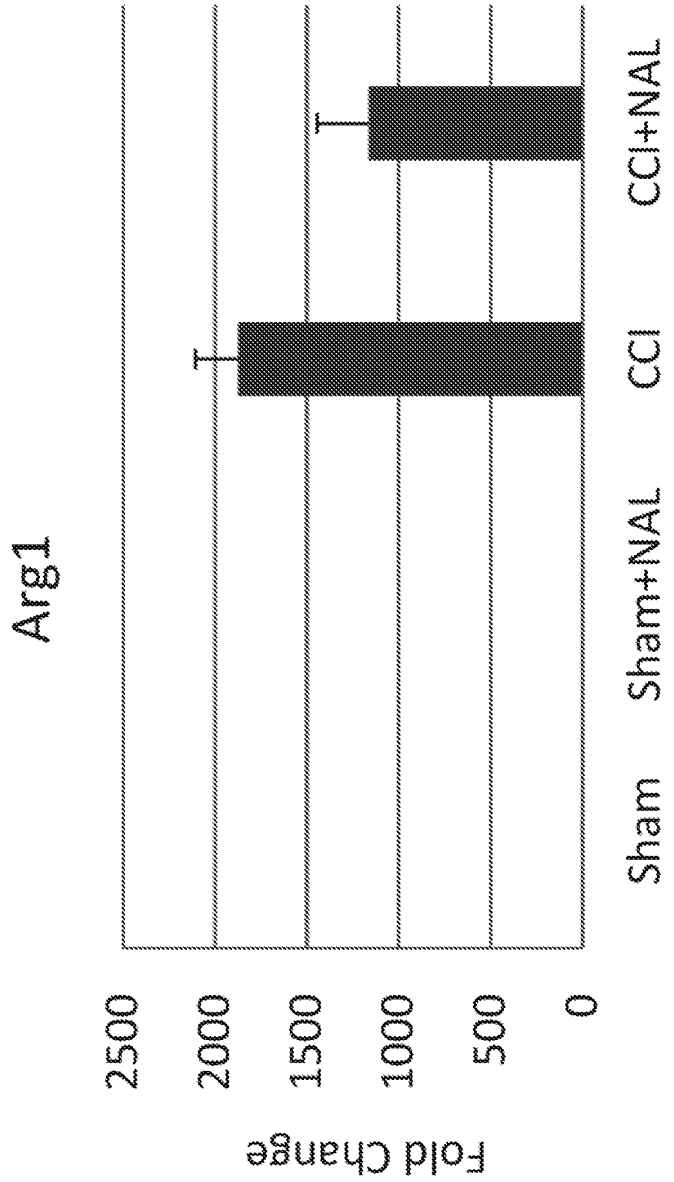

Arg1
Fold Change
2500
2000
1500
1000
500
0
Sham
Sham+NAL
CCI
CCI+NAL

Fig. 7

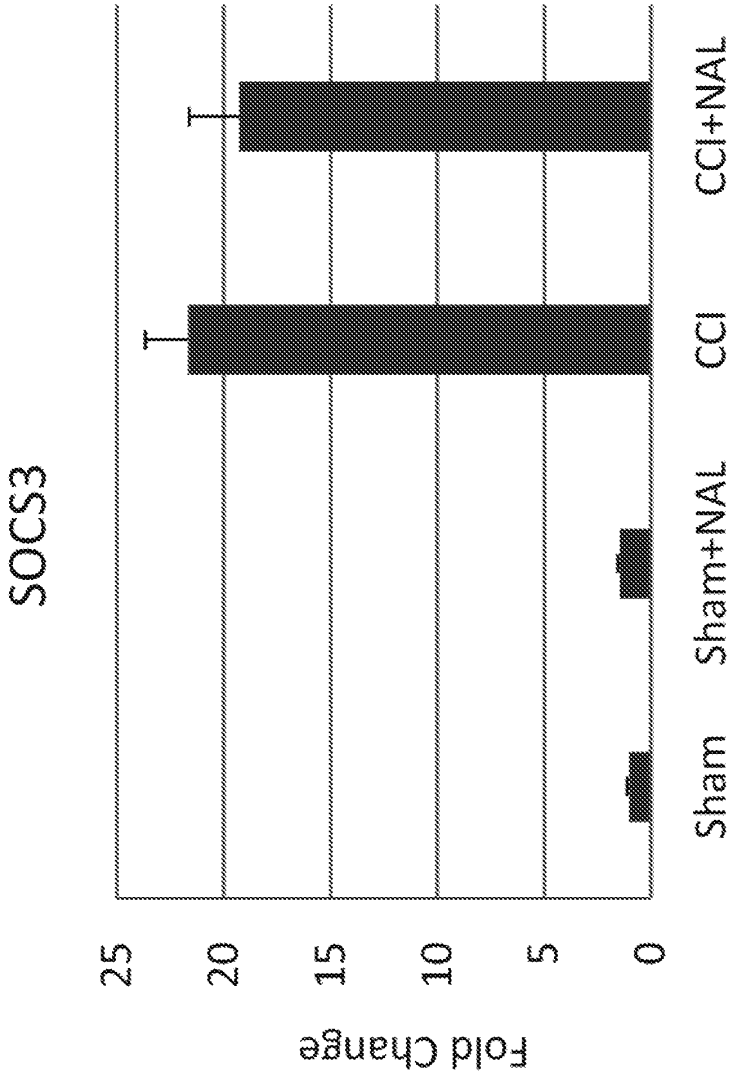


Fig. 8

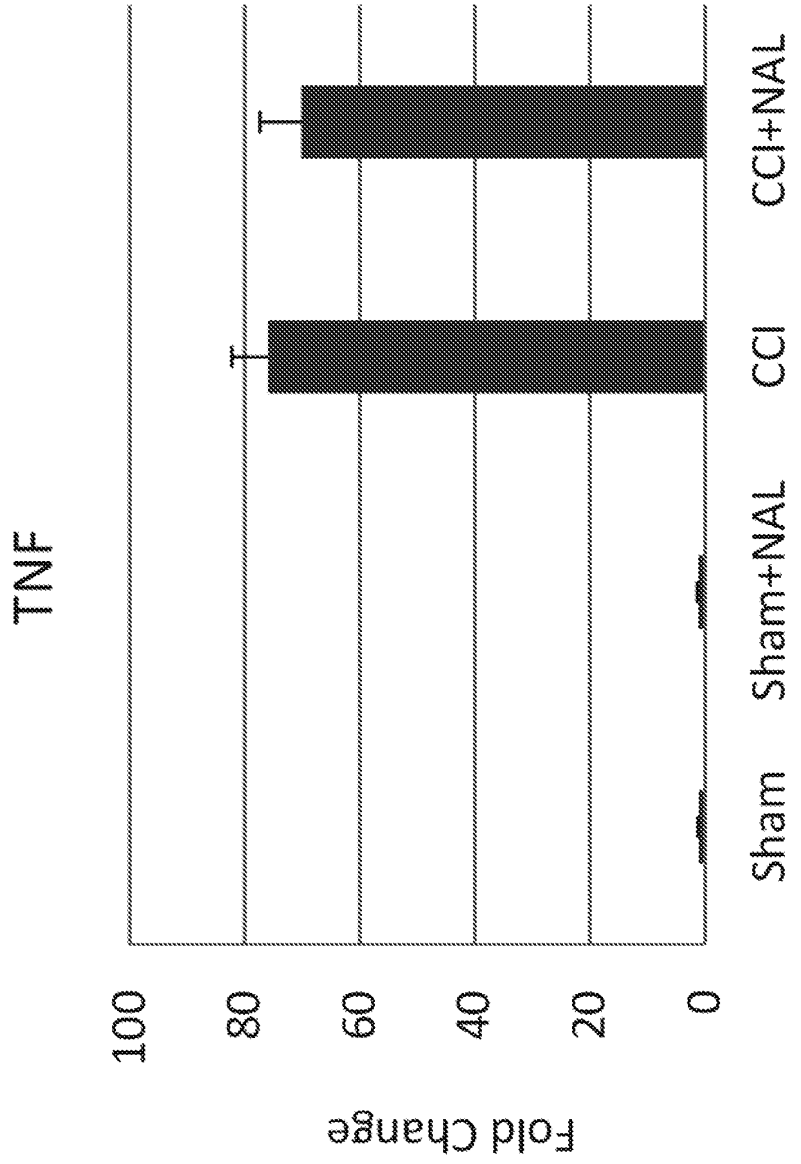


Fig. 9

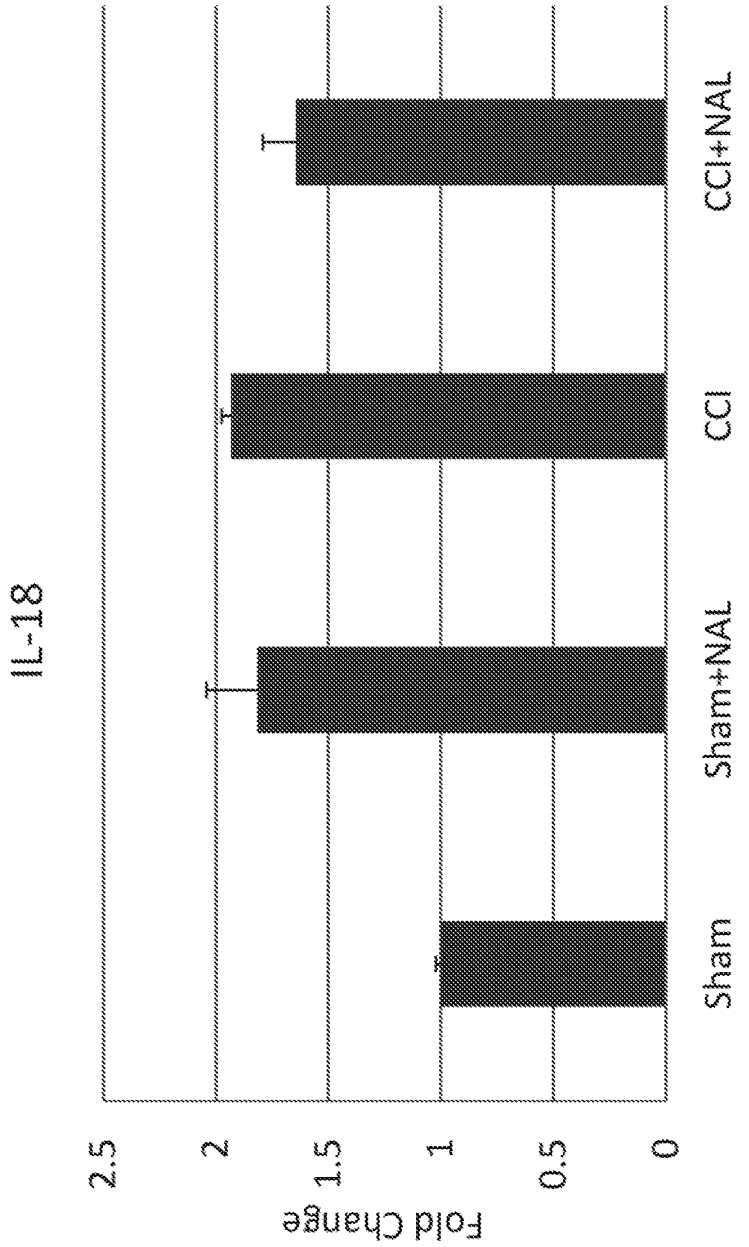


Fig. 10

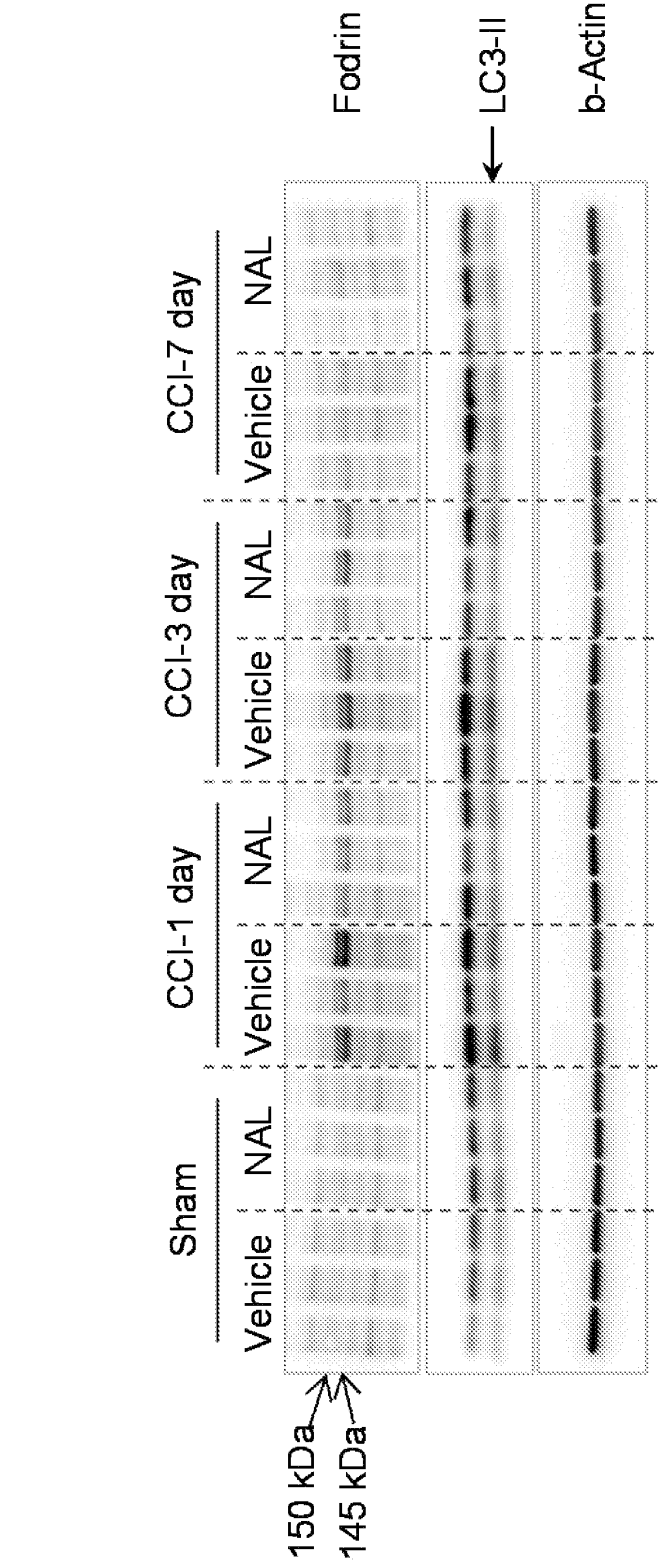

Fodrin
LC3-II
b-Actin
Sham
CCI-1 day
CCI-3 day
CCI-7 day
Vehicle
NAL
150 kDa
145 kDa

Fig. 11

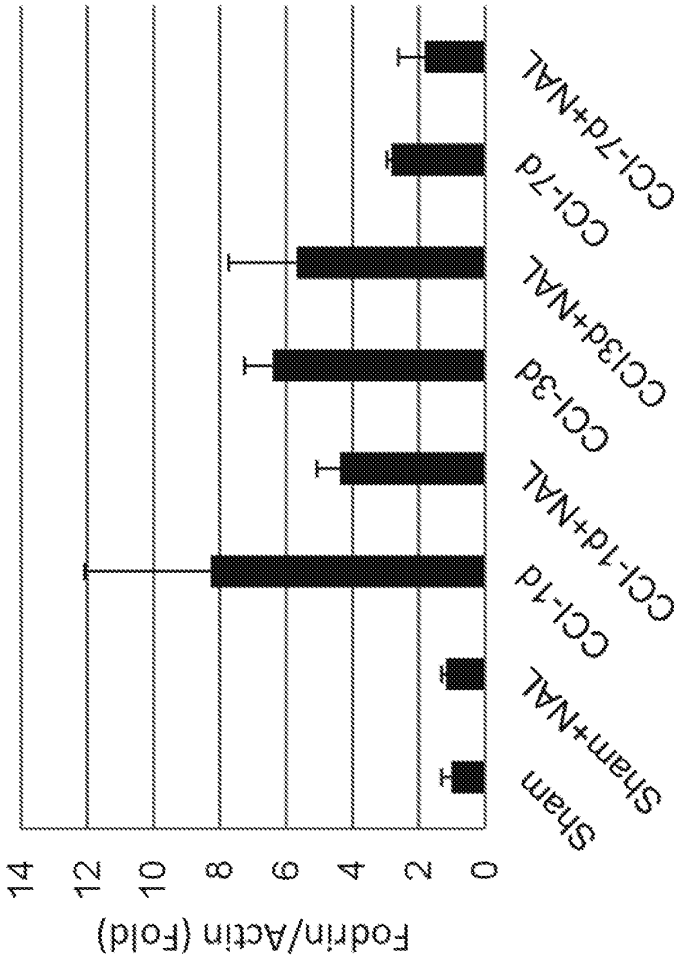

Sham
Sham+NAL
CCI-1d
CCI-1d+NAL
CCI-3d
CCI3d+NAL
CCI-7d
CCI-7d+NAL
0
2
4
6
8
10
12
14
Fodrin/Actin (Fold)

Fig. 12

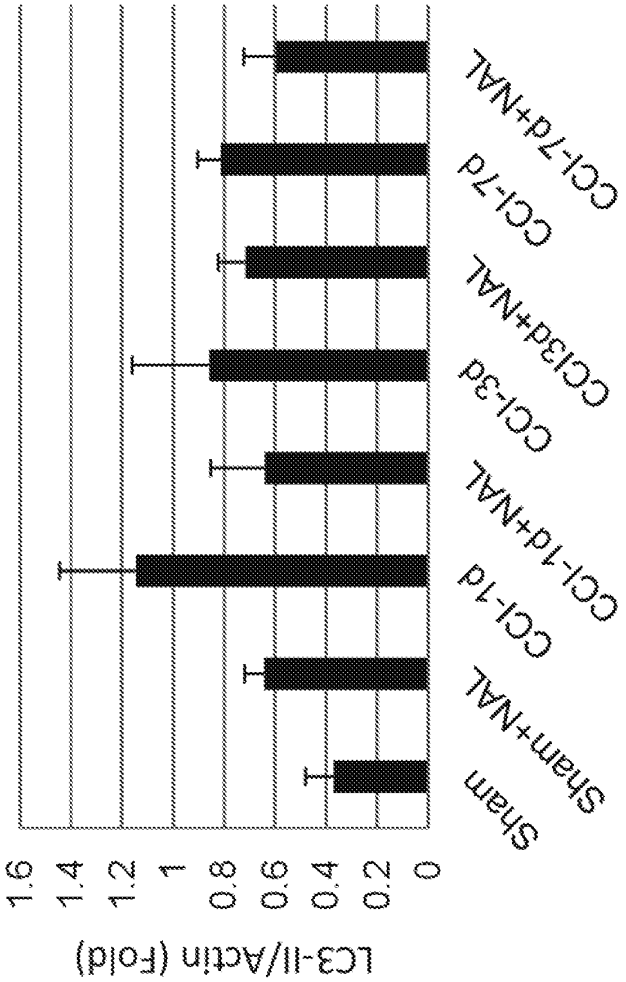

LC3-II/Actin (Fold)
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
Sham
Sham+NAL
CCl-1d
CCl-1d+NAL
CCl-3d
CCl3d+NAL
CCl-7d
CCl-7d+NAL

Fig. 13

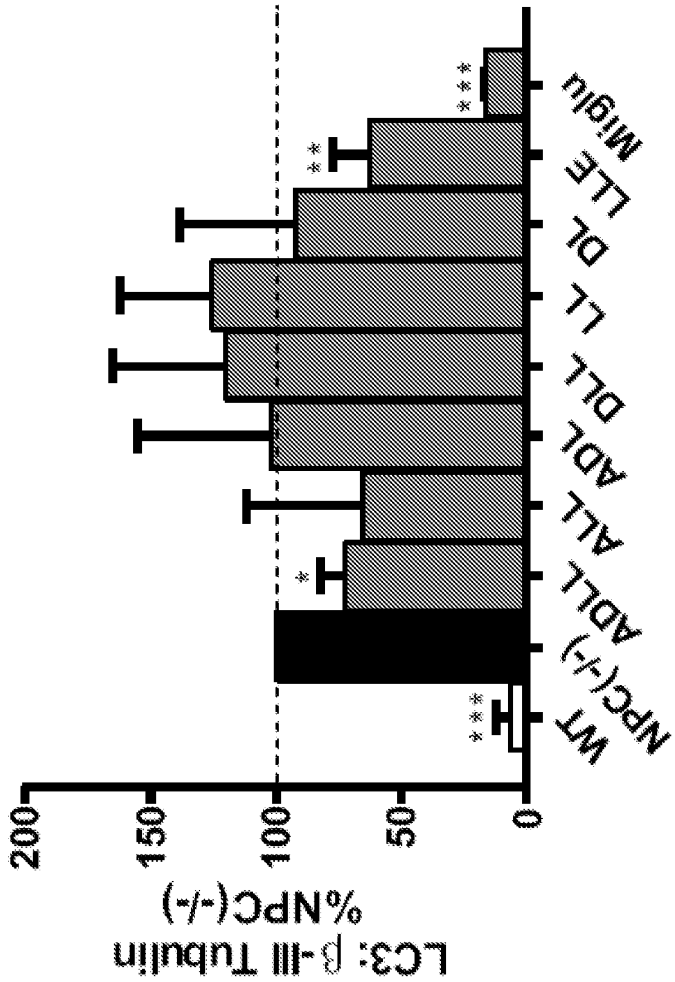

LC3: β-III Tubulin
%NPC(-/-)
200
150
100
50
0
WT
NPC(-/-)
ADLL
ALL
ADL
DLL
LL
DL
LLE
Miglu
***
**
*
***

Fig. 14

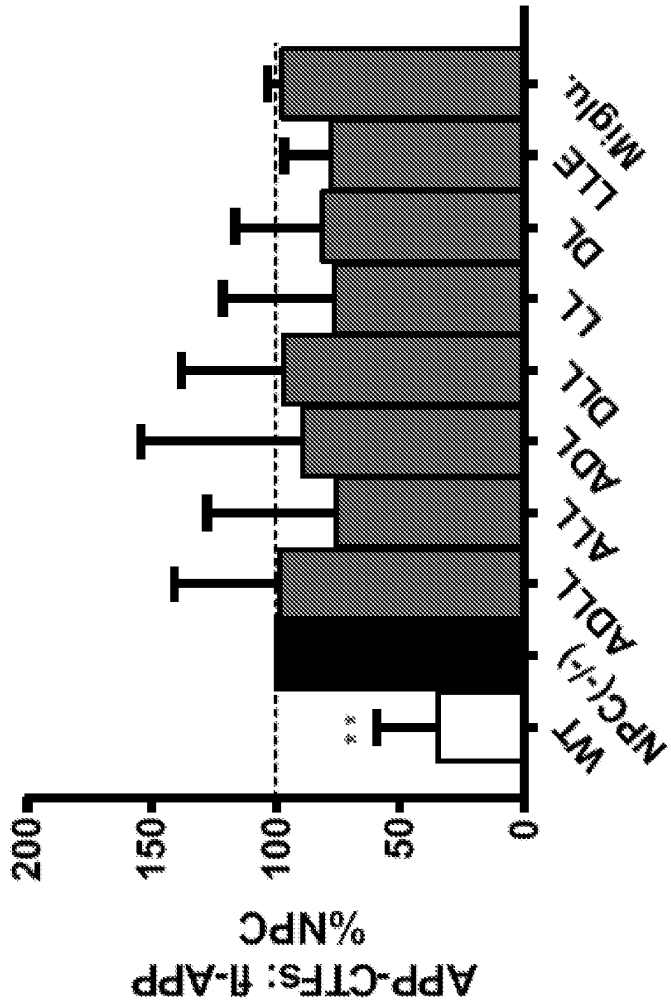

APP-CTFs: fl-APP
%NPC
200
150
100
50
0
**
WT
NPC(-/-)
ADLL
ALL
ADL
DLL
LL
DL
LLE
Miglu

Fig. 15

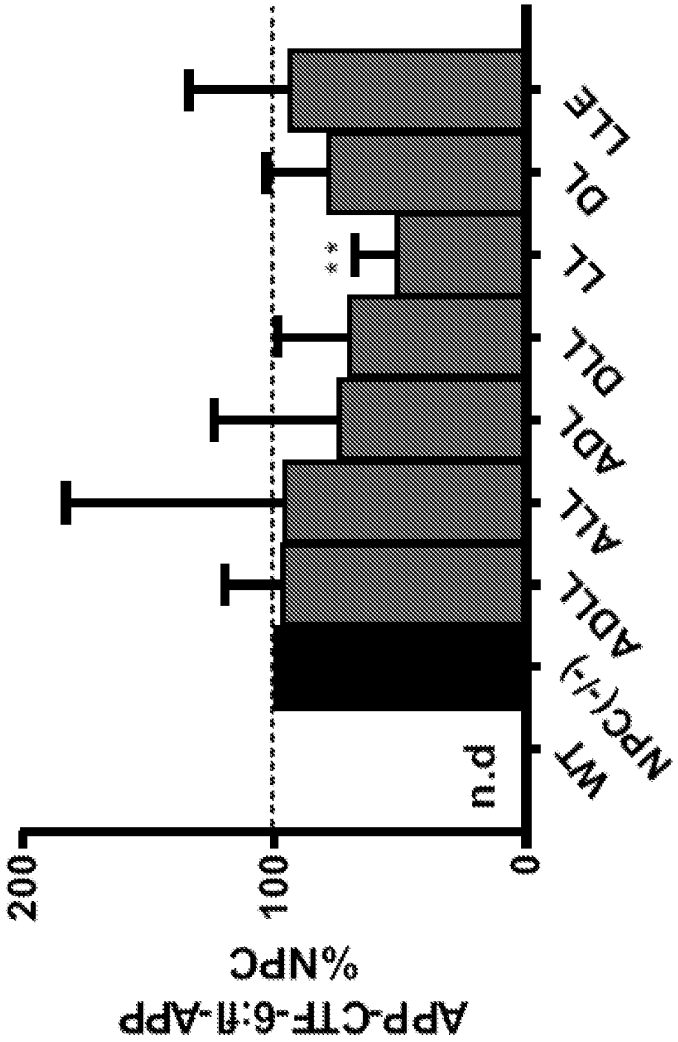


Fig. 16

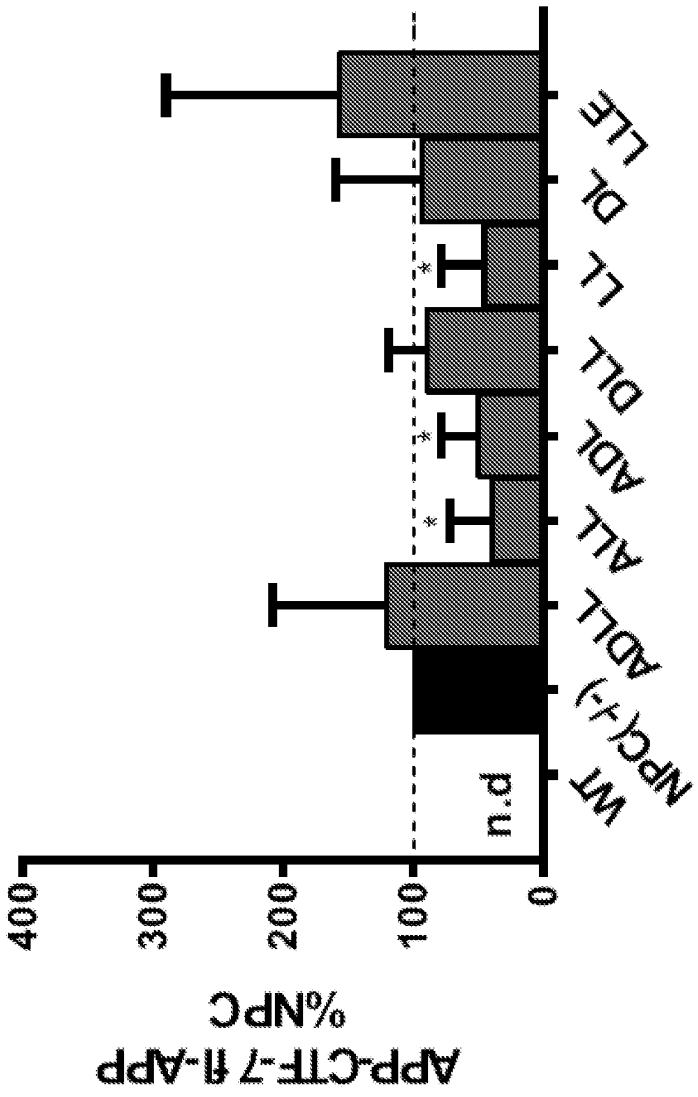

APP-CTF-γ /β-APP
%NPC
400
300
200
100
0
n.d
WT
NPC(-/-)
ADLL
ALL
ADL
DLL
LL
DL
LLE
*
*
*

Fig. 17

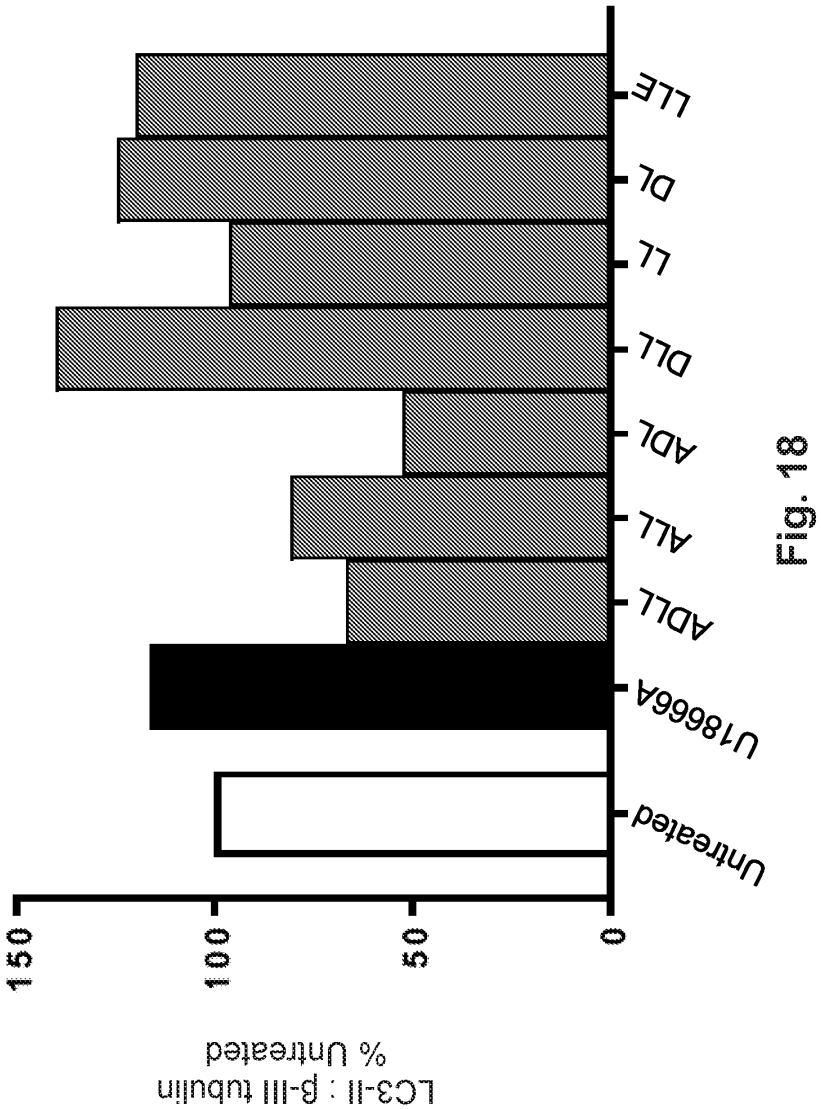

LC3-II : β-III tubulin
% Untreated
150
100
50
0
Untreated
U18666A
ADLL
ALL
ADL
DLL
LL
DL
LLE

Fig. 18

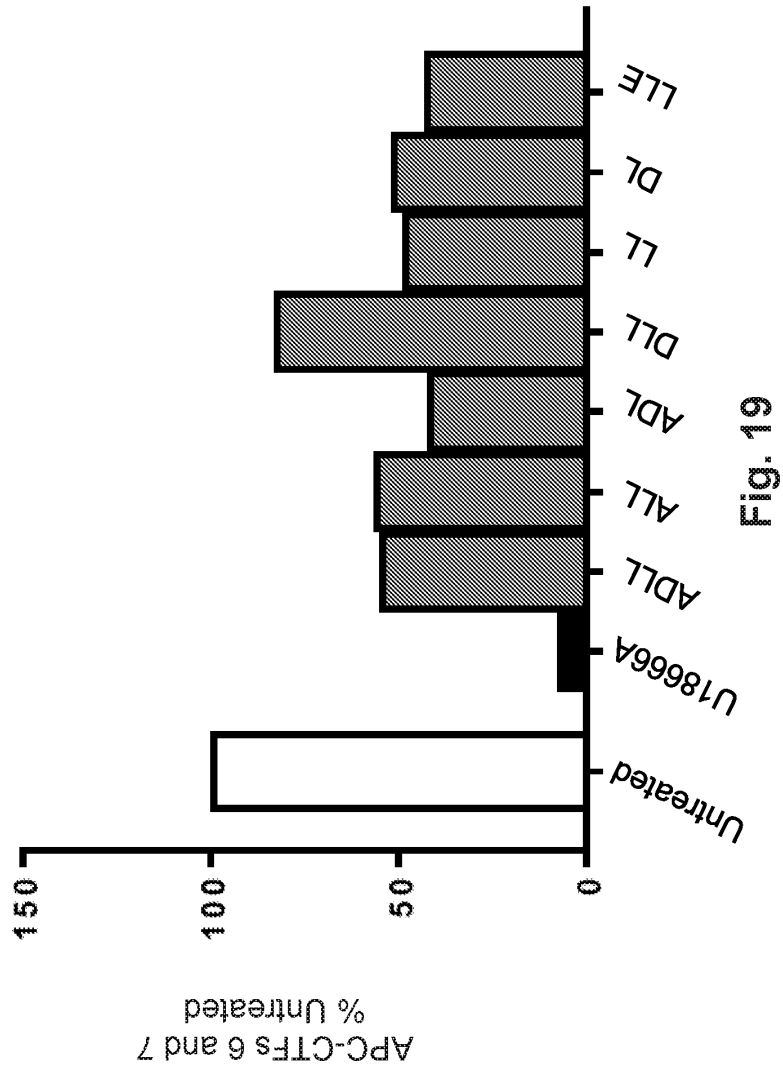

APC-CTFs 6 and 7
% Untreated
150
100
50
0
Untreated
U18666A
ADLL
ALL
ADL
DLL
LL
DL
LLE

Fig. 19

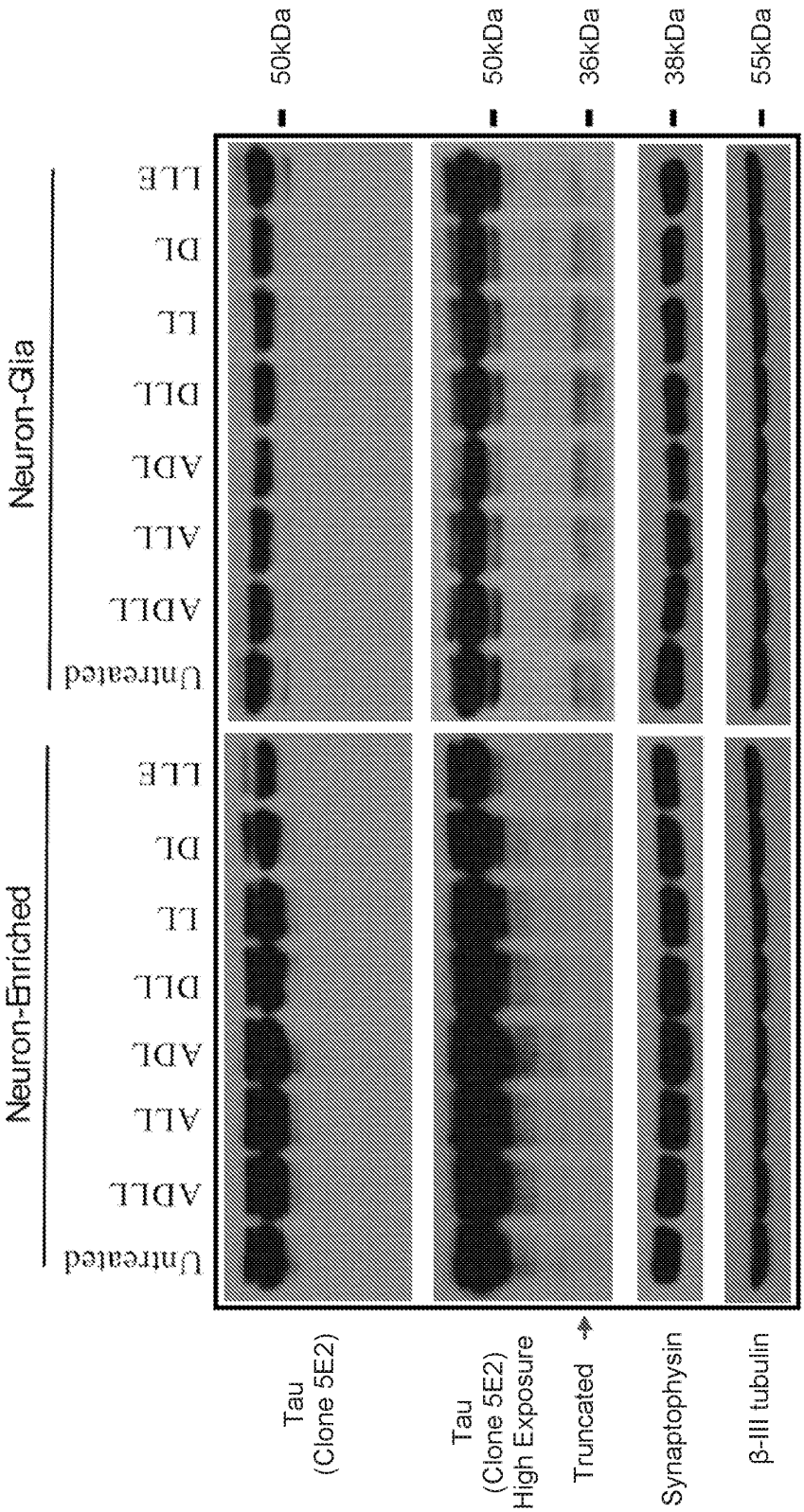

50kDa
50kDa
36kDa
38kDa
55kDa
Neuron-Glia
Neuron-Enriched
Untreated
ADLL
ALL
ADL
DLL
LL
DL
LLE
Tau (Clone 5E2)
Tau (Clone 5E2) High Exposure
Truncated
Synaptophysin
β-III tubulin

Fig. 20

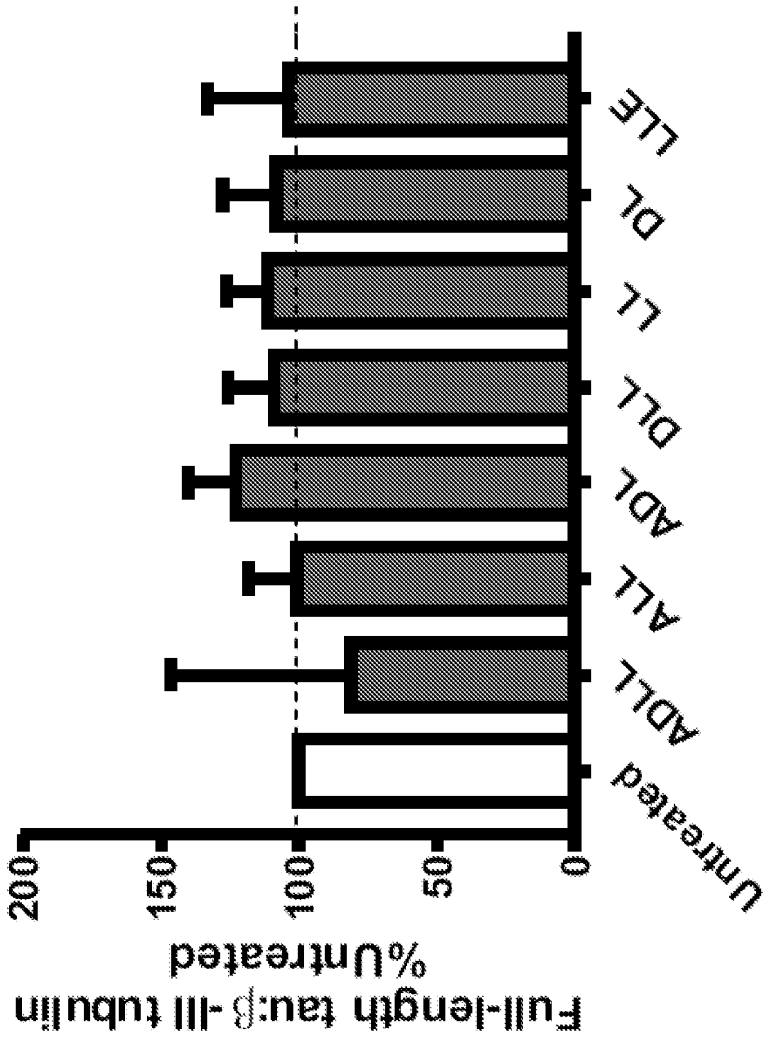

Full-length tau:β-III tubulin
%Untreated
200
150
100
50
0
Untreated
ADLL
ALL
ADL
DLL
LL
DL
LLE

Fig. 21

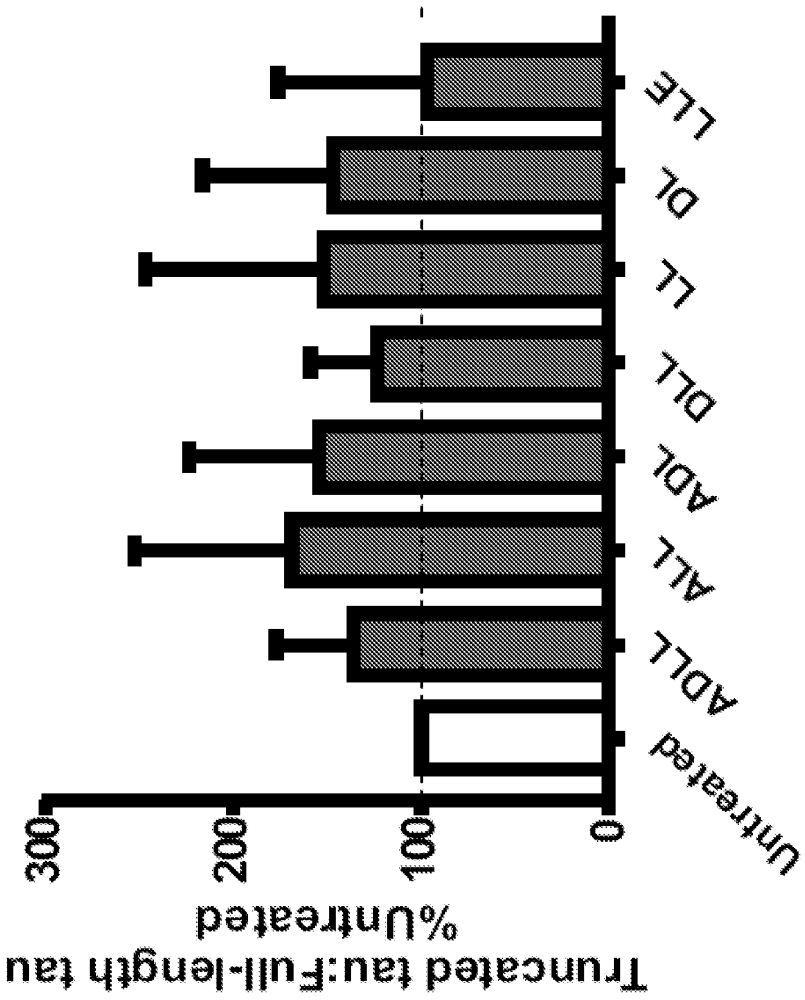

Truncated tau:Full-length tau
%Untreated
300
200
100
0
Untreated
ADLL
ALL
ADL
DLL
LL
DL
LLE

Fig. 22

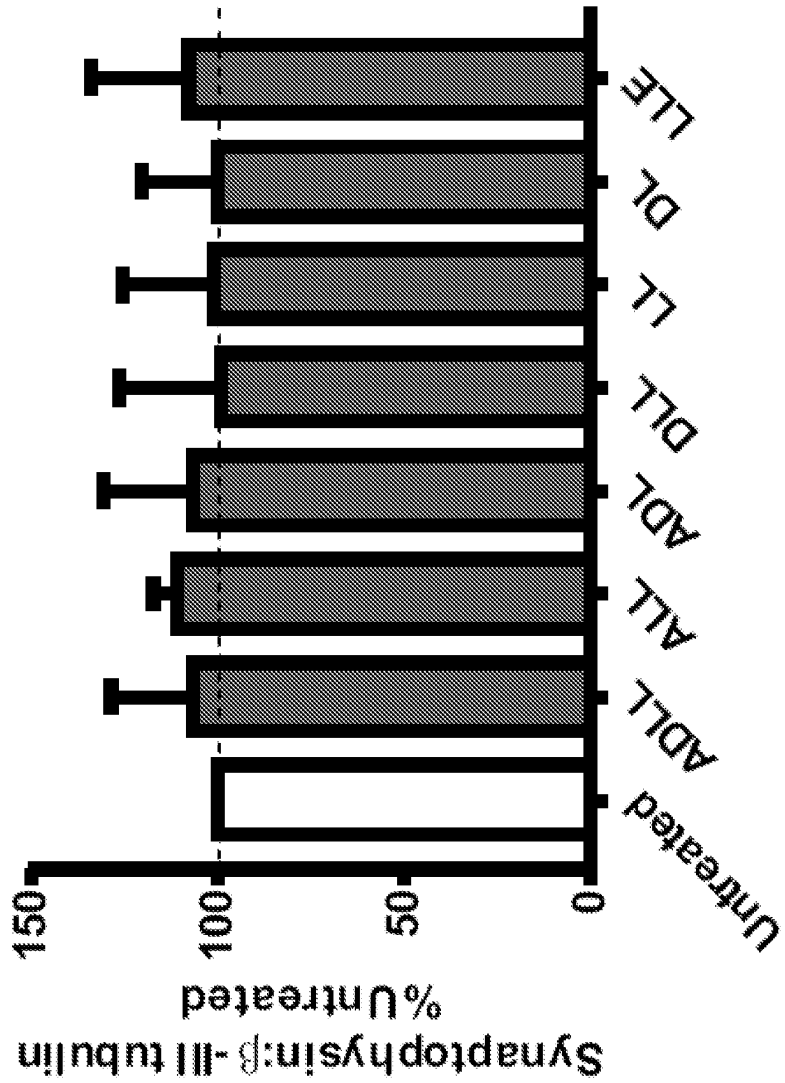

Synaptophysin:β-III tubulin
% Untreated
150
100
50
0
Untreated
ADLL
ALL
ADL
DLL
LL
DL
LLE

Fig. 23

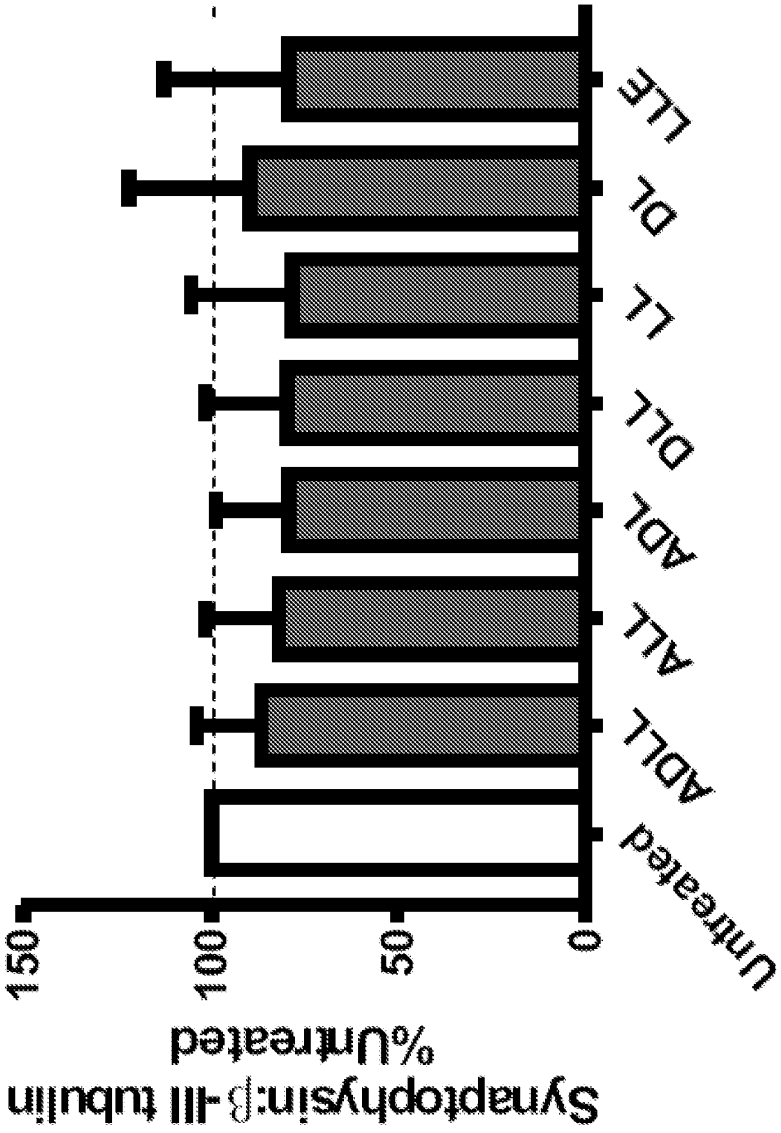

Synaptophysin:β-III tubulin
%Untreated
150
100
50
0
Untreated
ADLL
ALL
ADL
DLL
LL
DL
LLE

Fig. 24

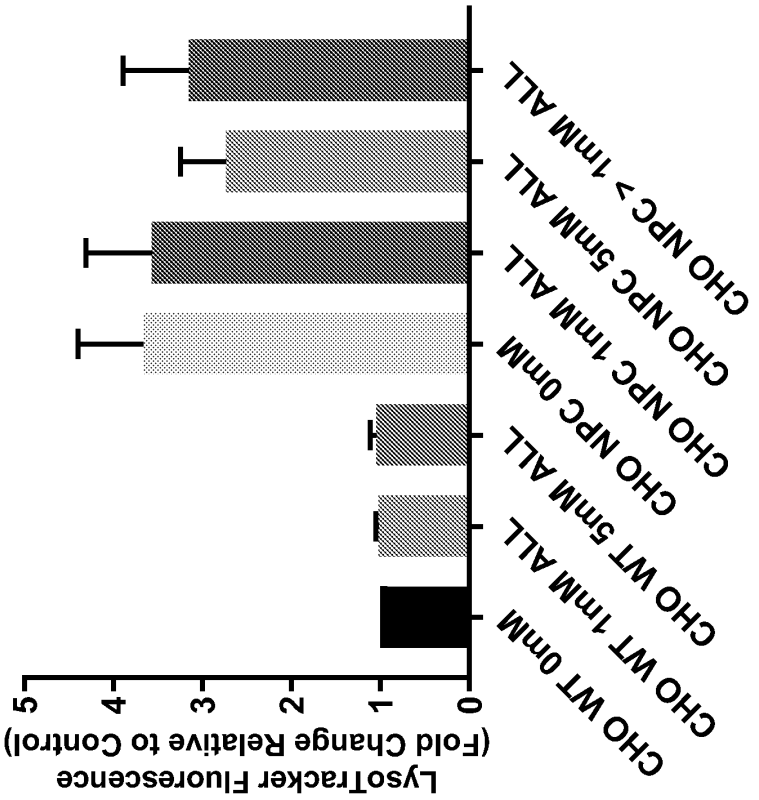

LysoTracker Fluorescence
(Fold Change Relative to Control)
0
1
2
3
4
5
CHO WT 0mM
CHO WT 1mM ALL
CHO WT 5mM ALL
CHO NPC 0mM
CHO NPC 1mM ALL
CHO NPC 5mM ALL
CHO NPC > 1mM ALL

Fig. 25

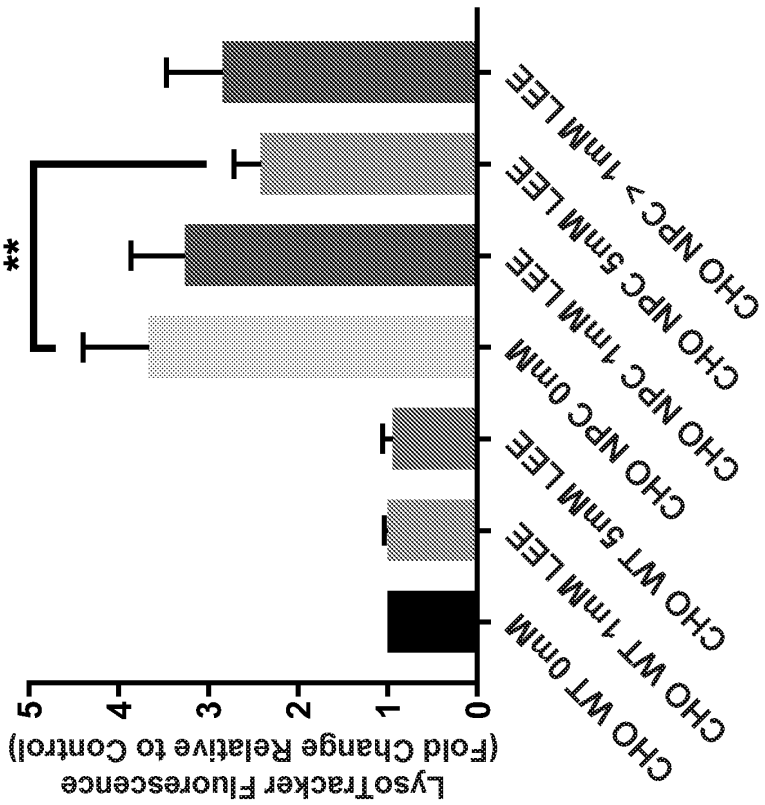

LysoTracker Fluorescence
(Fold Change Relative to Control)
0
1
2
3
4
5
**
CHO WT 0mM
CHO WT 1mM LEE
CHO WT 5mM LEE
CHO NPC 0mM
CHO NPC 1mM LEE
CHO NPC 5mM LEE
CHO NPC > 1mM LEE

Fig. 26

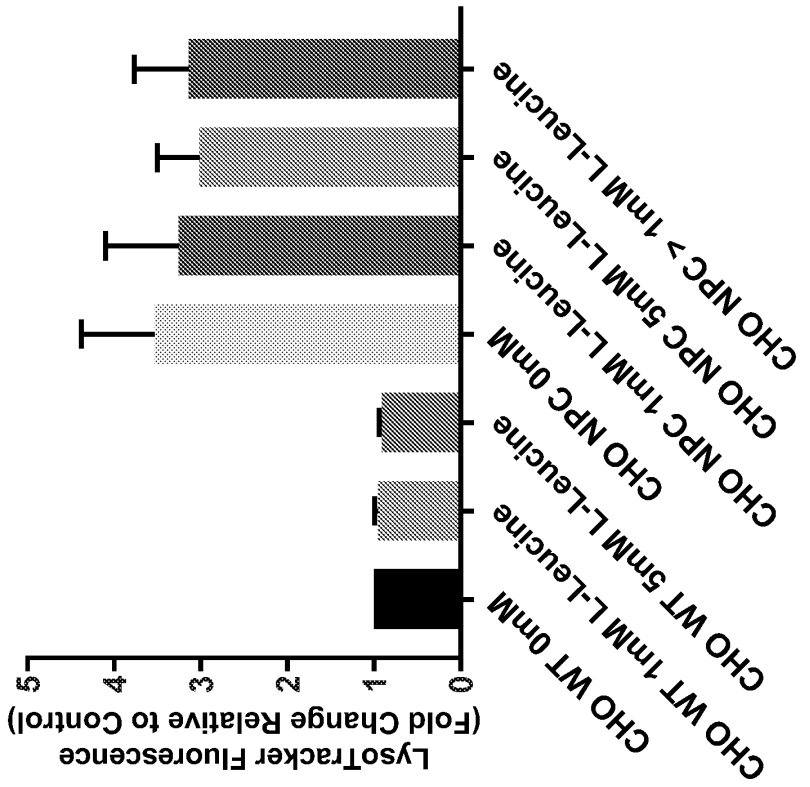

LysoTracker Fluorescence
(Fold Change Relative to Control)
0
1
2
3
4
5
CHO WT 0mM L-Leucine
CHO WT 1mM L-Leucine
CHO WT 5mM L-Leucine
CHO NPC 0mM L-Leucine
CHO NPC 1mM L-Leucine
CHO NPC 5mM L-Leucine
CHO NPC > 1mM L-Leucine

Fig. 27

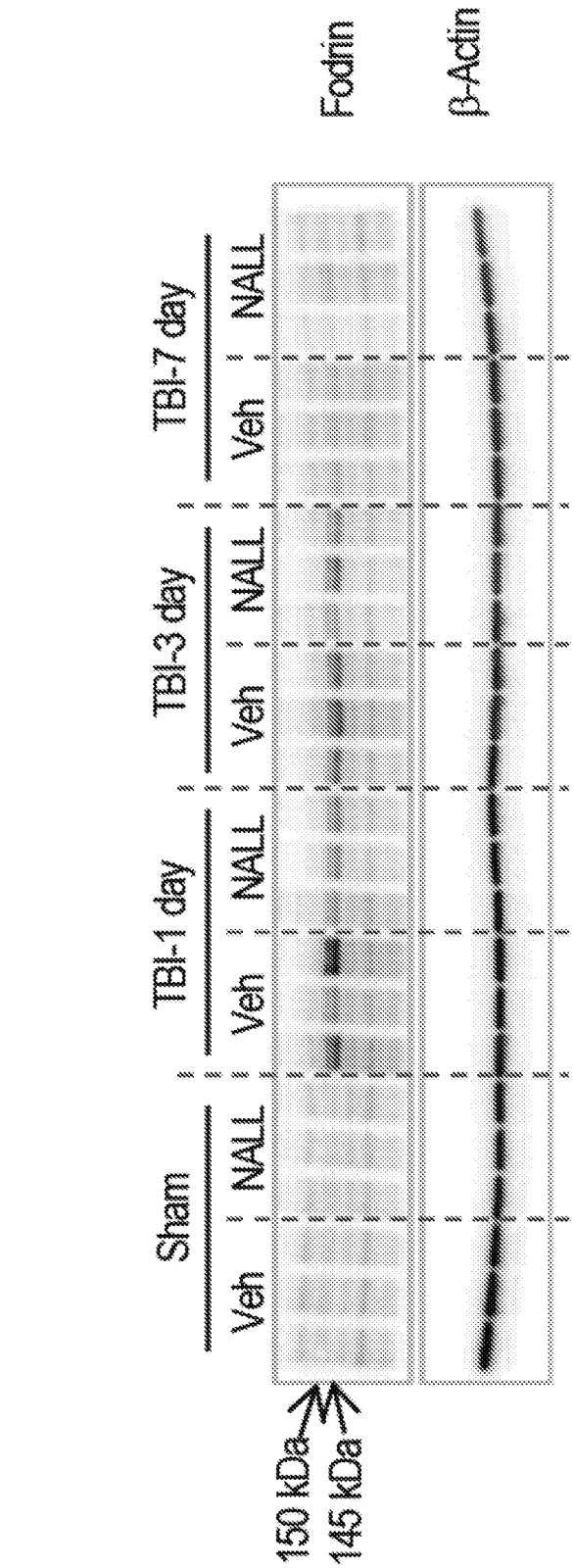

Fodrin
β-Actin
Sham
TBI-1 day
TBI-3 day
TBI-7 day
Veh
NALL
Veh
NALL
Veh
NALL
Veh
NALL
150 kDa
145 kDa

Fig. 28

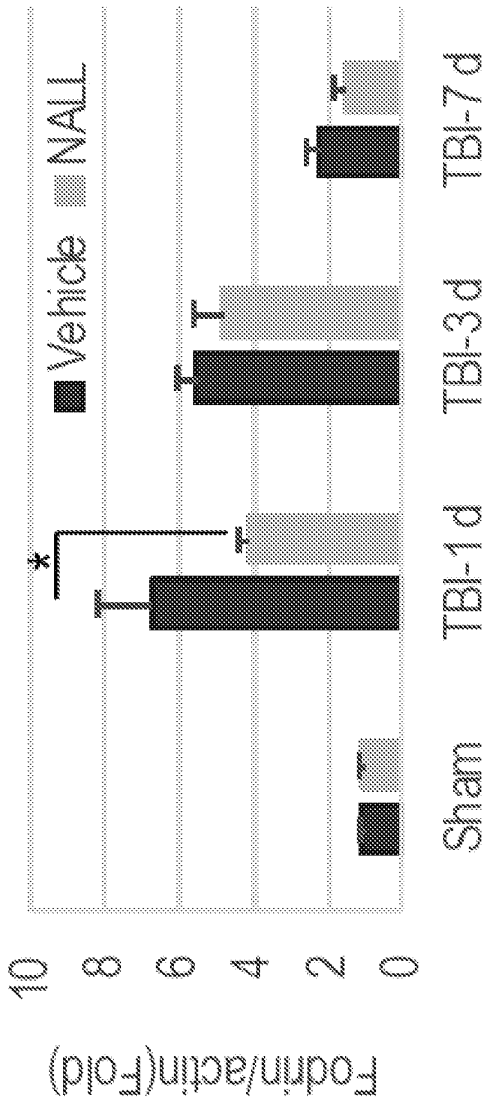

Vehicle
NALL
Sham
TBI-1 d
TBI-3 d
TBI-7 d
*
10
8
6
4
2
0
Fodrin/actin(Fold)

Fig. 29

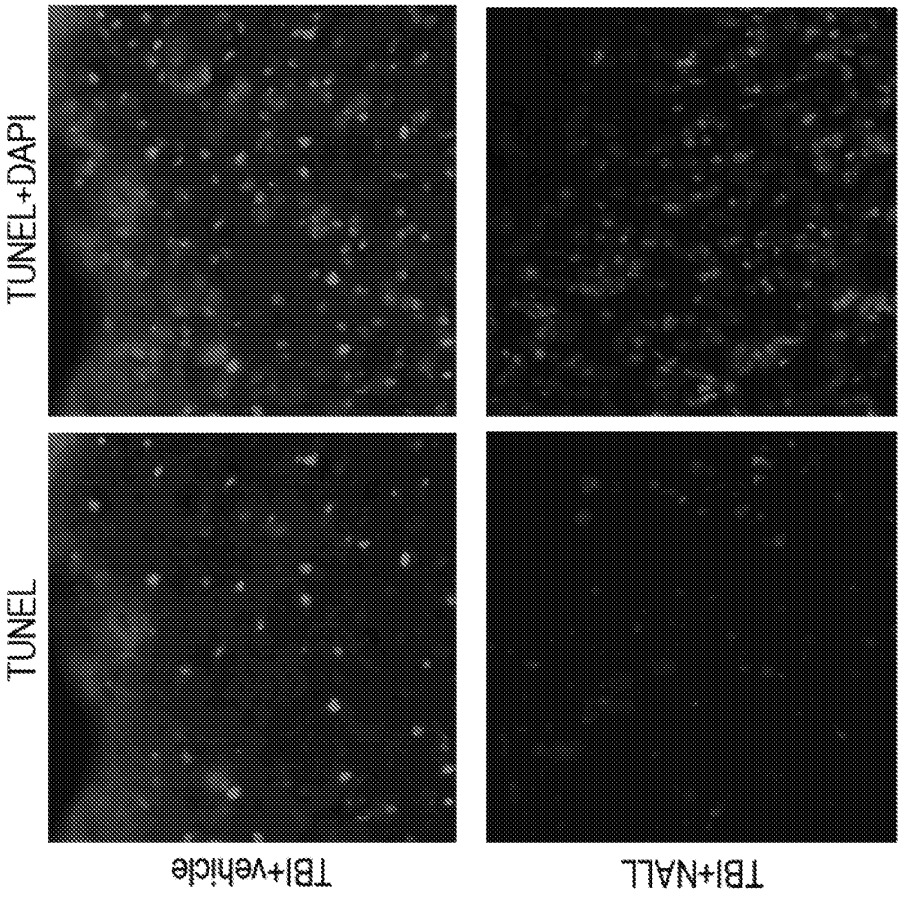


Fig. 30

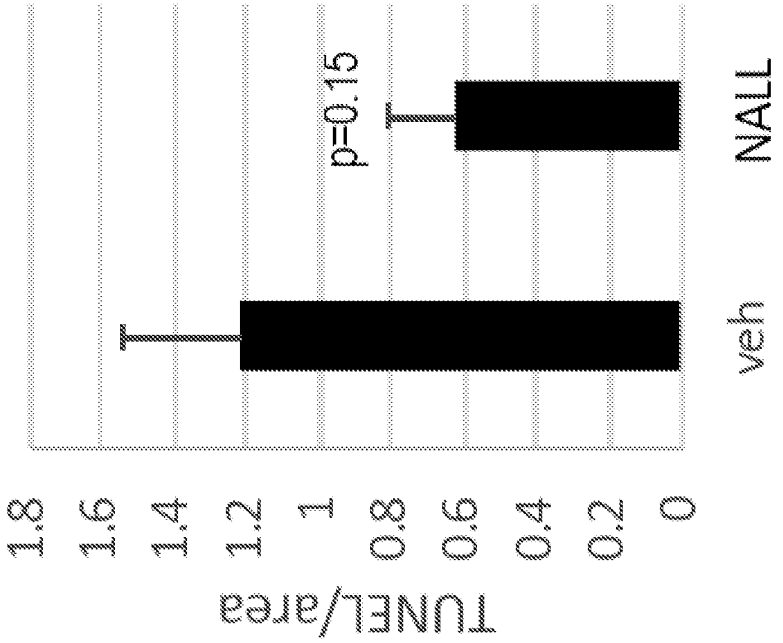


Fig. 31

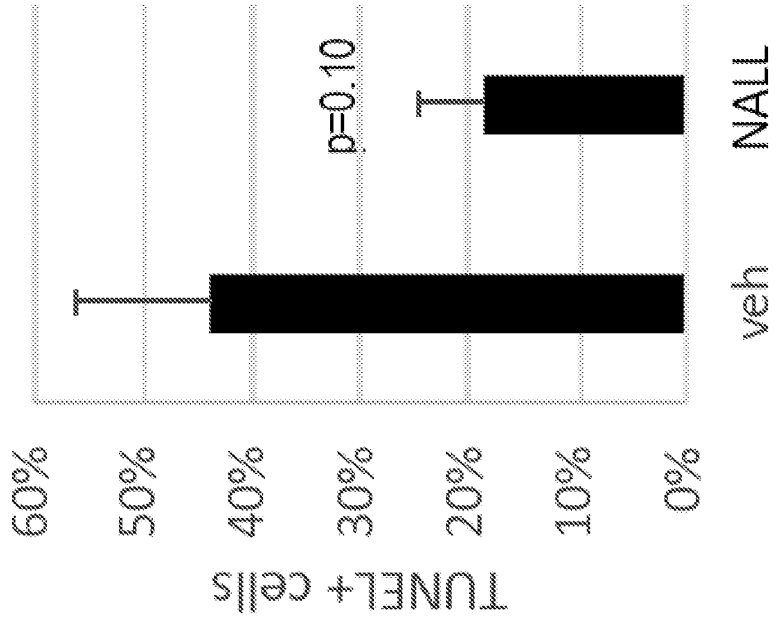


Fig. 32

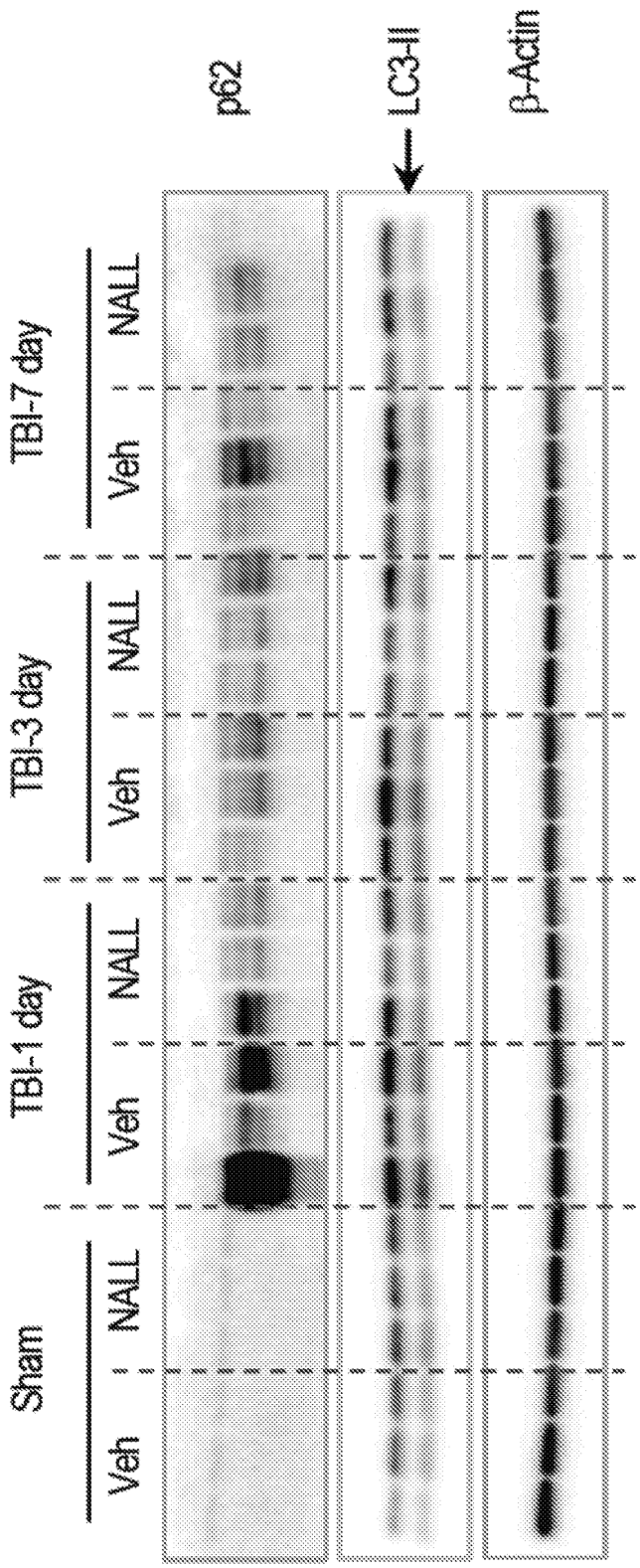

p62
LC3-II
β-Actin
Sham
Veh
NALL
TBI-1 day
Veh
NALL
TBI-3 day
Veh
NALL
TBI-7 day
Veh
NALL

Fig. 33

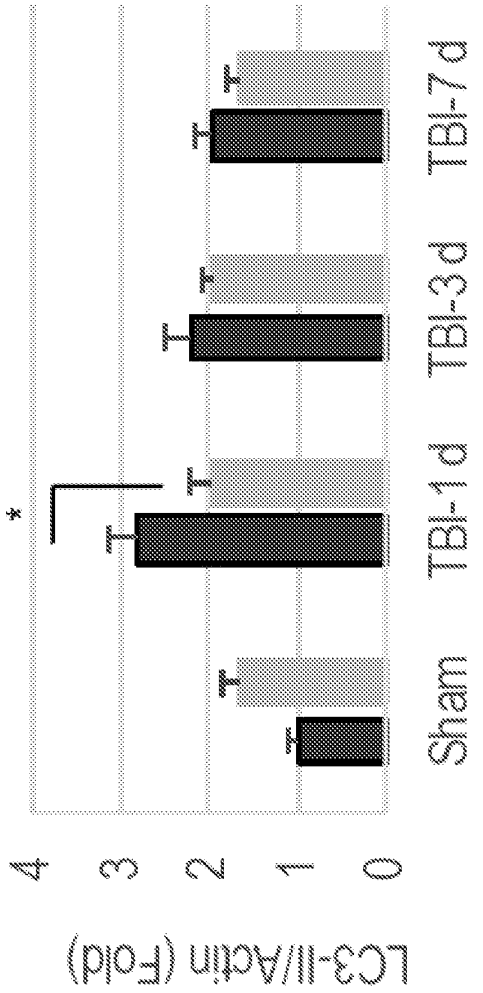


Fig. 34

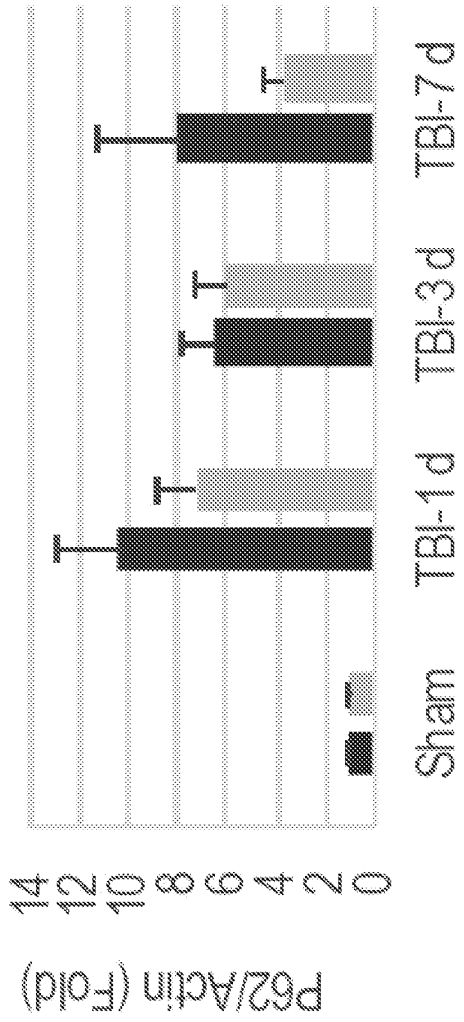

P62/Actin (Fold)
0
2
4
6
8
10
12
14
Sham
TBI-1d
TBI-3d
TBI-7d
Vehicle
NALL

Fig. 35

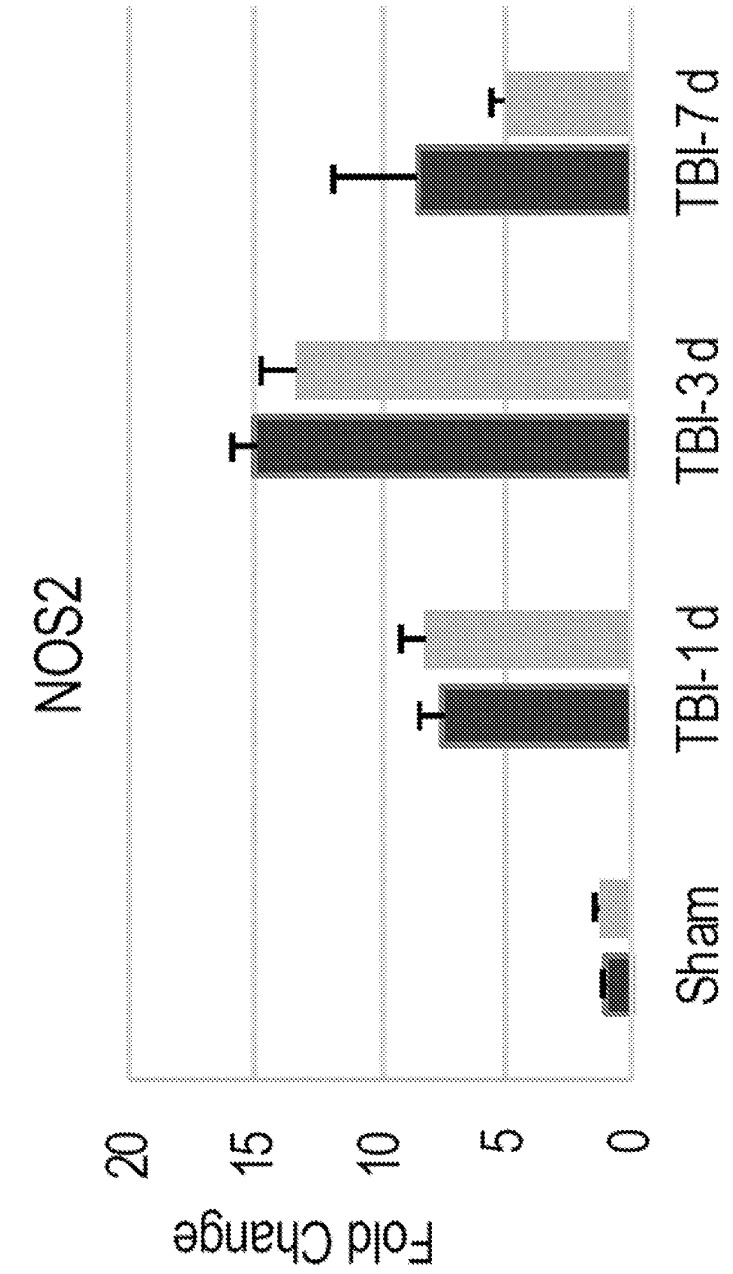

NOS2
Fold Change
20
15
10
5
0
Sham
TBI-1 d
TBI-3 d
TBI-7 d
Vehicle
NALL

Fig. 36

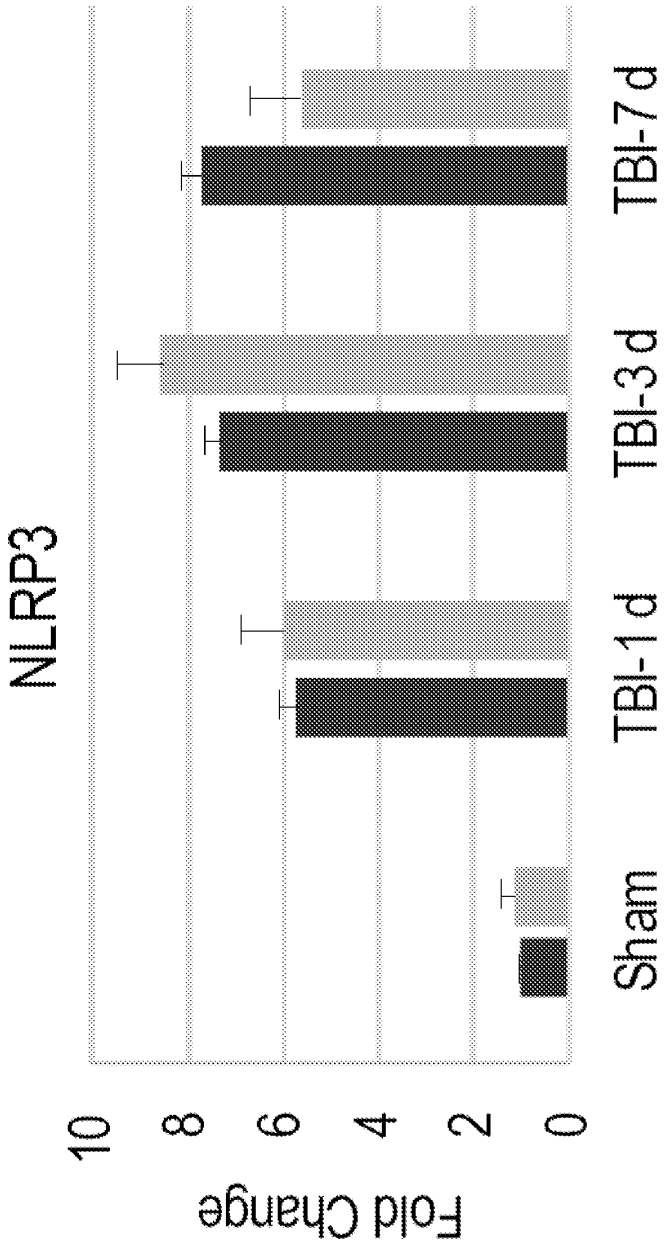

NLRP3
Fold Change
10
8
6
4
2
0
Sham
TBI-1 d
TBI-3 d
TBI-7 d
Vehicle
NALL

Fig. 37

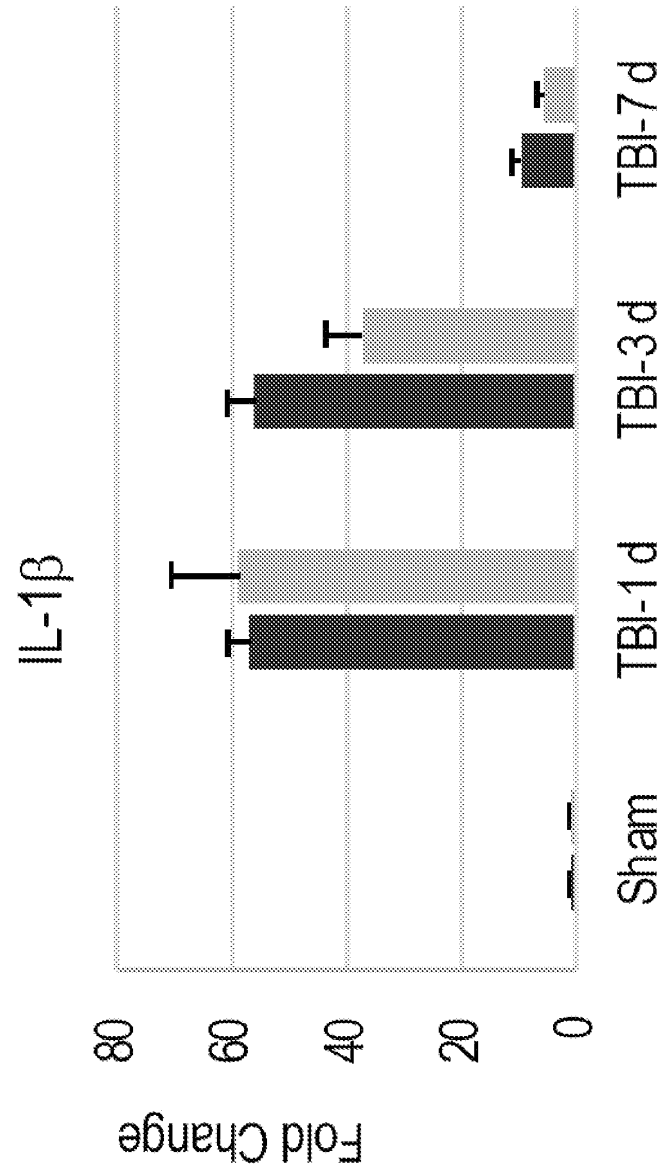

IL-1β
Fold Change
80
60
40
20
0
Sham
TBI-1 d
TBI-3 d
TBI-7 d
Vehicle
NALL

Fig. 38

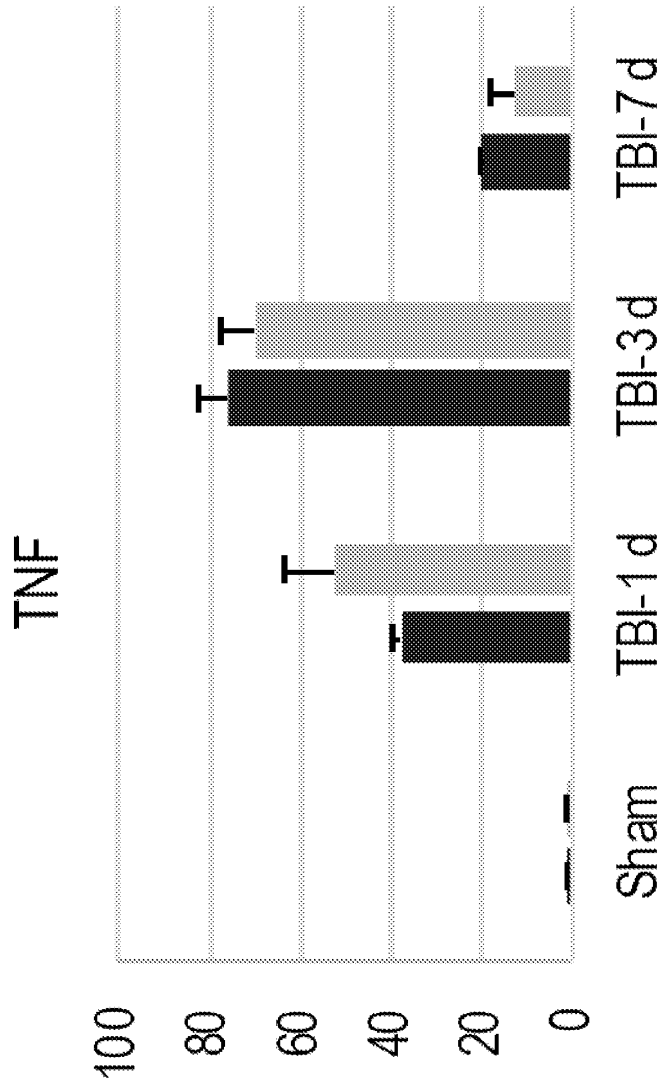


Fig. 39

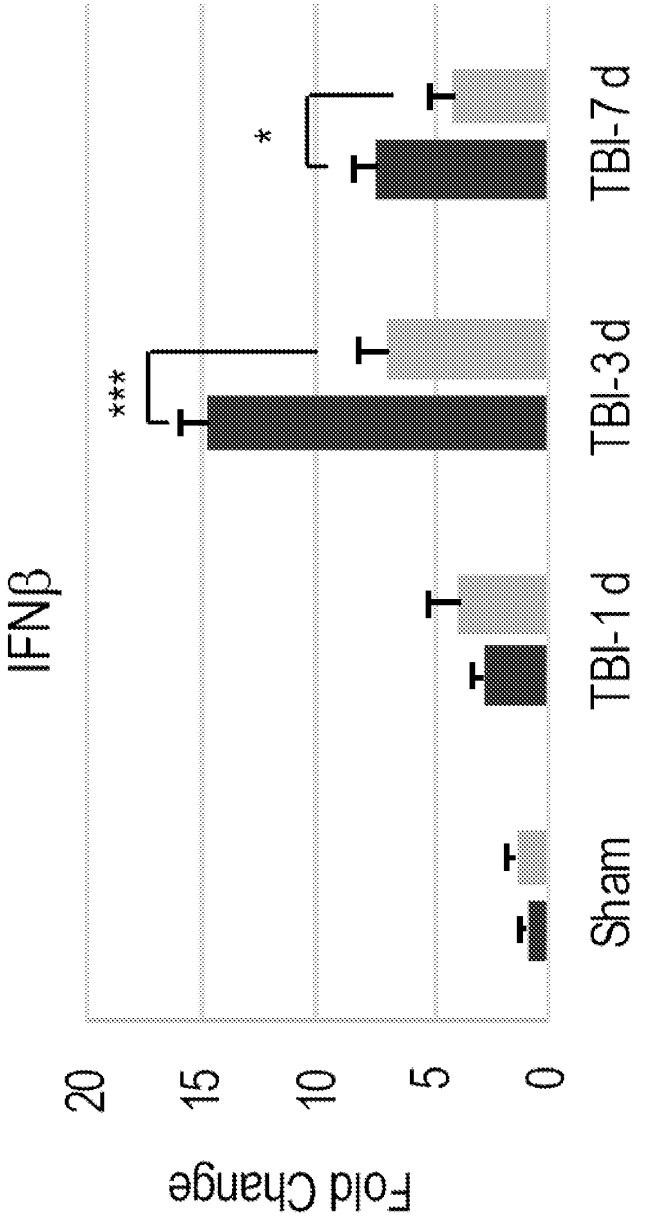

IFNβ
Fold Change
20
15
10
5
0
***
*
Sham
TBI-1 d
TBI-3 d
TBI-7 d
Vehicle
NALL

Fig. 40

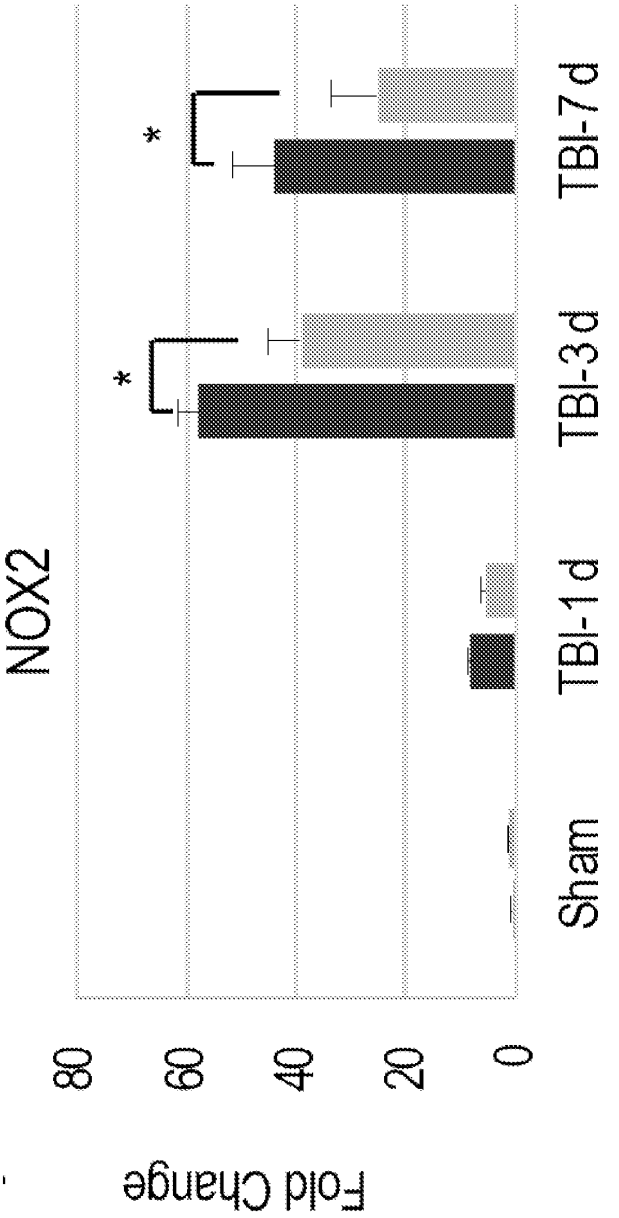

NOX2
Fold Change
80
60
40
20
0
*
*
Sham
TBI-1 d
TBI-3 d
TBI-7 d
Vehicle
NALL

Fig. 41

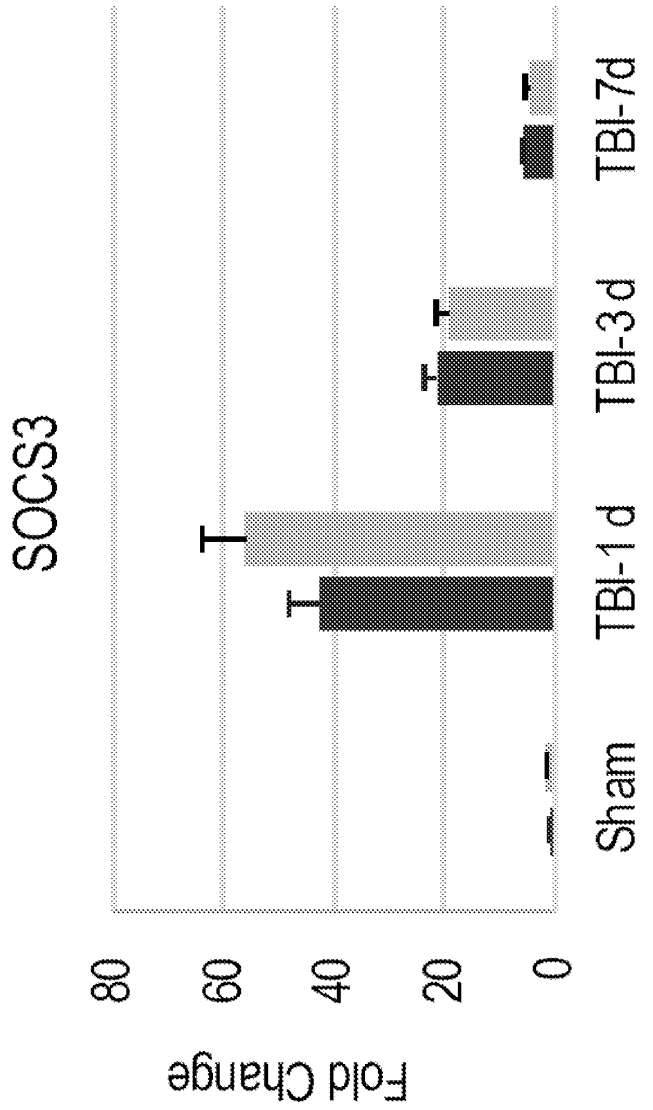

SOCS3
Fold Change
80
60
40
20
0
Sham
TBI-1 d
TBI-3 d
TBI-7d
Vehicle
NALL

Fig. 42

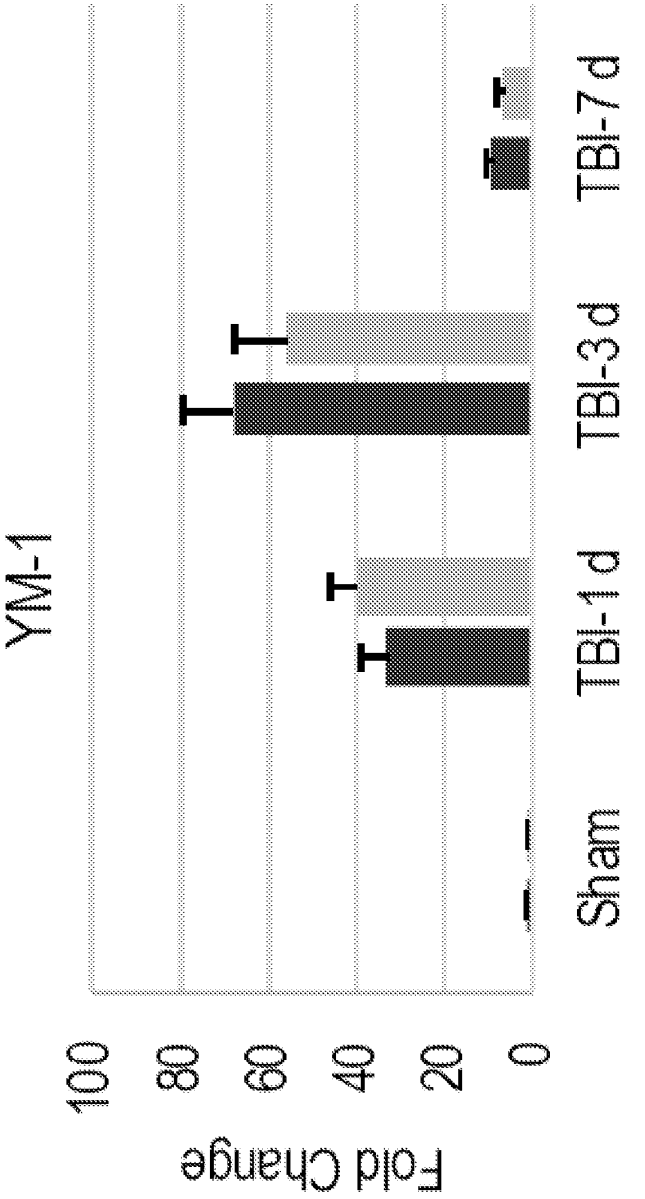

YM-1
Fold Change
100
80
60
40
20
0
Sham
TBI-1 d
TBI-3 d
TBI-7 d
Vehicle
NALL

Fig. 43

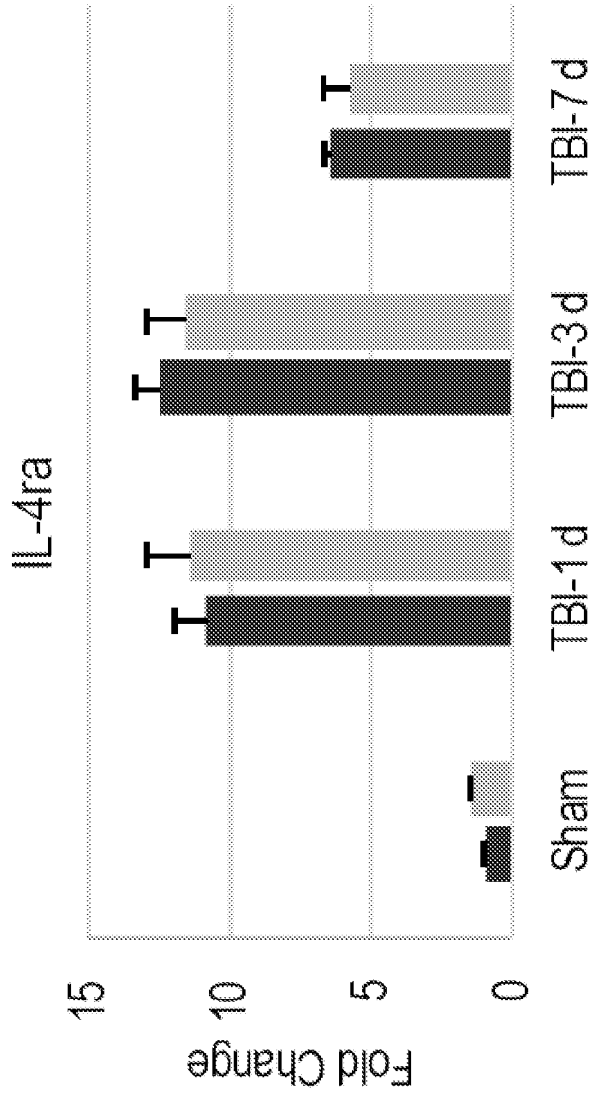

IL-4ra
Fold Change
15
10
5
0
Sham
TBI-1 d
TBI-3 d
TBI-7 d
Vehicle
NALL

Fig. 44

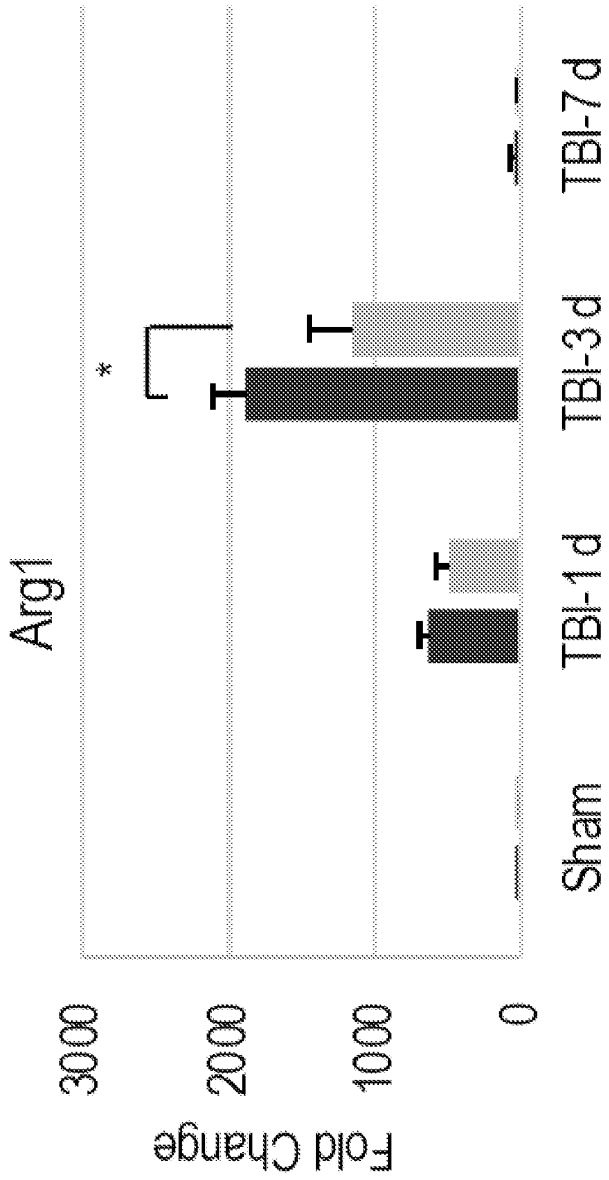

Arg1
Fold Change
30000
20000
10000
0
*
Sham
TBI-1d
TBI-3d
TBI-7d
Vehicle
NALL

Fig. 45

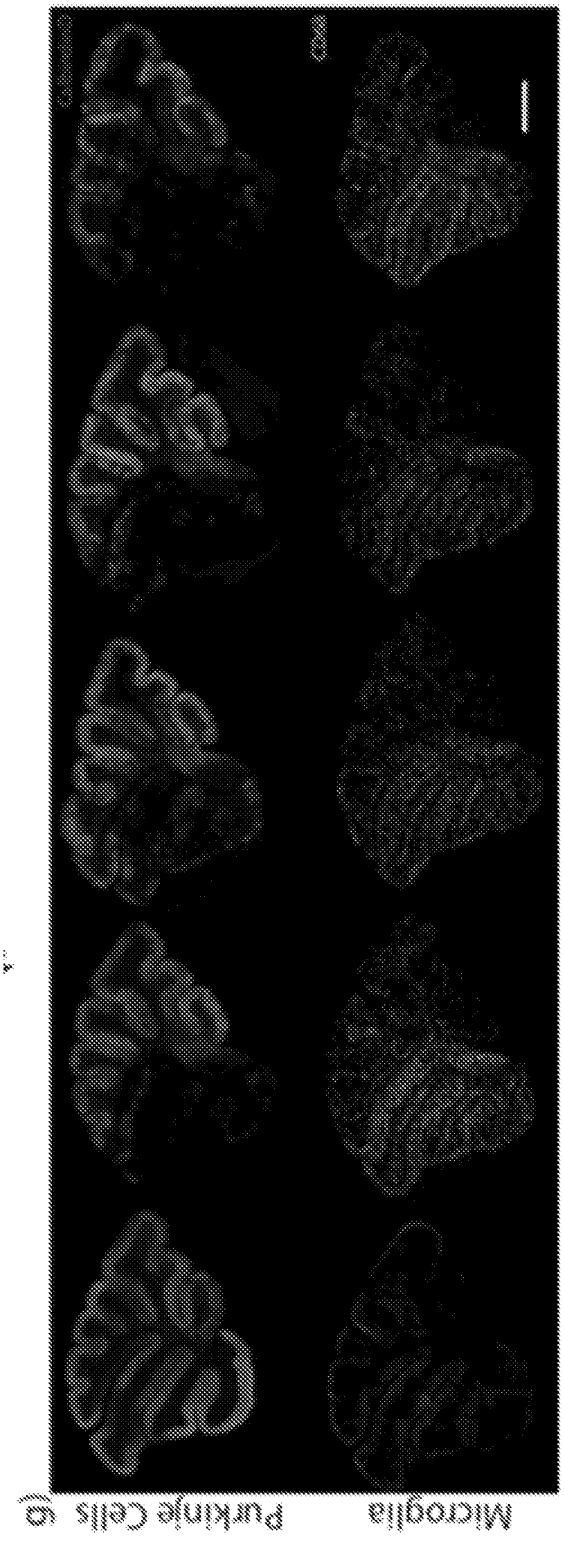

Microglia
Purkinje cells
+/+ Npc1 UT
-/- Npc1 UT
-/- Npc1 ADLL
-/- Npc1 ALL
-/- Npc1 ADL

Fig. 46

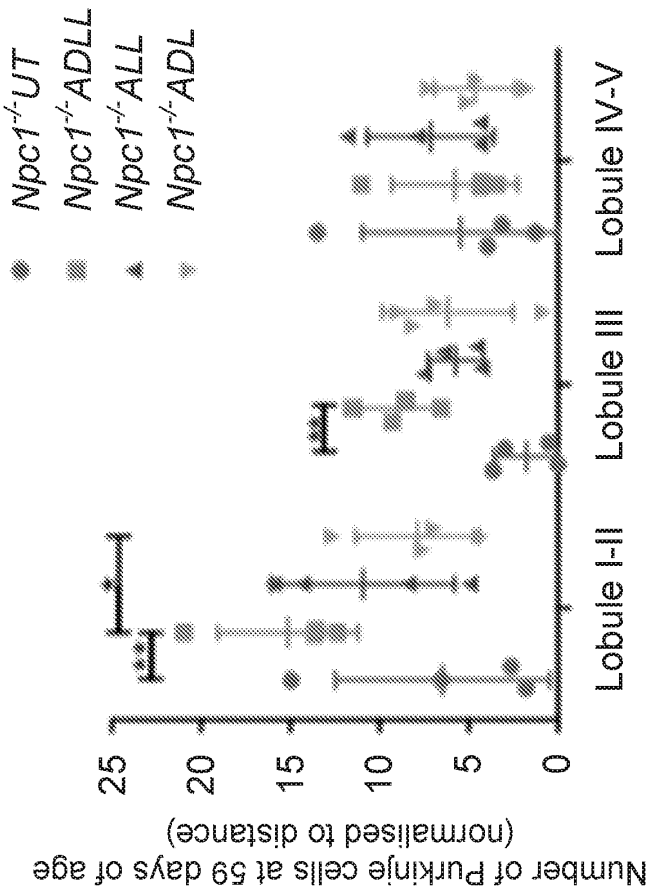

Npc1-/-UT
Npc1-/-ADLL
Npc1-/-ALL
Npc1-/-ADL
Number of Purkinje cells at 59 days of age
(normalised to distance)
25
20
15
10
5
0
Lobule I-II
Lobule III
Lobule IV-V

Fig. 47

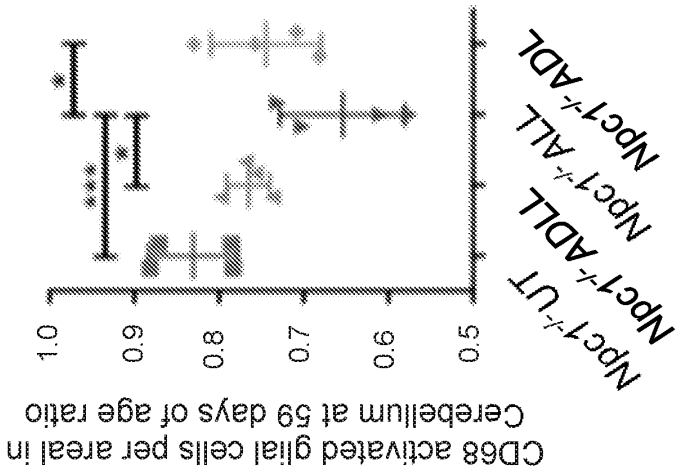

CD68 activated glial cells per areal in Cerebellum at 59 days of age ratio
1.0
0.9
0.8
0.7
0.6
0.5
Npc1-/- UT
Npc1-/- ADLL
Npc1-/- ALL
Npc1-/- ADL

Fig. 48

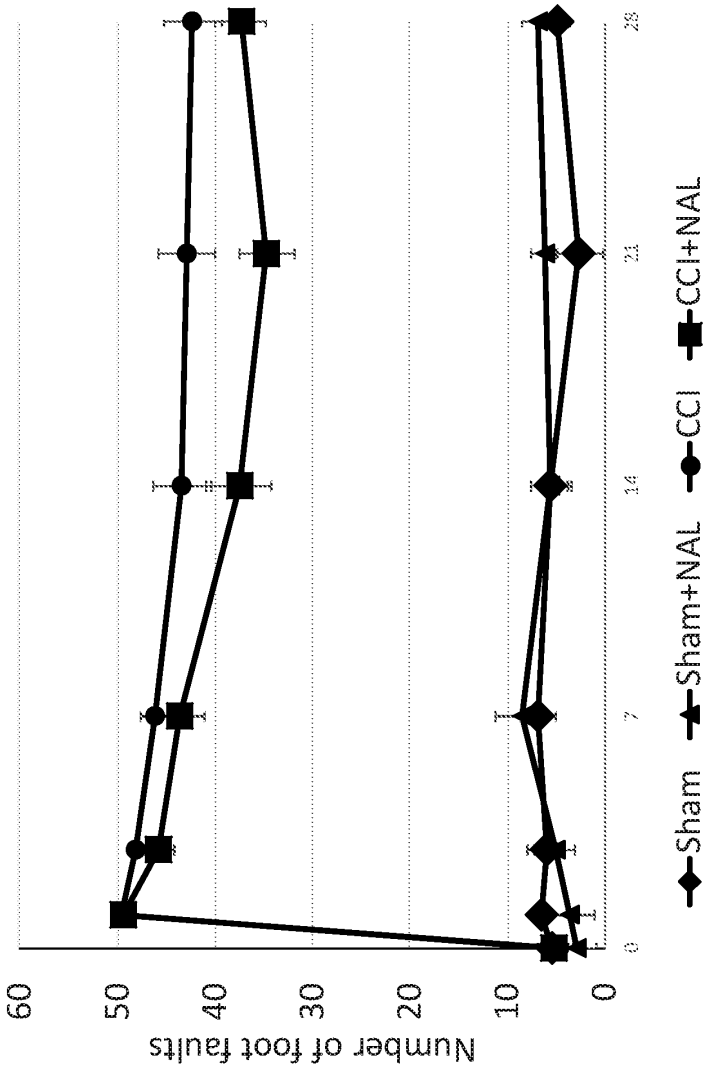

Number of foot faults
60
50
40
30
20
10
0
0
7
14
21
28
Sham
Sham+NAL
CCI
CCI+NAL

Fig. 49

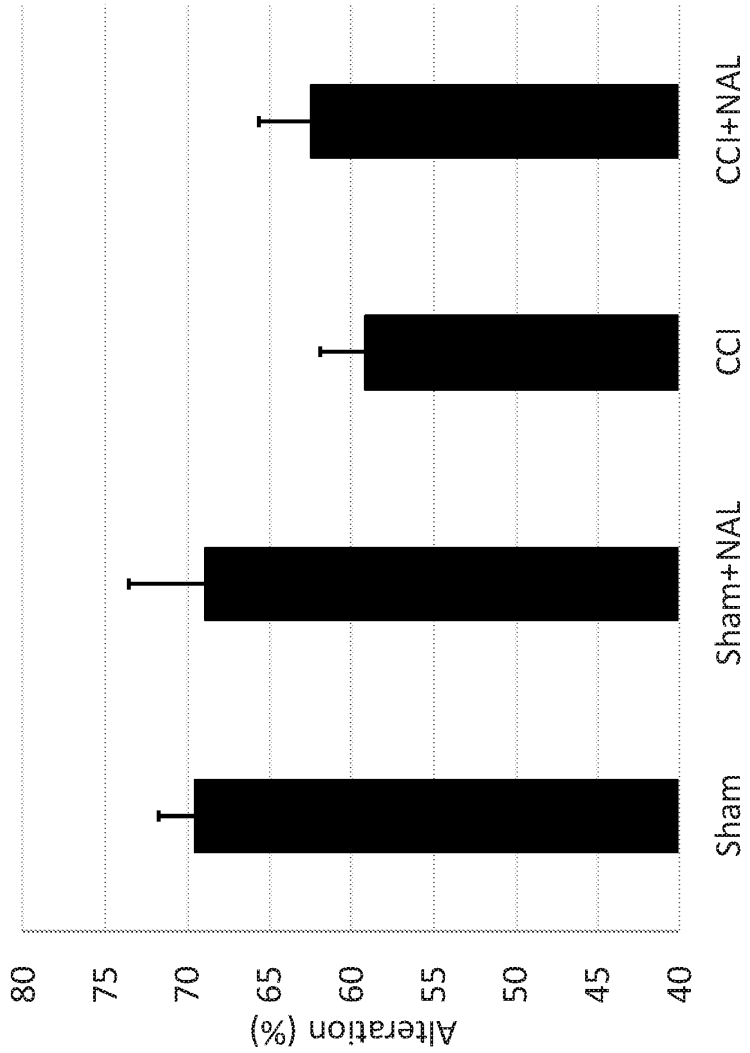


Fig. 50

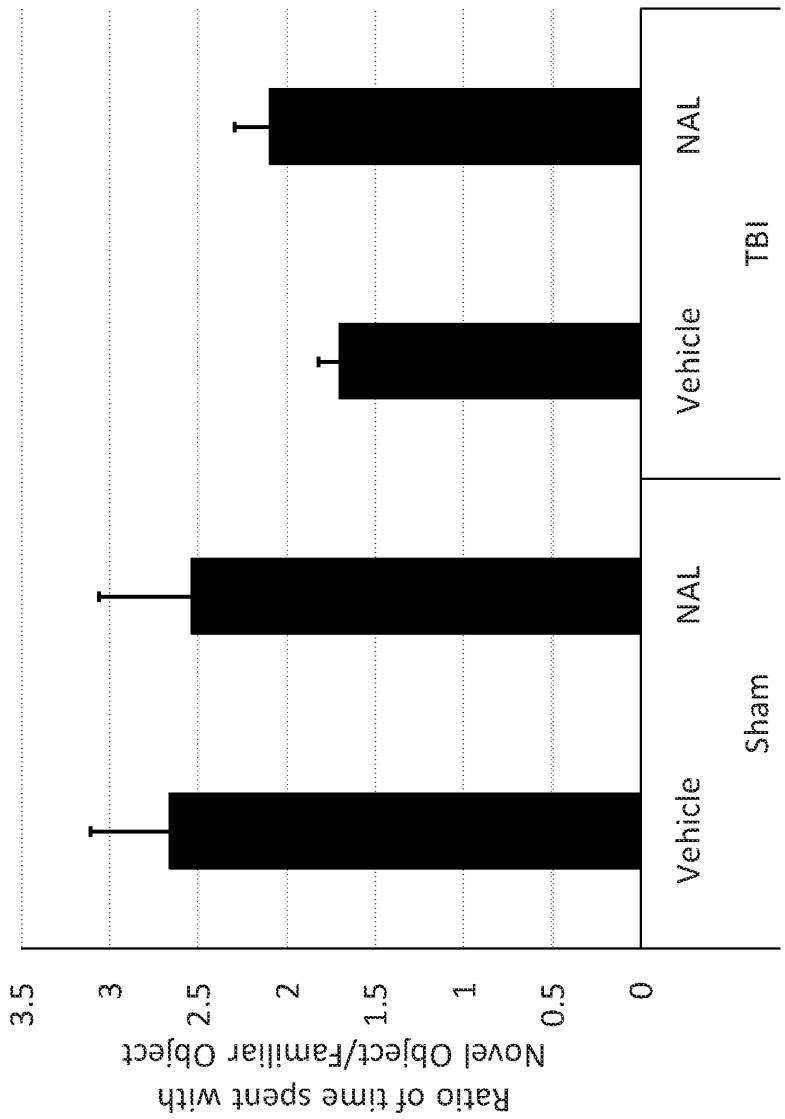

Ratio of time spent with
Novel Object/Familiar Object
3.5
3
2.5
2
1.5
1
0.5
0
Vehicle
NAL
Sham
Vehicle
NAL
TBI

Fig. 51