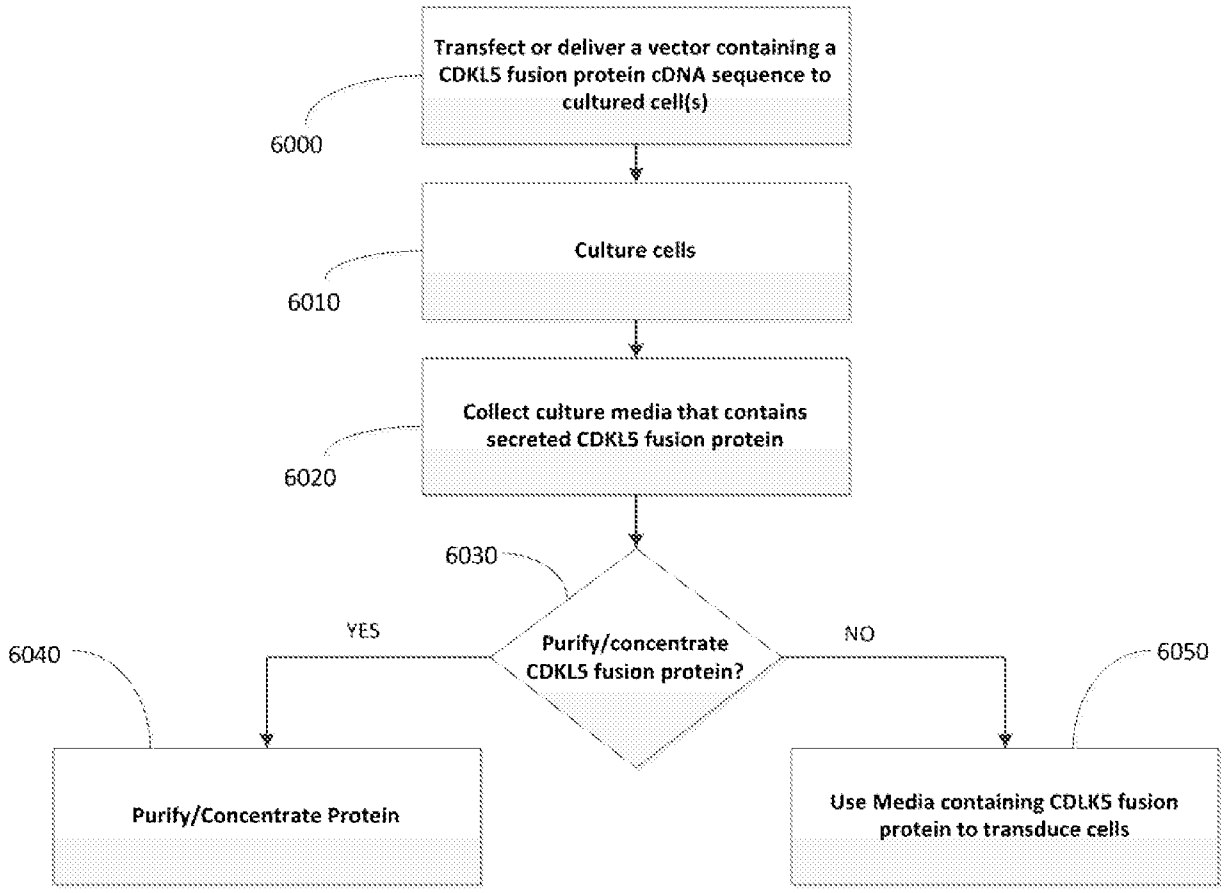

Transfect or deliver a vector containing a CDKL5 fusion protein cDNA sequence to cultured cell(s)
6000
Culture cells
6010
Collect culture media that contains secreted CDKL5 fusion protein
6020
6030
Purify/concentrate CDKL5 fusion protein?
YES
NO
6040
6050
Purify/Concentrate Protein
Use Media containing CDLK5 fusion protein to transduce cells

Fig. 1

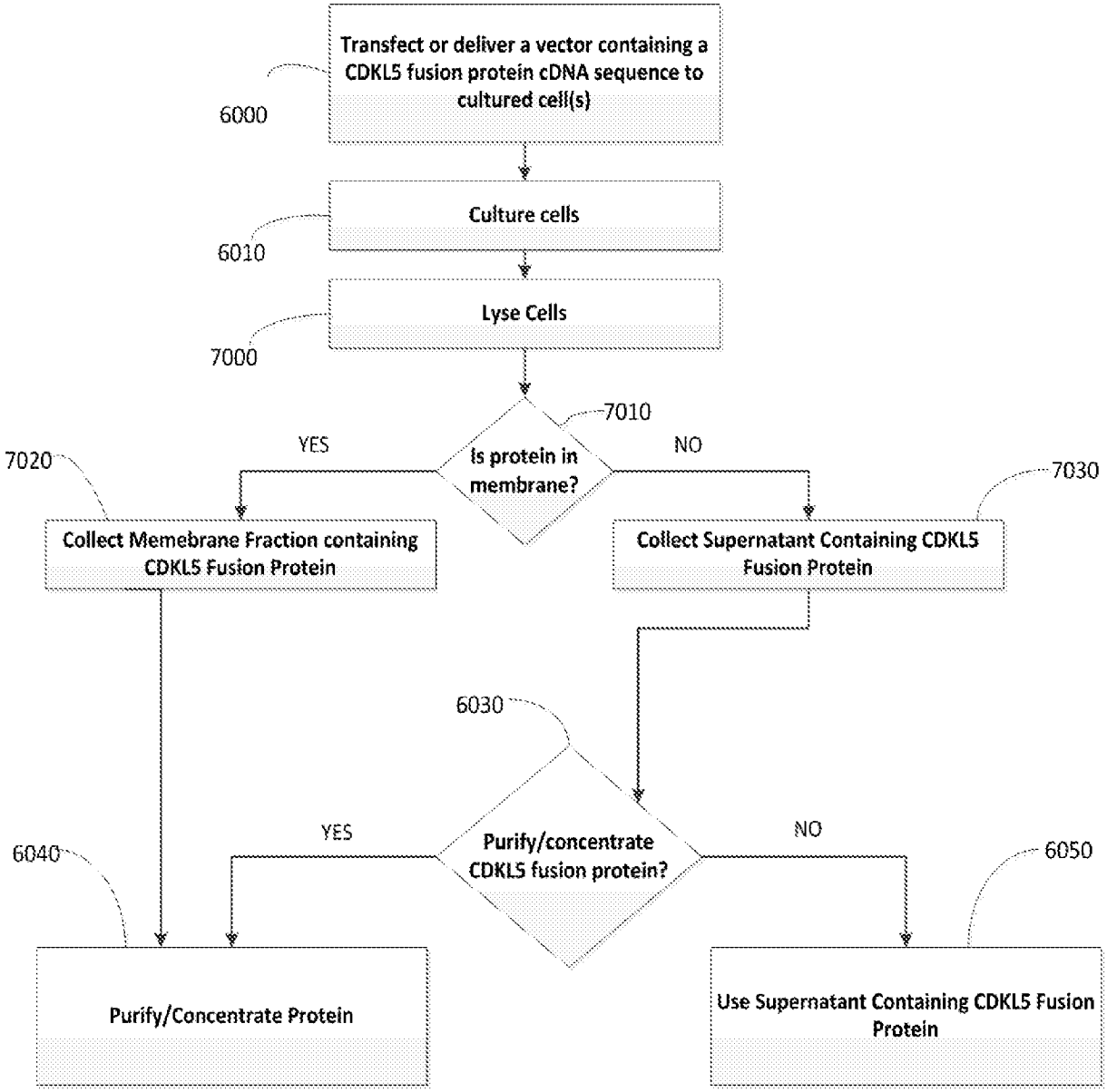

Transfect or deliver a vector containing a CDKL5 fusion protein cDNA sequence to cultured cell(s)
6000
Culture cells
6010
Lyse Cells
7000
Is protein in membrane?
7010
YES
NO
7020
7030
Collect Memebrane Fraction containing CDKL5 Fusion Protein
Collect Supernatant Containing CDKL5 Fusion Protein
6030
Purify/concentrate CDKL5 fusion protein?
YES
NO
6040
6050
Purify/Concentrate Protein
Use Supernatant Containing CDKL5 Fusion Protein

Fig. 2

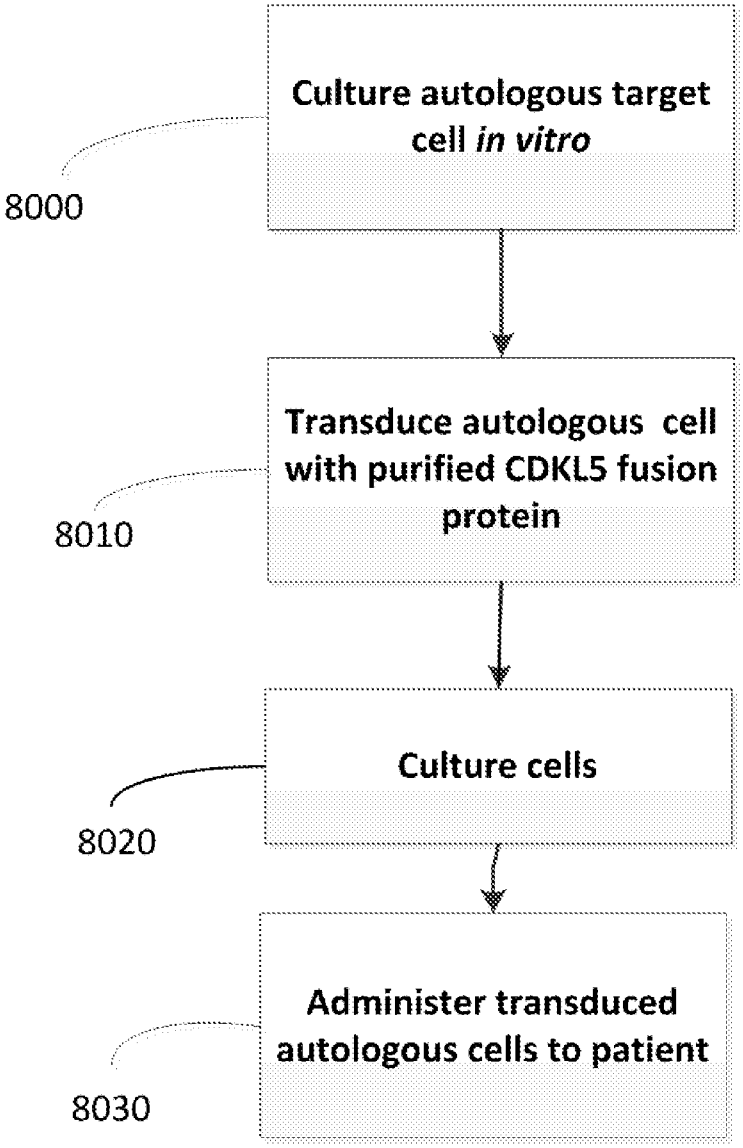

Culture autologous target cell *in vitro*
8000
Transduce autologous cell with purified CDKL5 fusion protein
8010
Culture cells
8020
Administer transduced autologous cells to patient
8030

Fig. 3

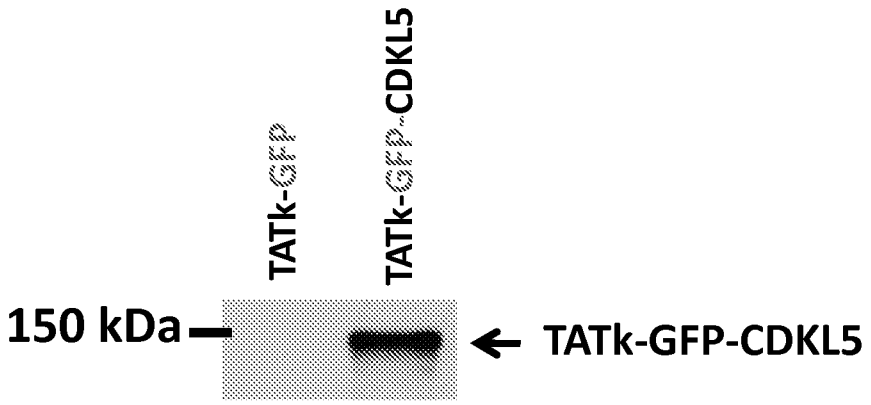

TATk-GFP
TATk-GFP-CDKL5
150 kDa
TATk-GFP-CDKL5

Fig. 4A

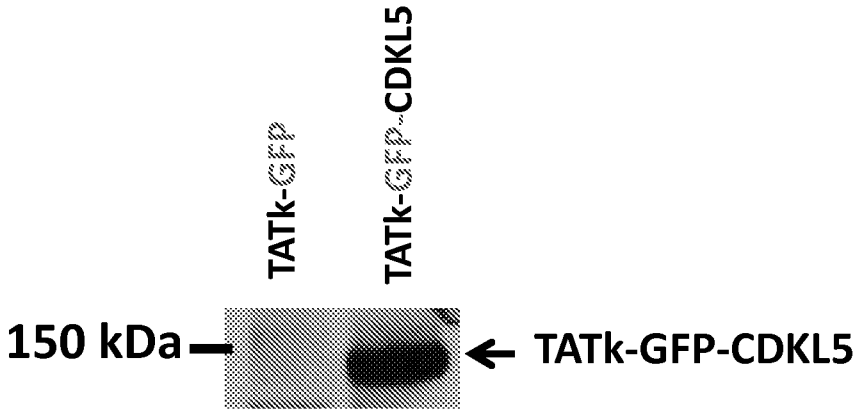

TATk-GFP
TATk-GFP-CDKL5
150 kDa
TATk-GFP-CDKL5

Fig. 4B

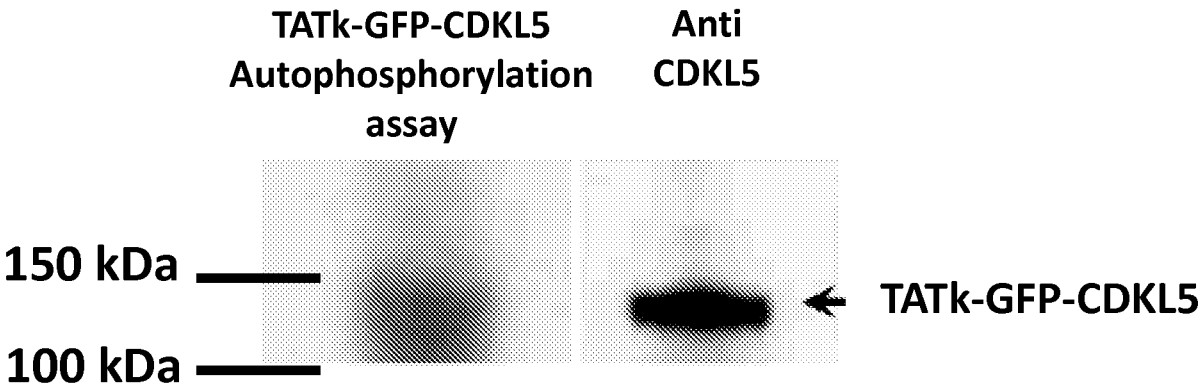


Fig. 5A Fig. 5B

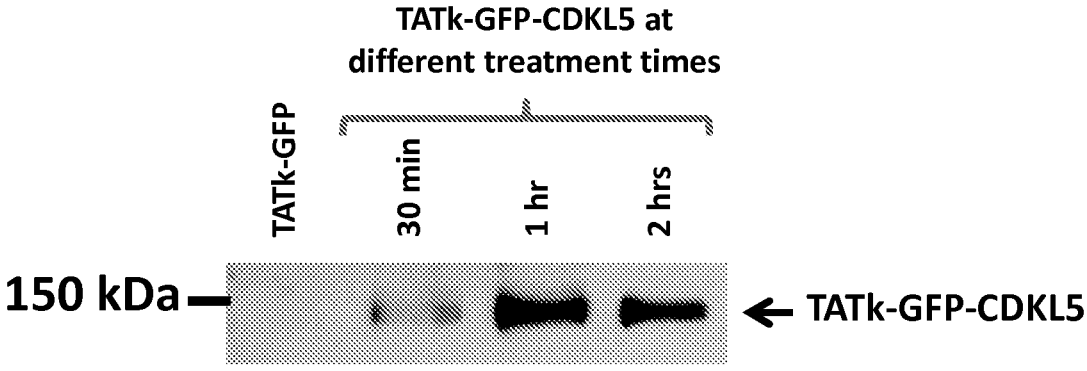


Fig. 6

Untreated 293T

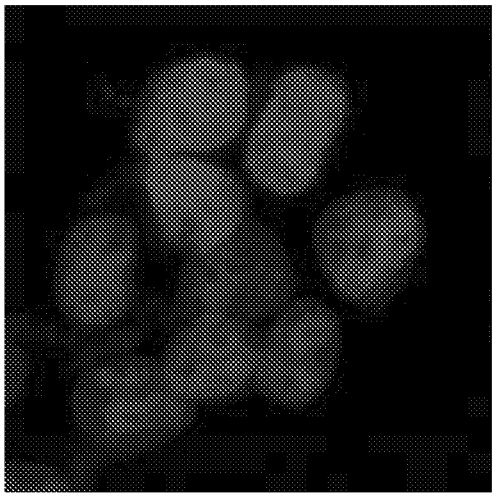


Fig. 7A

TATk-GFP-CDKL5 treated 293T

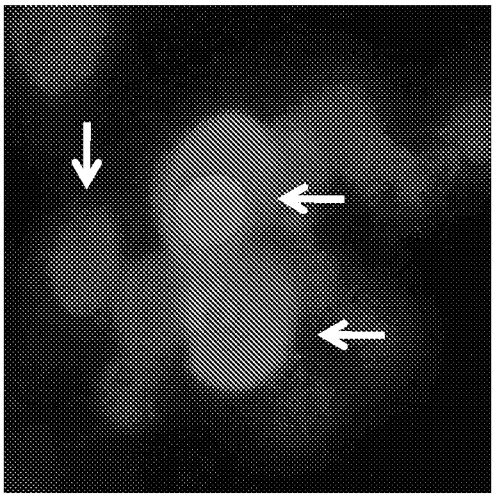


Fig. 7B

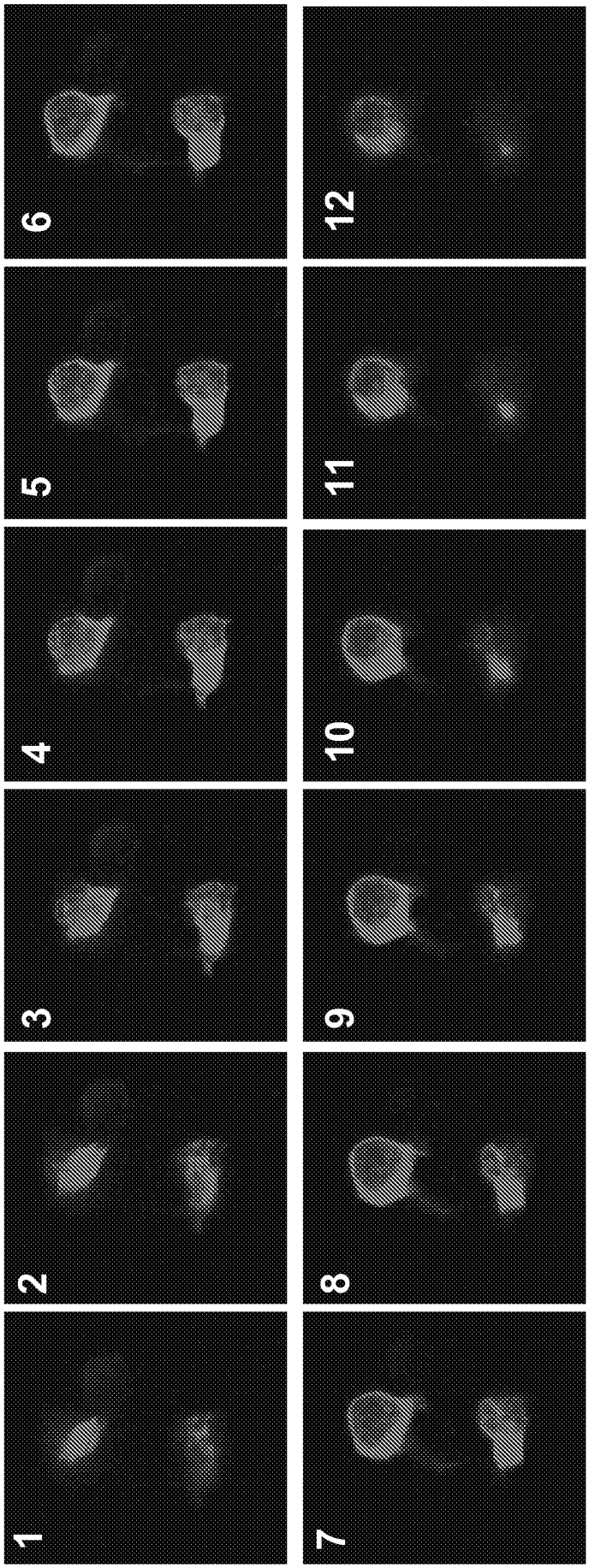


Fig. 8

TATk-GFP
treated SH-SY5Y

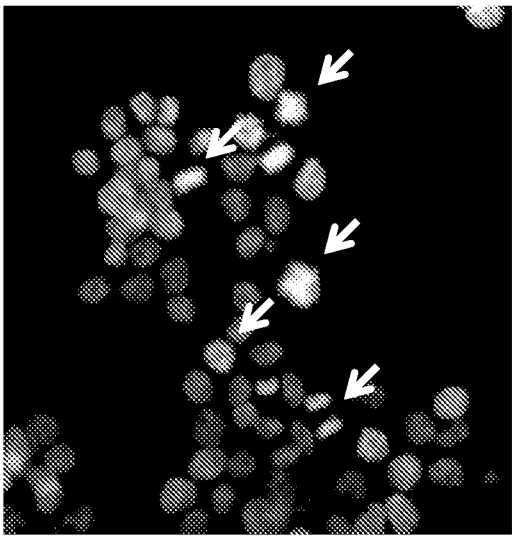


Fig. 9A

TATk-GFP-CDKL5
treated SH-SY5Y

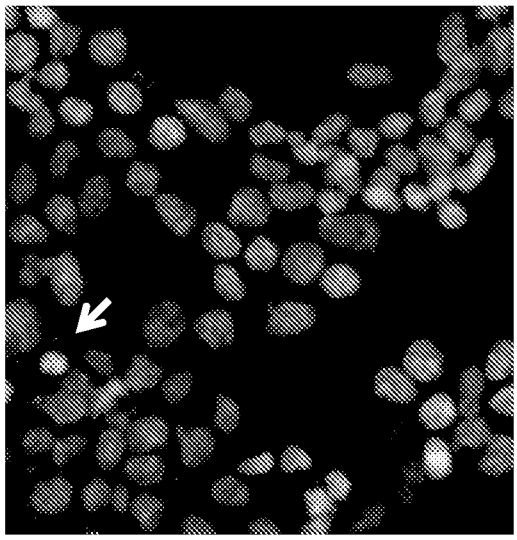


Fig. 9B

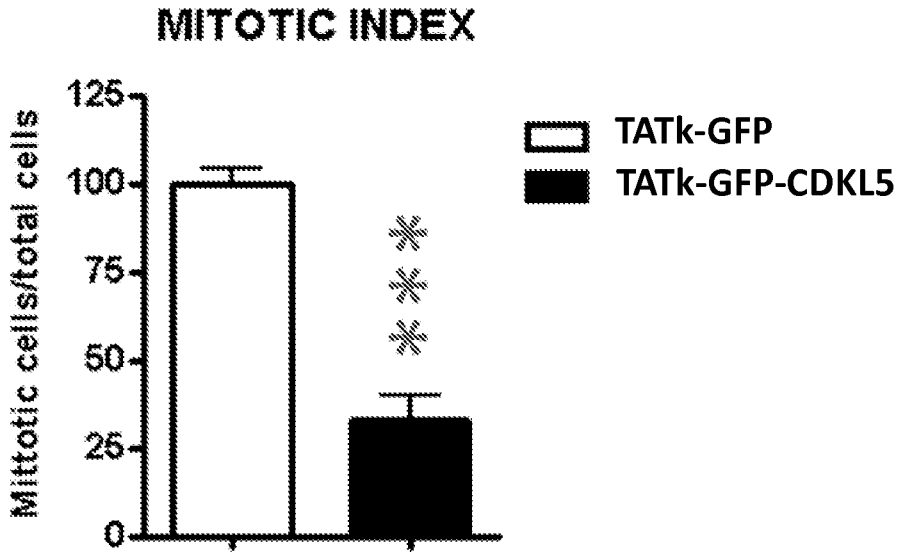


Fig. 10

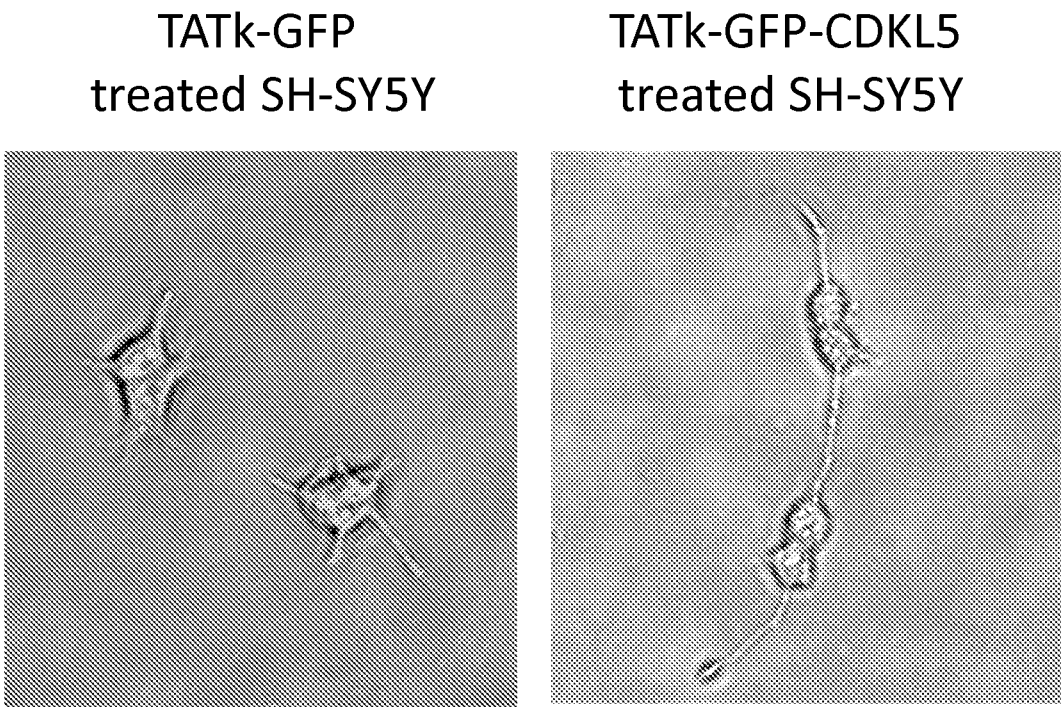


Fig. 11A

Fig. 11B

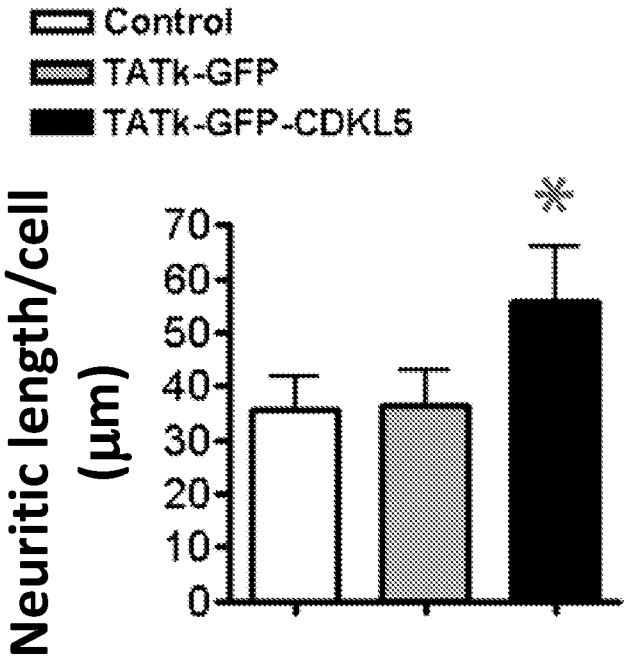


Fig. 12

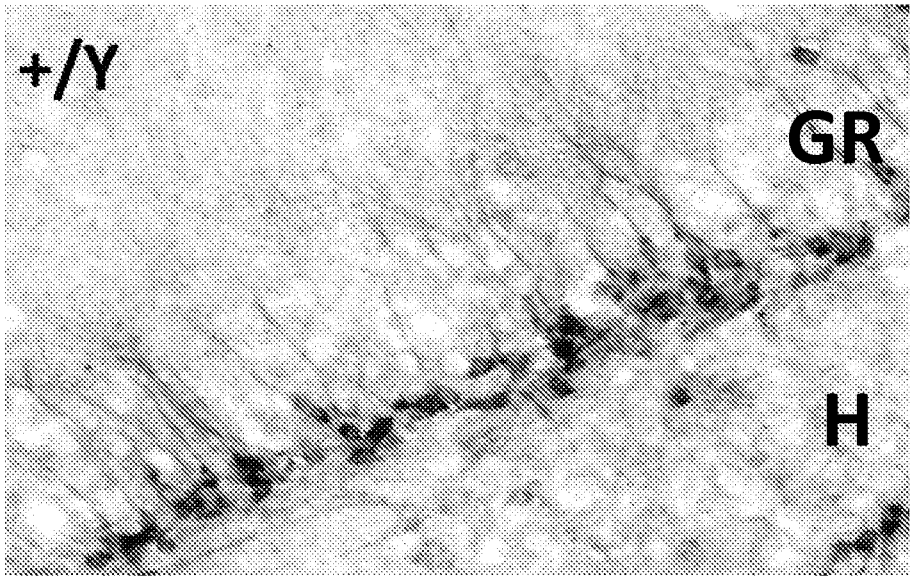


Fig. 13A

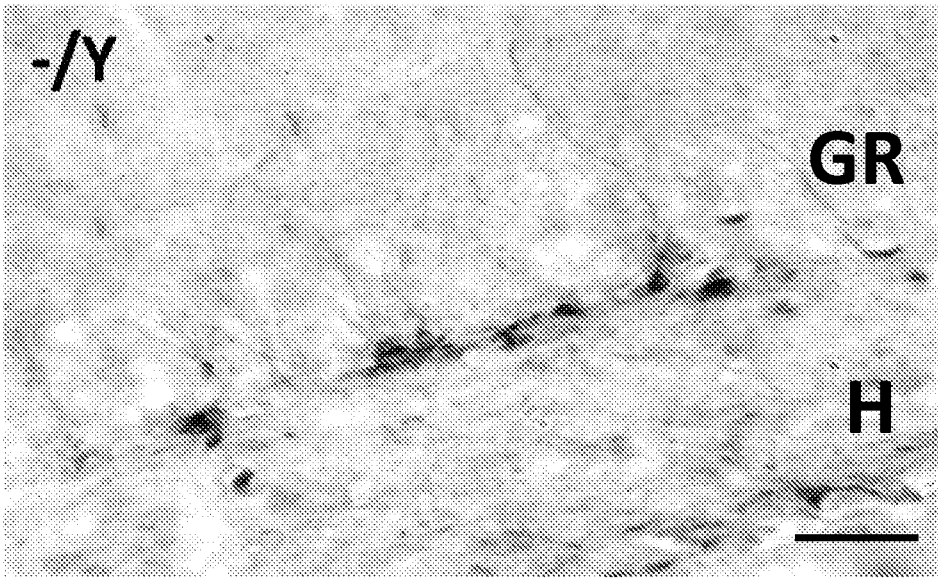


Fig. 13B

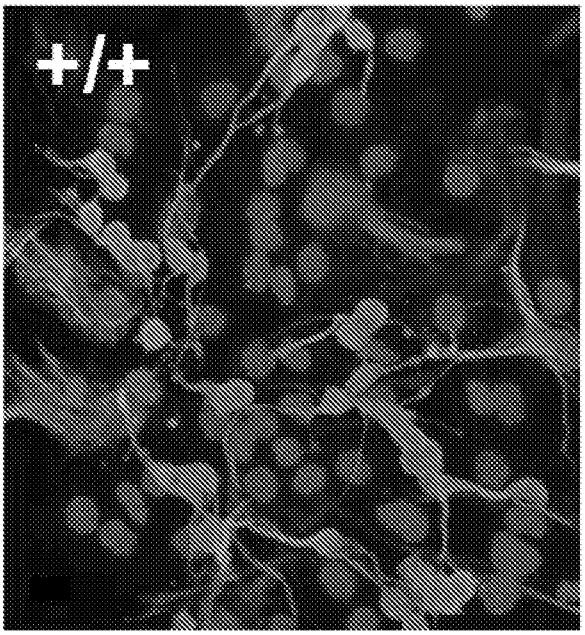


Fig. 14A

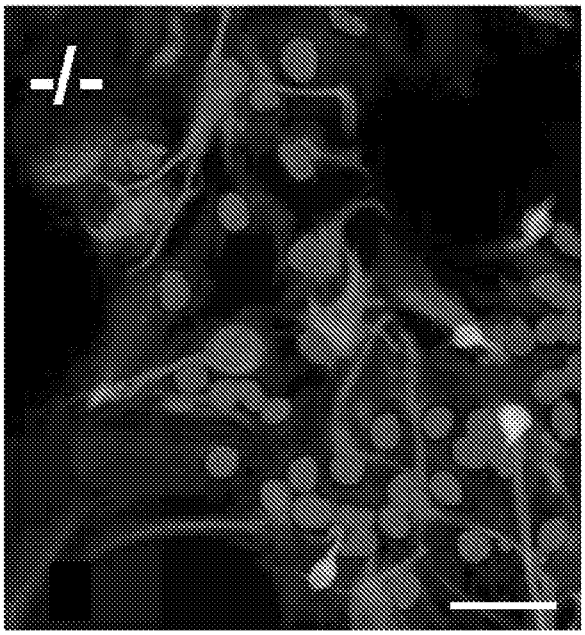


Fig. 14B

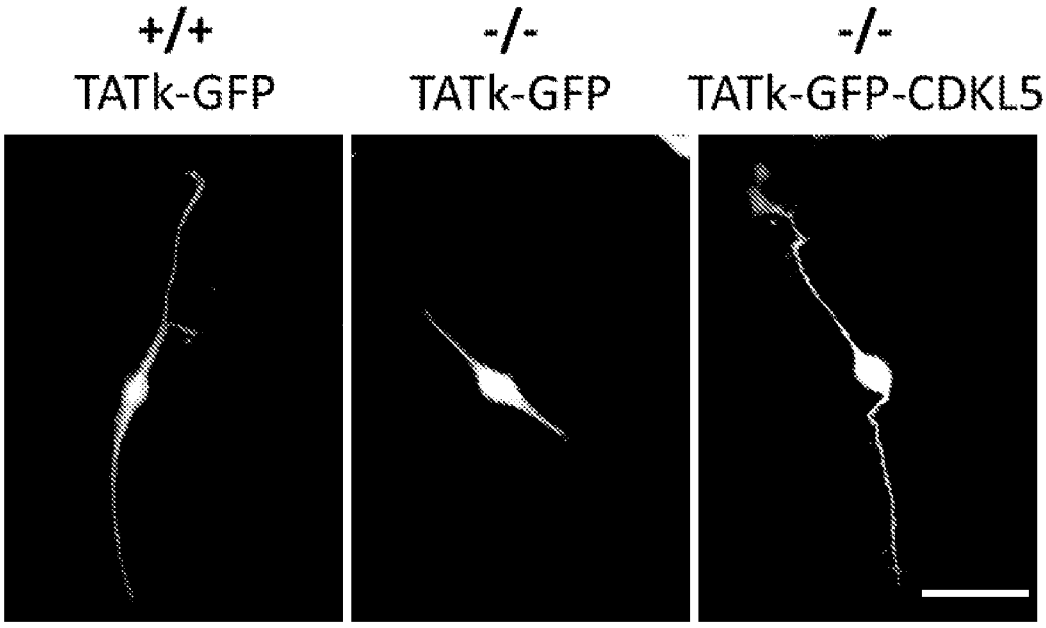


Fig. 15A Fig. 15B Fig. 15C

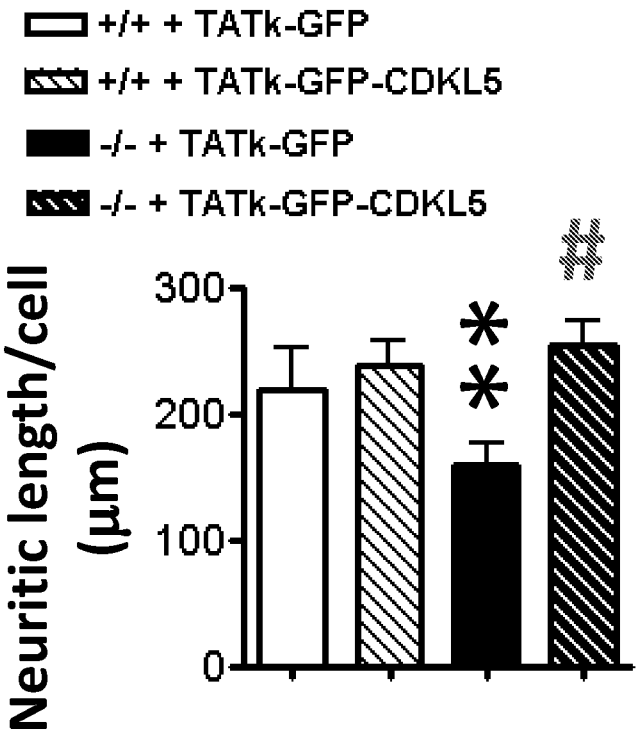


Fig. 16

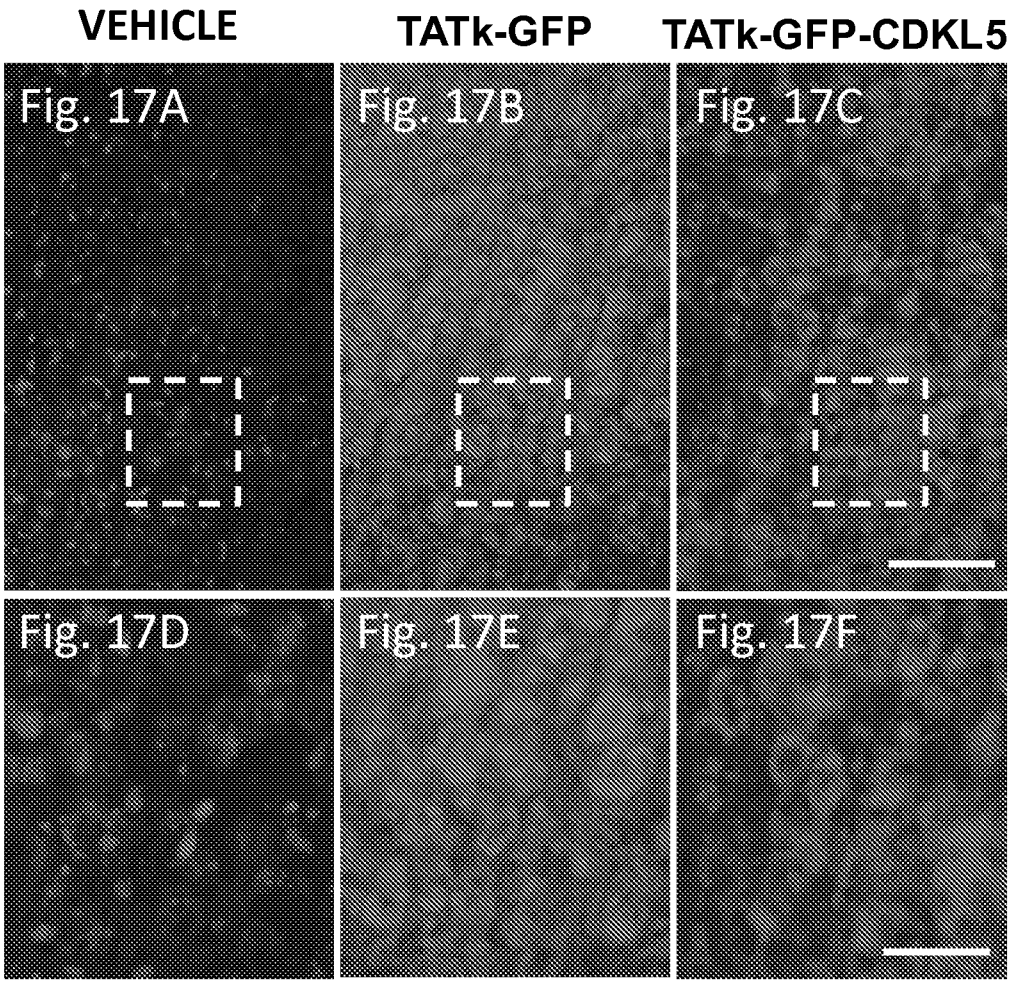

VEHICLE
TATk-GFP
TATk-GFP-CDKL5
Fig. 17A
Fig. 17B
Fig. 17C
Fig. 17D
Fig. 17E
Fig. 17F

Fig. 17A-F

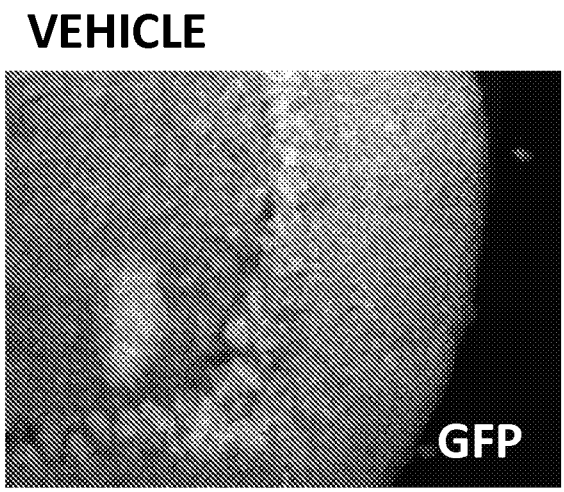


Fig. 18A

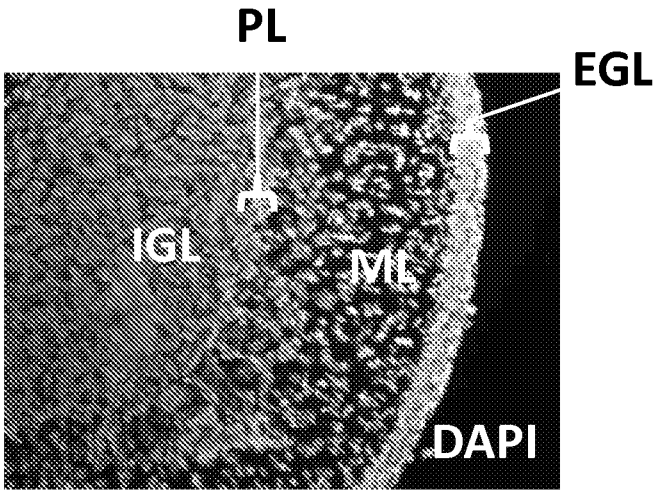


Fig. 18B

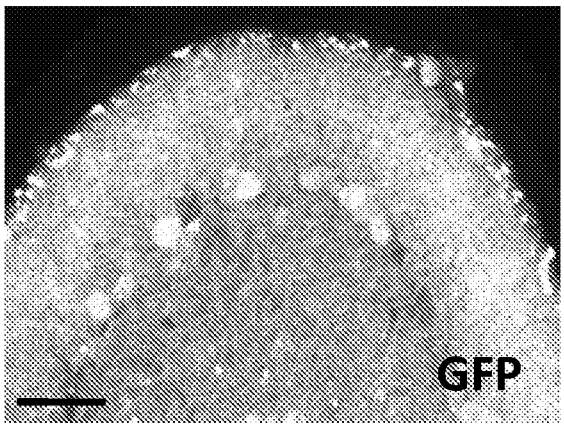


Fig. 18C

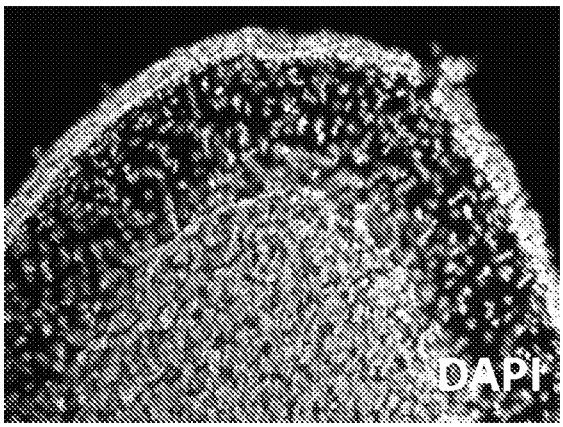


Fig. 18D

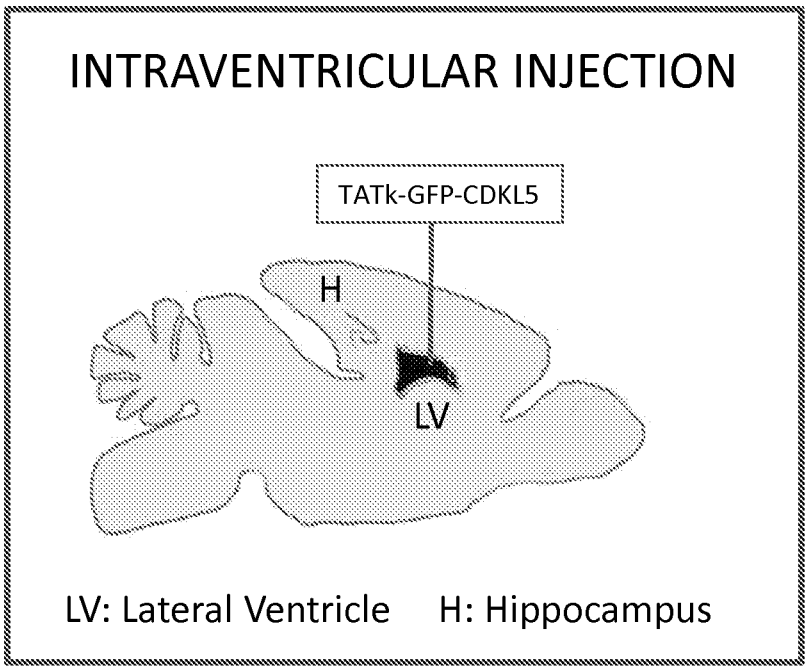

INTRAVENTRICULAR INJECTION
TATk-GFP-CDKL5
H
LV
LV: Lateral Ventricle
H: Hippocampus

Fig. 19

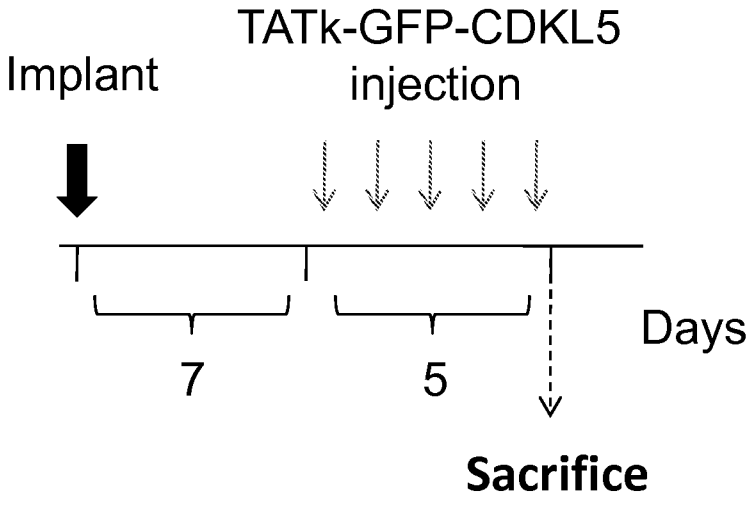

TATk-GFP-CDKL5
injection
Implant
Days
7
5
Sacrifice

Fig. 20

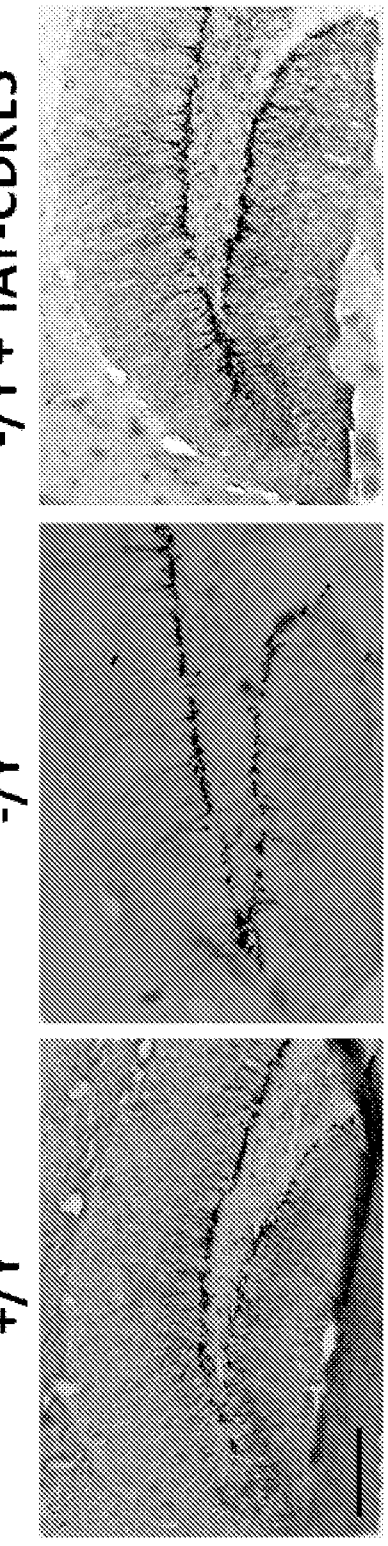


Fig. 21A Fig. 21B Fig. 21C

+/Y

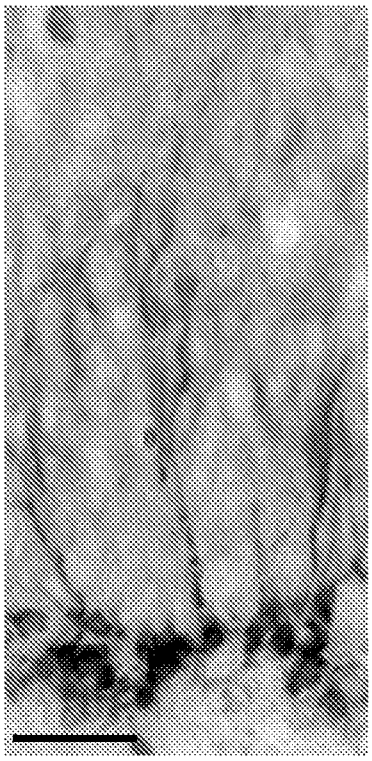


Fig. 22A

-/Y

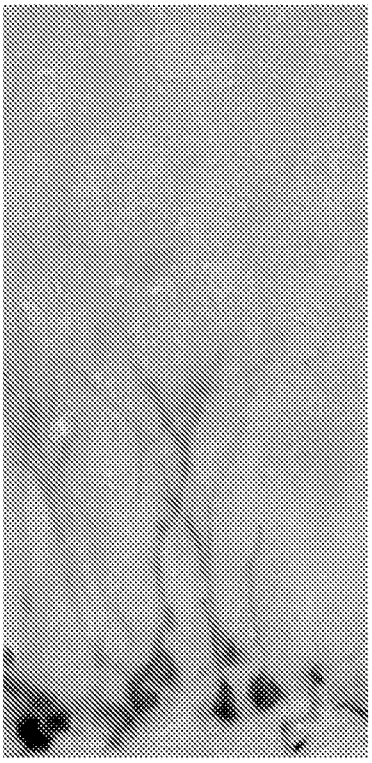


Fig. 22B

-/Y +TATk-GFP-CDKL5

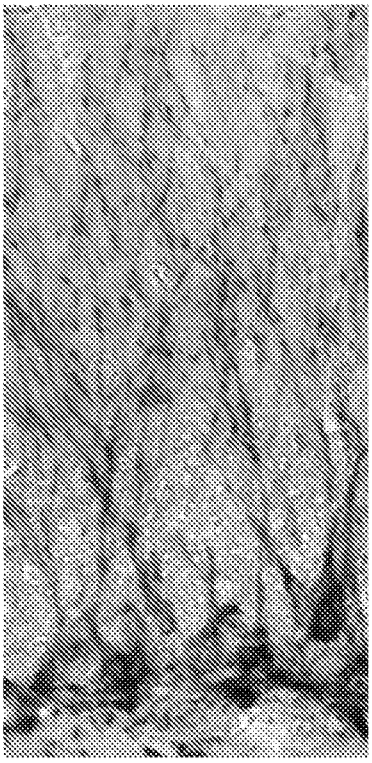


Fig. 22C

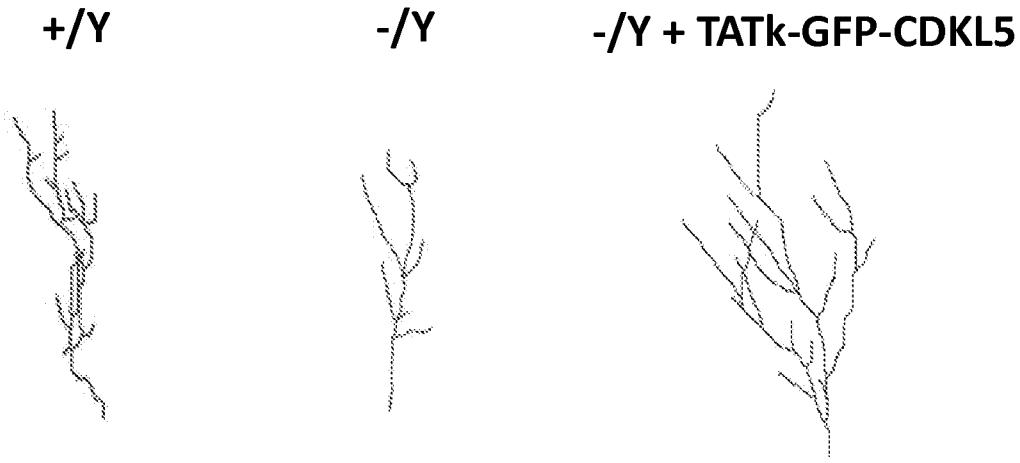


Fig. 23A Fig. 23B Fig. 23C

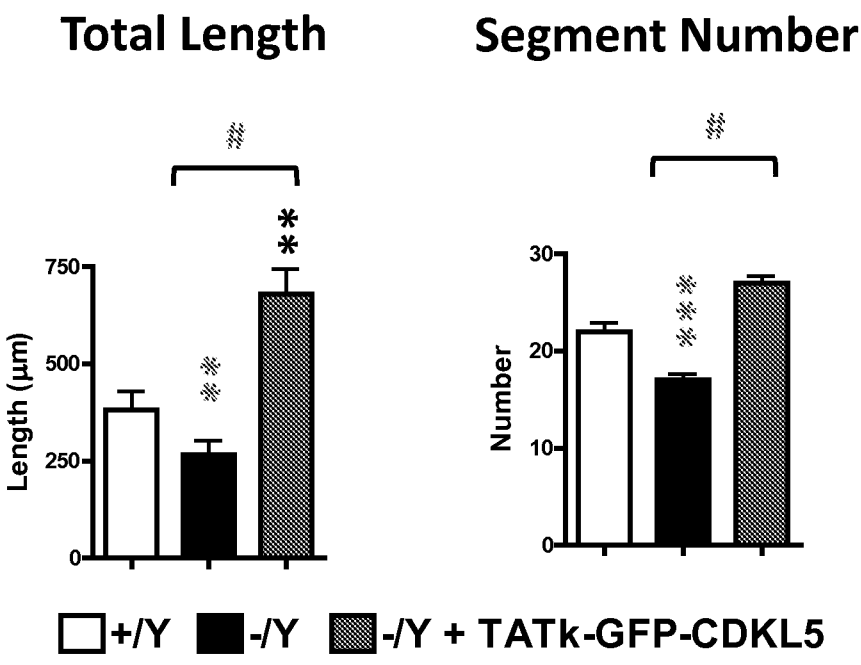


Fig. 24A Fig. 24B

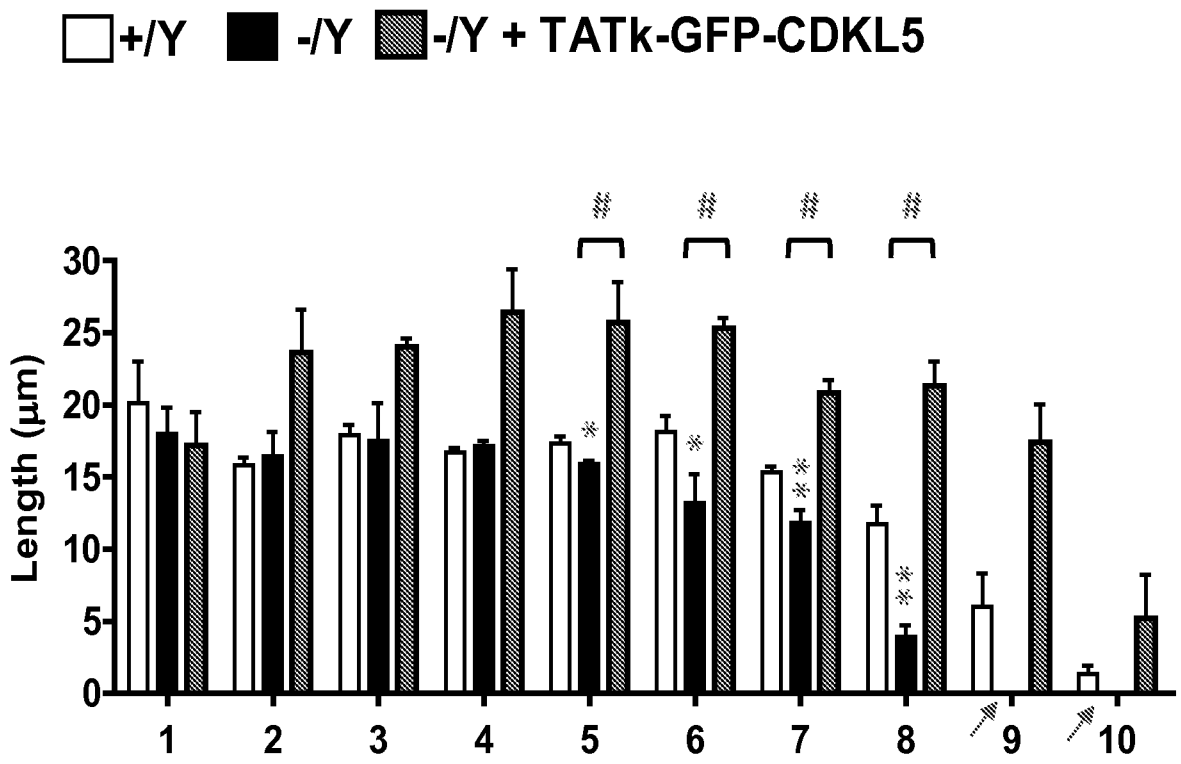


Fig. 25A

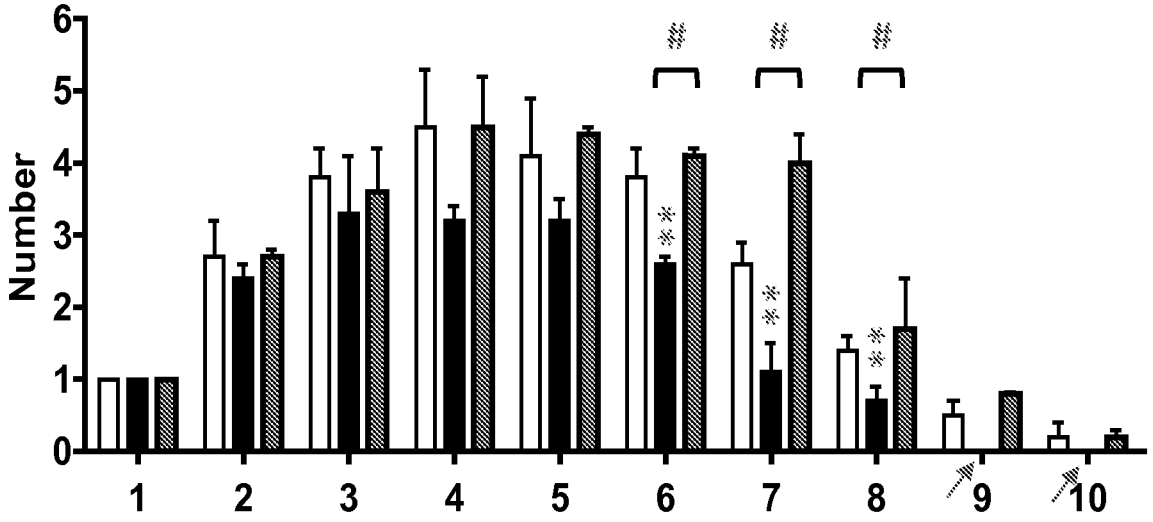


Fig. 25B


+/Y
-/Y
-/Y + TATk-GFP-CDKL5

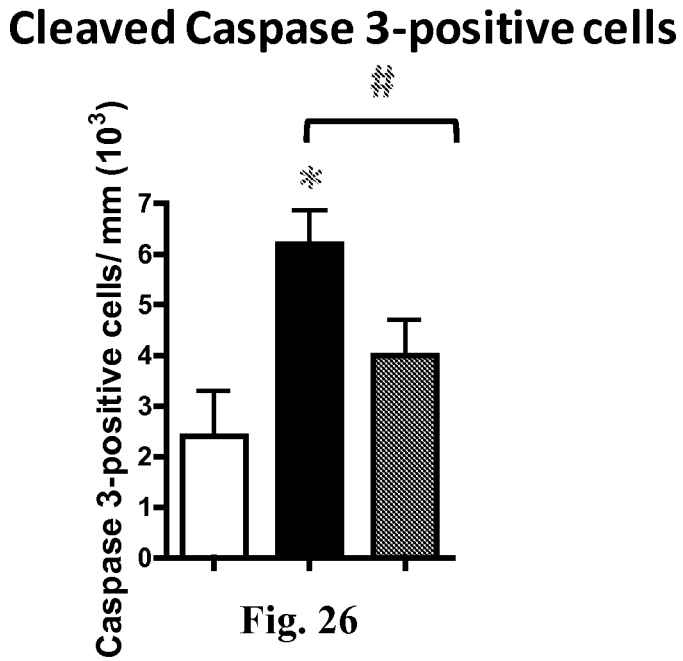

Cleaved Caspase 3-positive cells
Caspase 3-positive cells/ mm (10^3)
0
1
2
3
4
5
6
7
*
#

Fig. 26

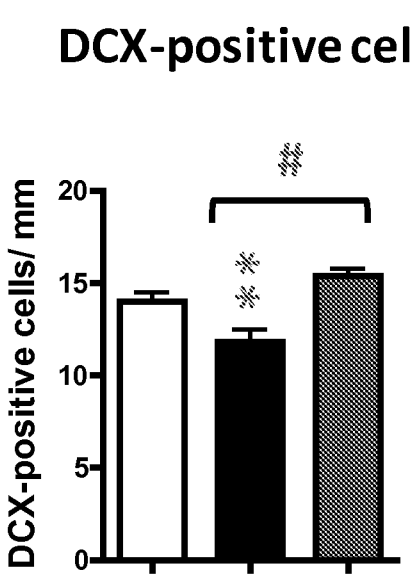

DCX-positive cells
DCX-positive cells/ mm
0
5
10
15
20
*
#

Fig. 27

SYN

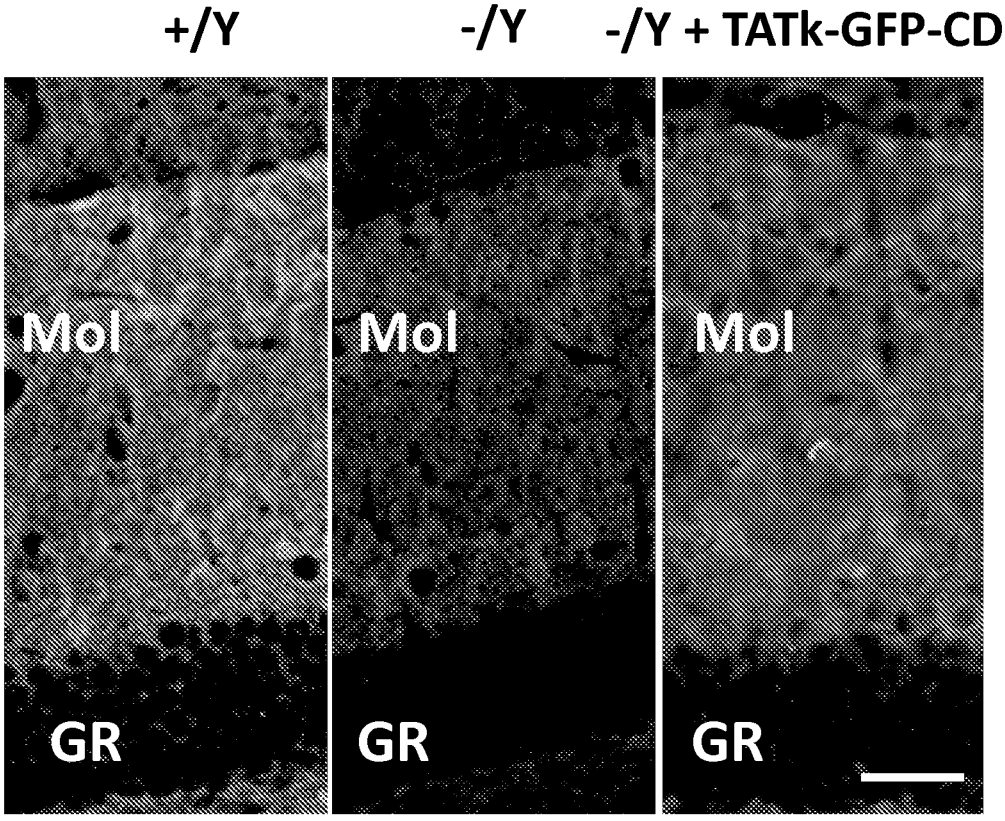


Fig. 28A Fig. 28B Fig. 28C

P-AKT

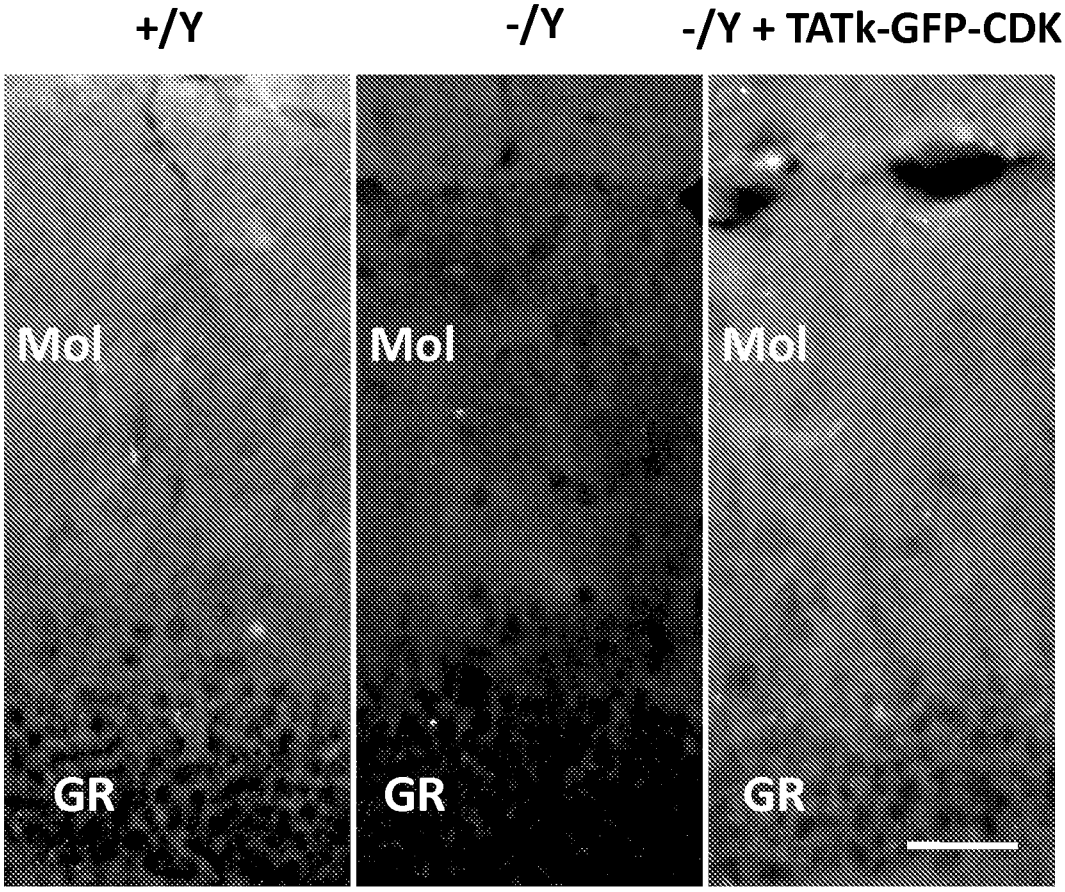


Fig. 29A Fig. 29B Fig. 29C



Hippocampus (molecular layer)

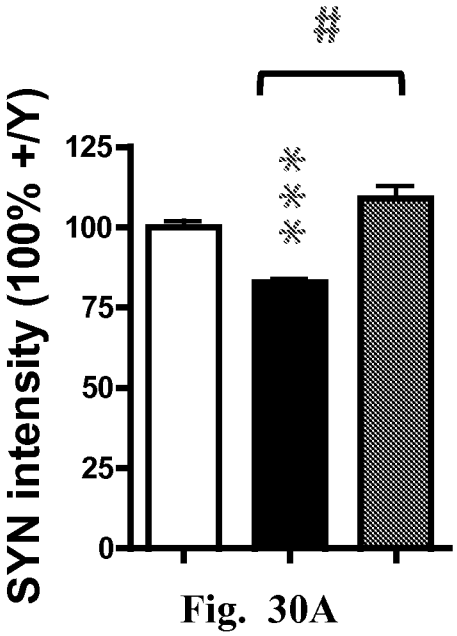


Fig. 30A

Cortex (layer III)

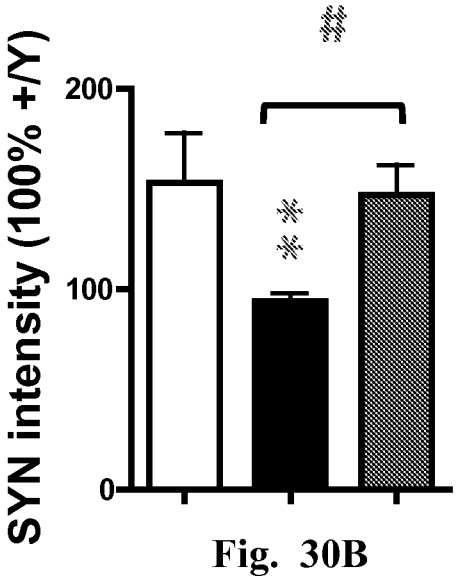


Fig. 30B

Hippocampus (molecular layer)

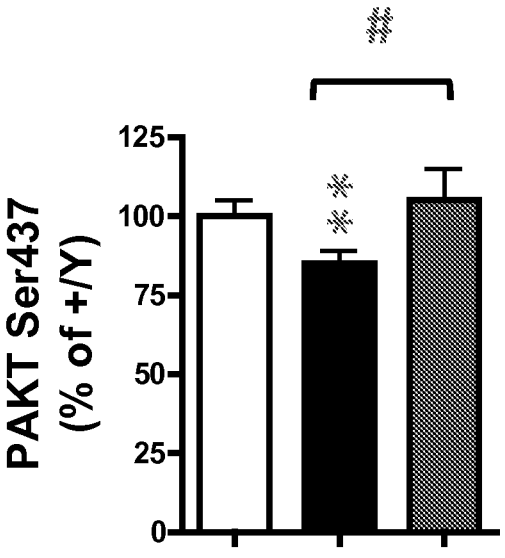


Fig. 31A

Cortex (layer V)

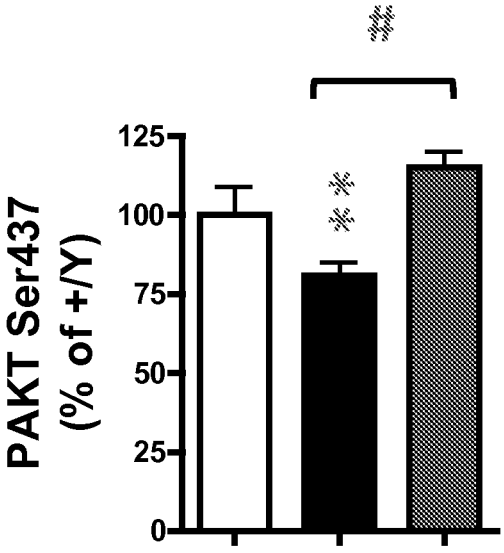


Fig. 31B

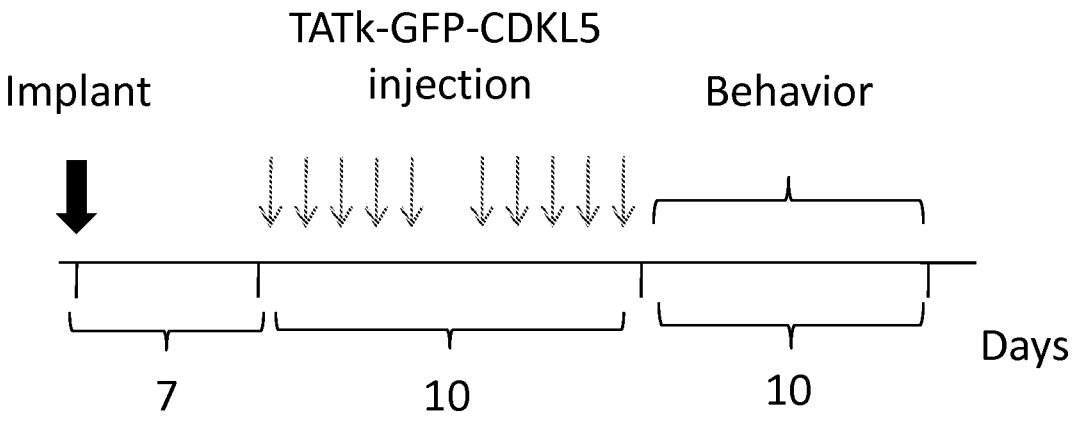


Fig. 32

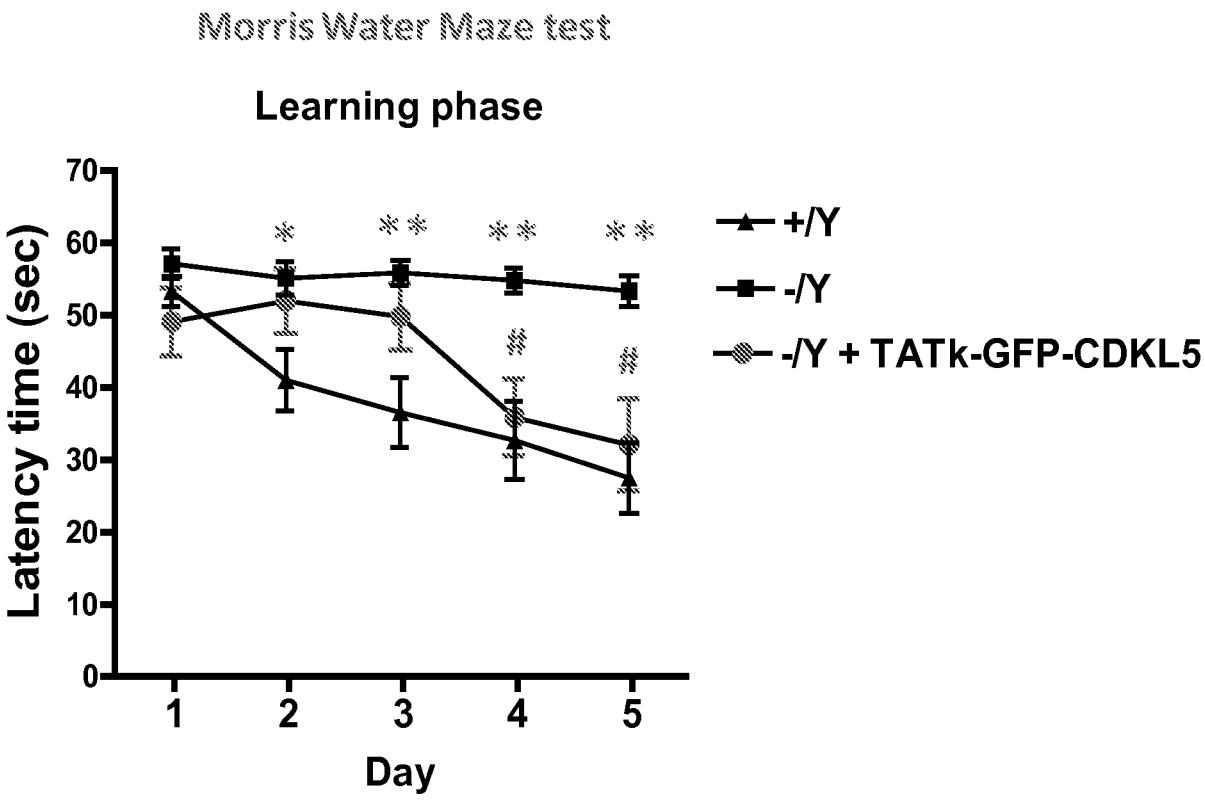


Fig. 33

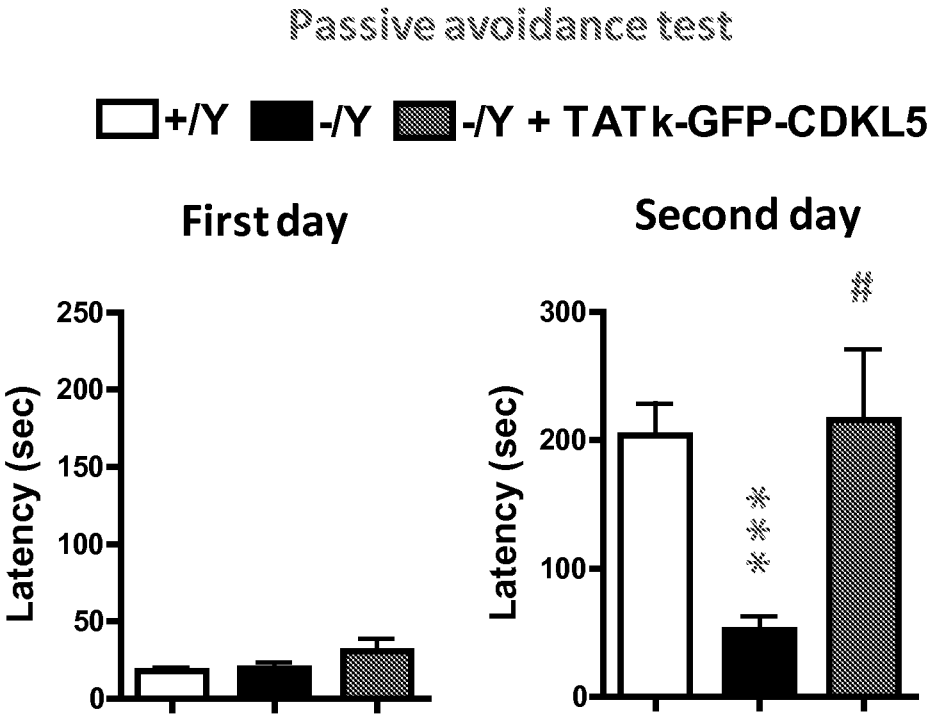


Fig. 34A

Fig. 34B

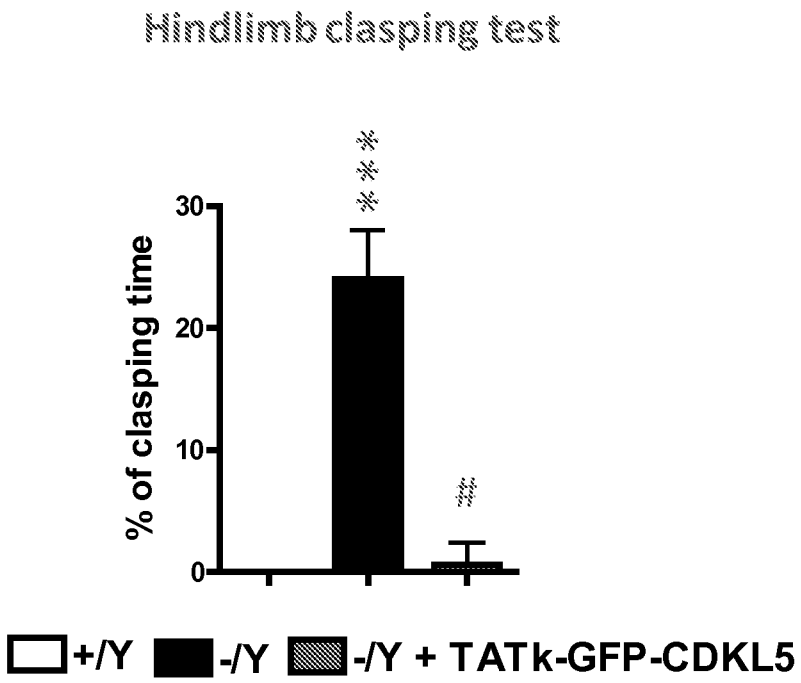


Fig. 35A

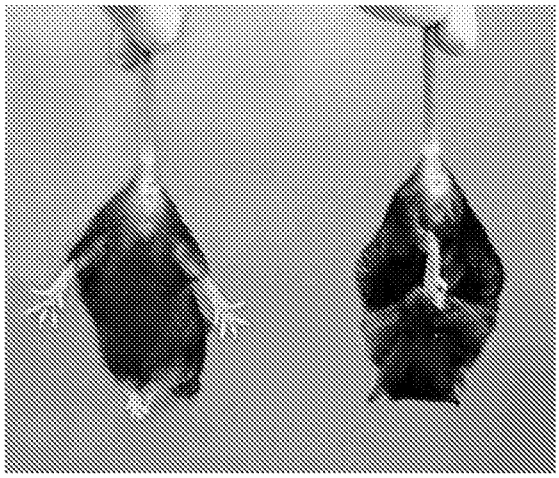


Fig. 35B

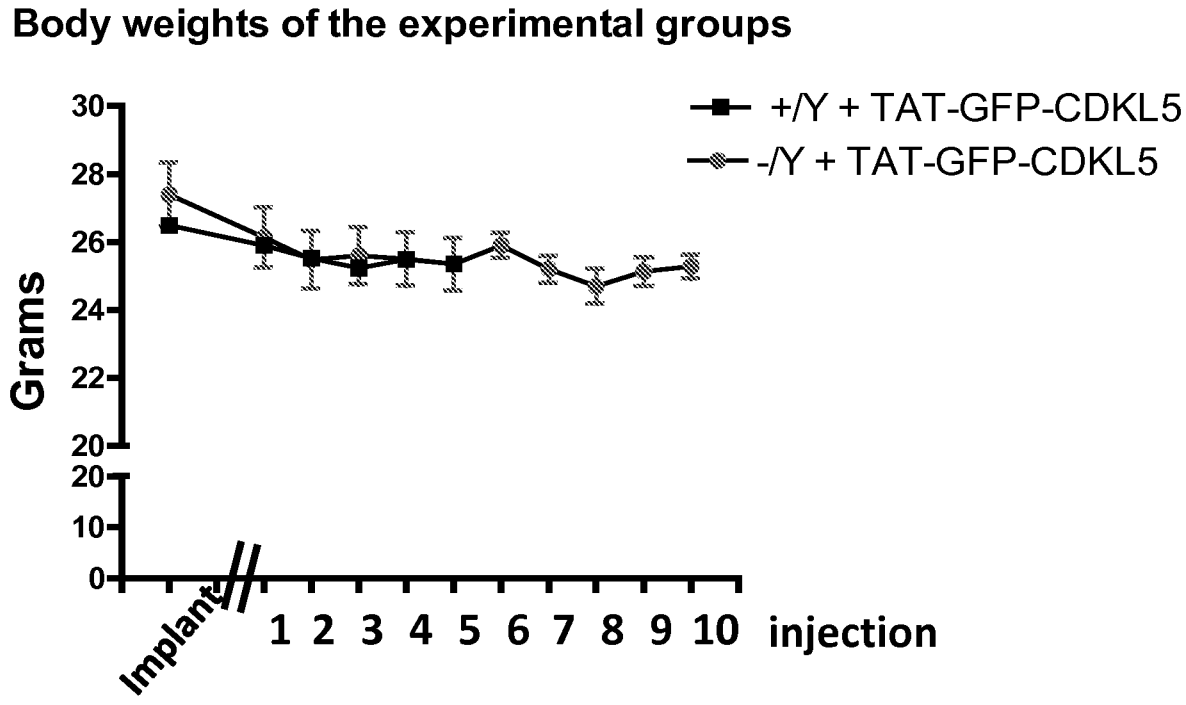

Body weights of the experimental groups
+/Y + TAT-GFP-CDKL5
-/Y + TAT-GFP-CDKL5
Grams
30
28
26
24
22
20
20
10
0
Implant
1 2 3 4 5 6 7 8 9 10
injection

Fig. 36