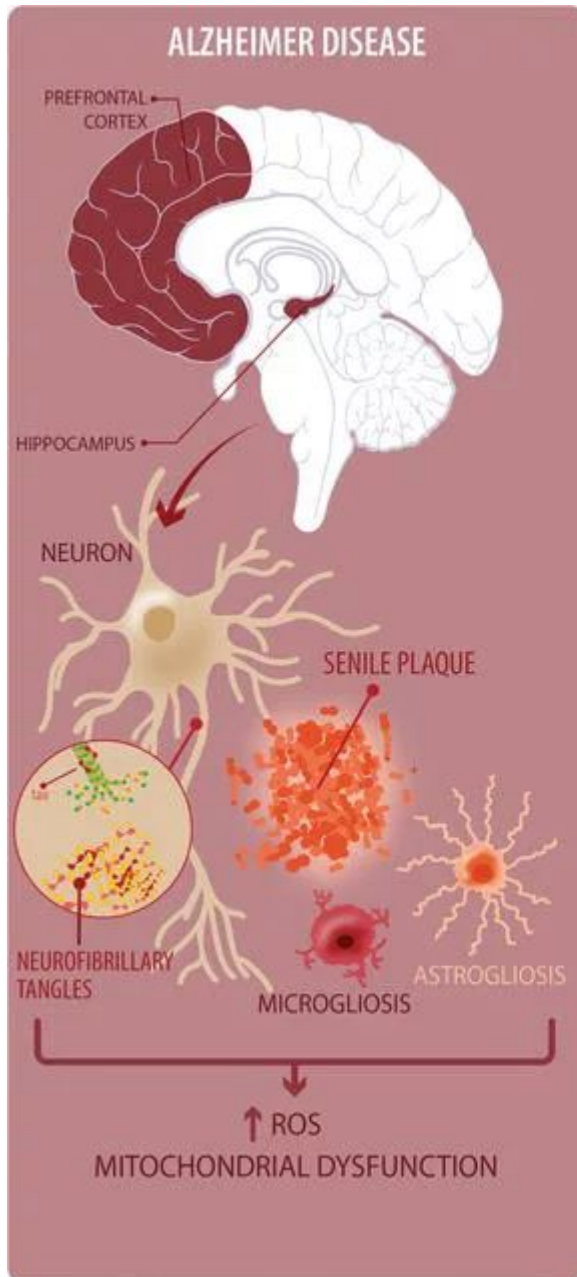




Severe reactive astrocytes precipitate pathological hallmarks of Alzheimer's disease via H_2O_2^- production

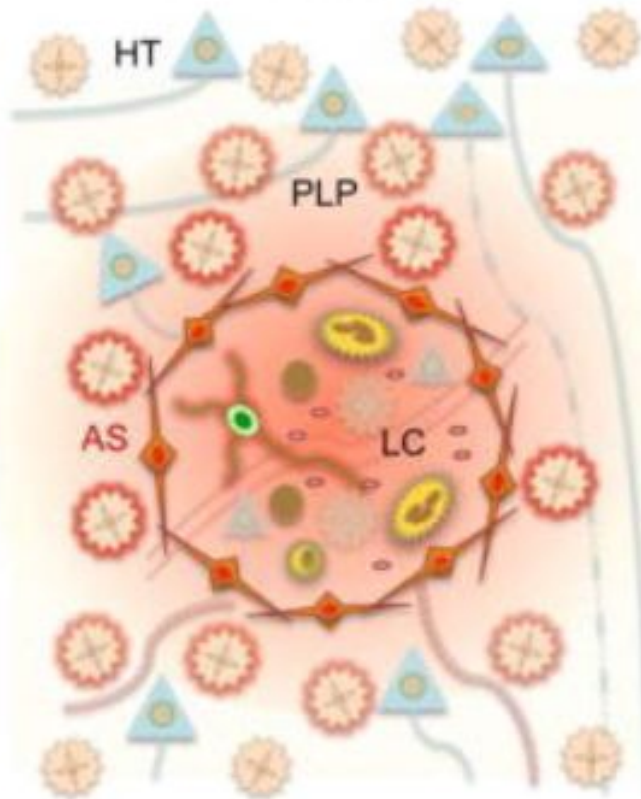
Heejung Chun ^{1,2,3}, Hyeonjoo Im³, You Jung Kang⁴, Yunha Kim³, Jin Hee Shin⁵, Woojin Won^{1,6}, Jiwoon Lim¹, Yeonha Ju^{1,7,8}, Yongmin Mason Park^{1,7,8}, Sunpil Kim^{1,6}, Seung Eun Lee⁹, Jaekwang Lee², Junsung Woo², Yujin Hwang³, Hyesun Cho^{3,10}, Seonmi Jo ^{2,11}, Jong-Hyun Park ¹², Daesoo Kim ¹¹, Doo Yeon Kim ¹³, Jeong-Sun Seo^{10,14}, Byoung Joo Gwag⁵, Young Soo Kim ¹⁵, Ki Duk Park^{8,12,16}, Bong-Kiun Kaang ¹⁷, Hansang Cho^{4,18,19}, Hoon Ryu ^{3,20}  and C. Justin Lee ^{1,2,6,7} 



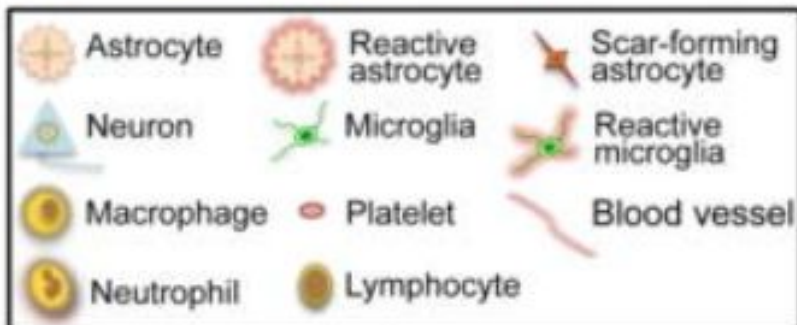
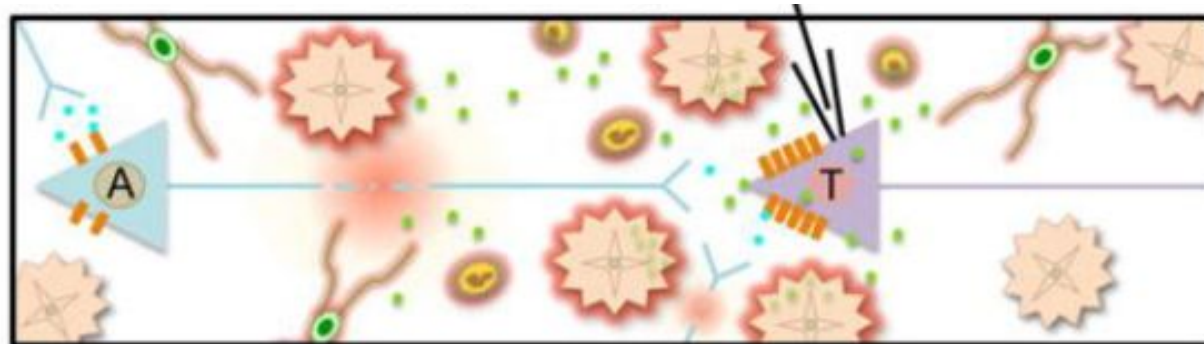
AD:

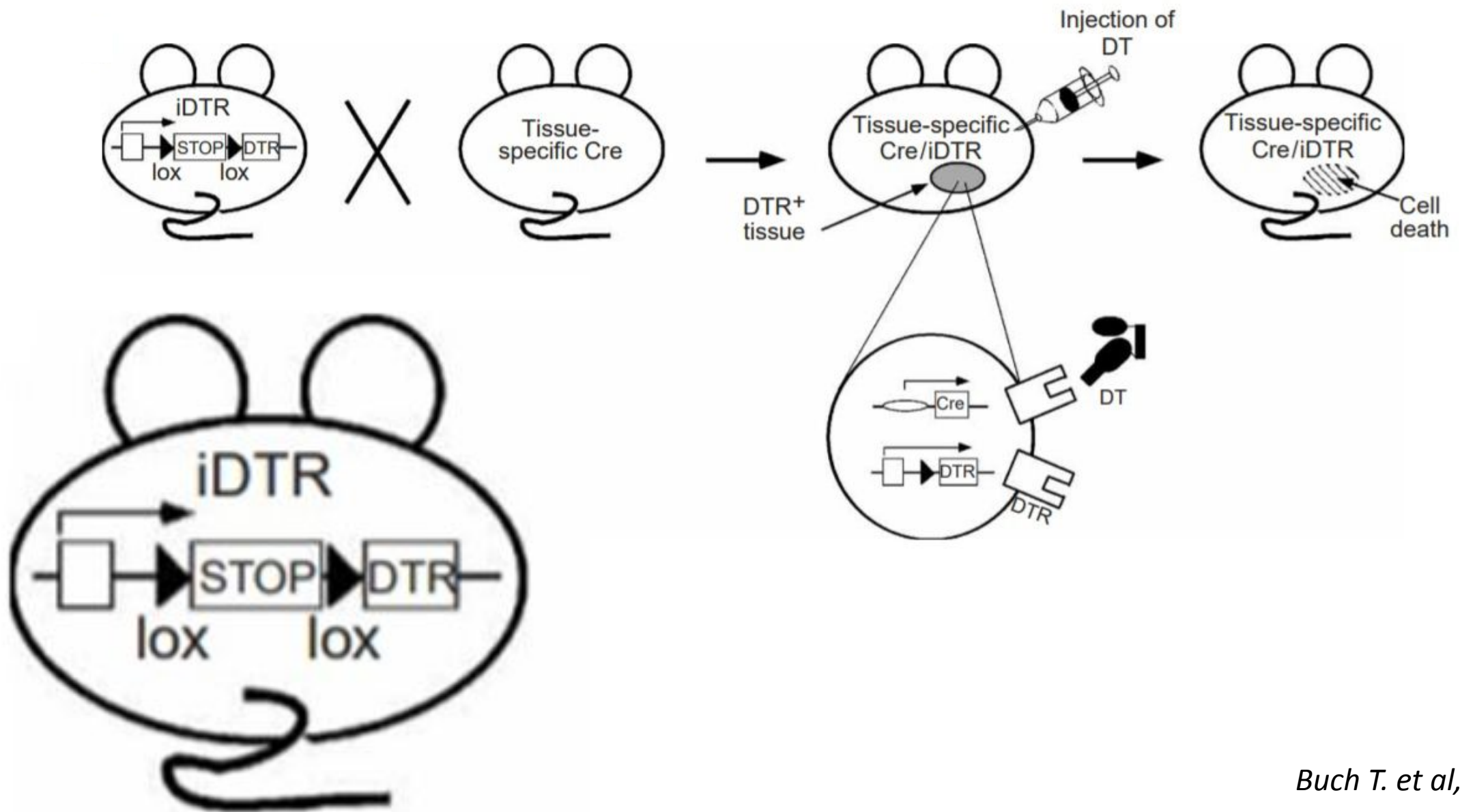
- Накопление β A и p-тау
- Мультиклеточный глиальный ответ;
нейровоспаление
 - реактивный астроглиоз
 - активация микроглии
- Нейродегенерация

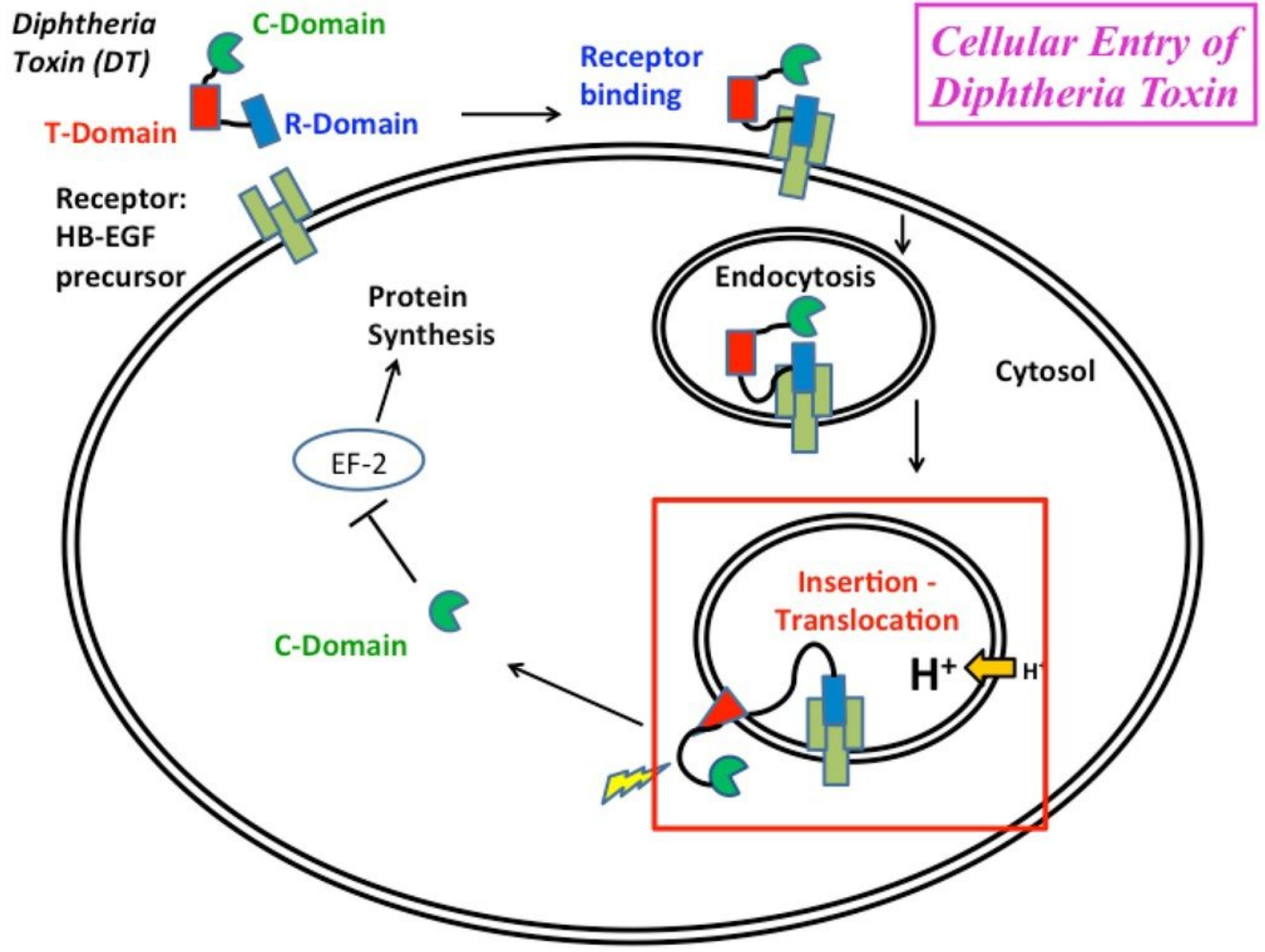
Focal lesion with scar formation

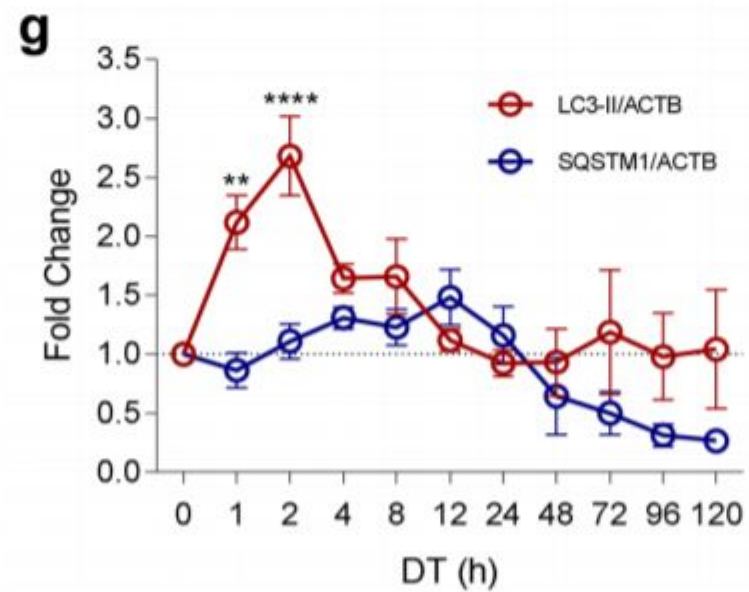
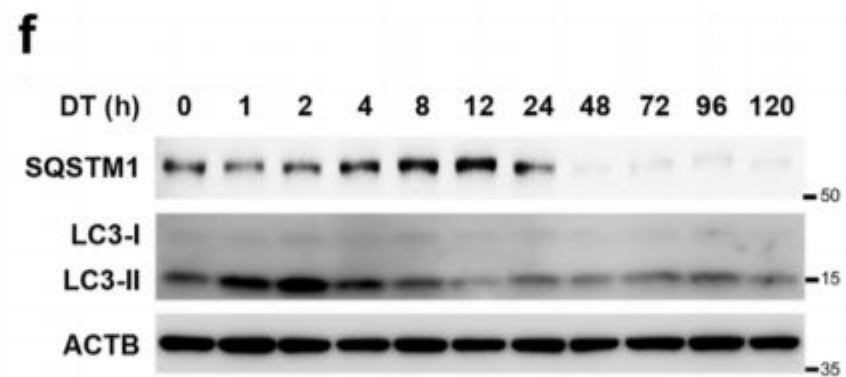
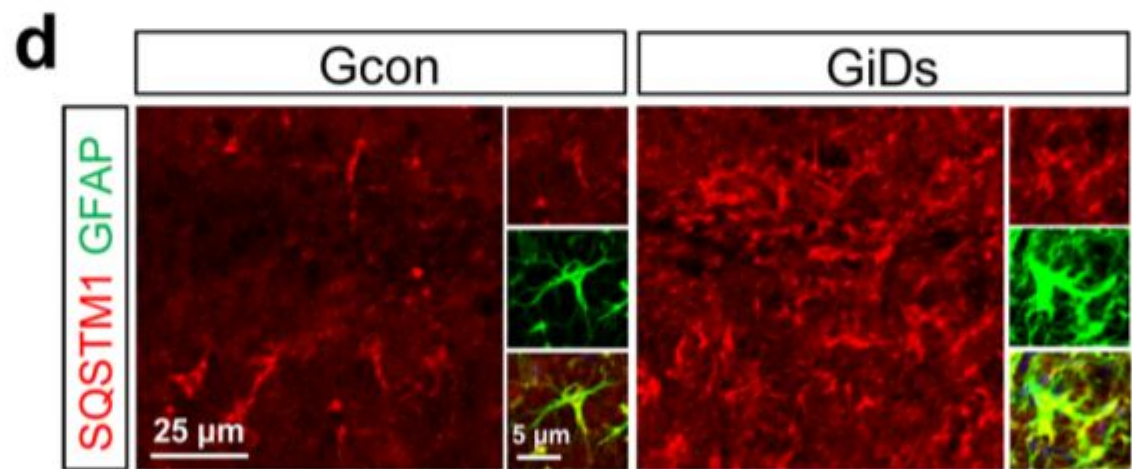
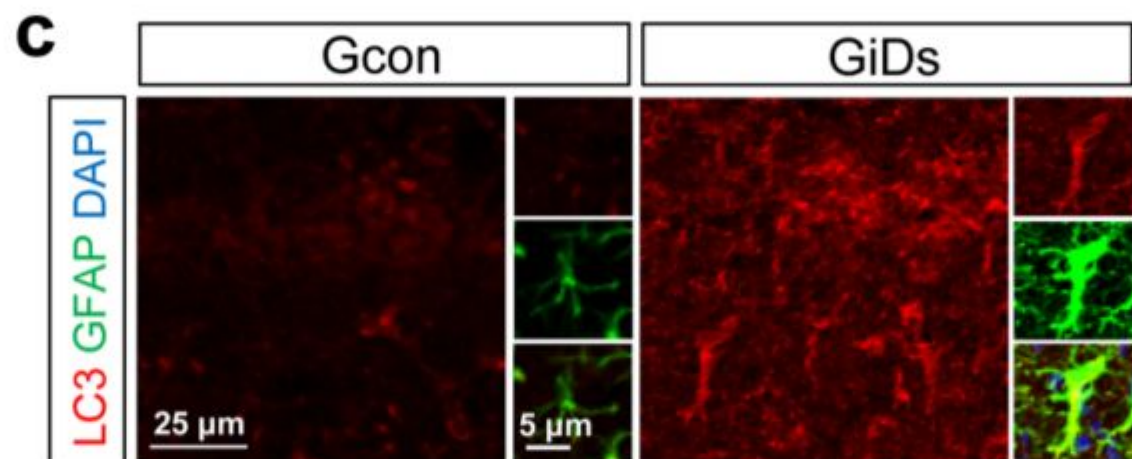


- Изоляция очага поражения
 - механический барьер
 - «химический» барьер
- Регуляция воспаления
- Регуляция проницаемости ГЭБ
- Посттравматическое ремоделирование нервной цепи
- Стимуляция регенерации

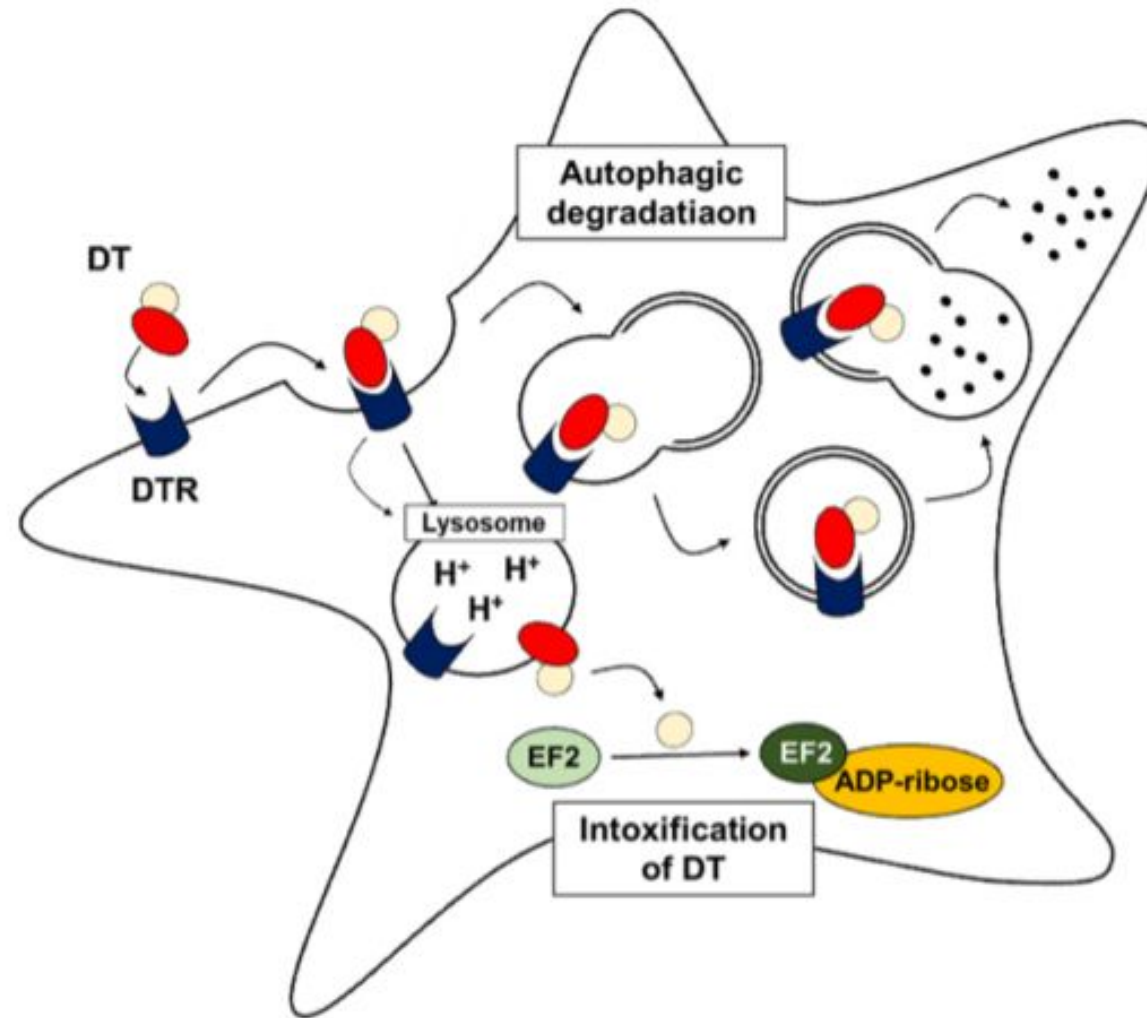


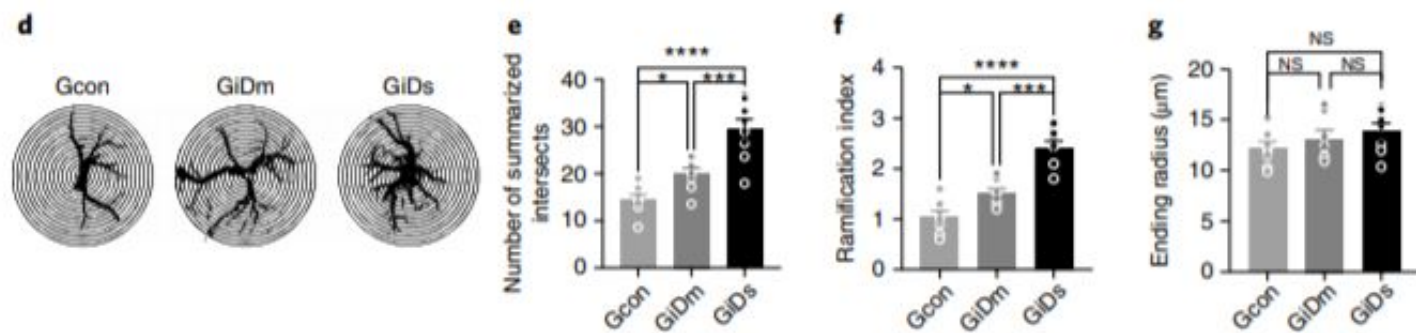
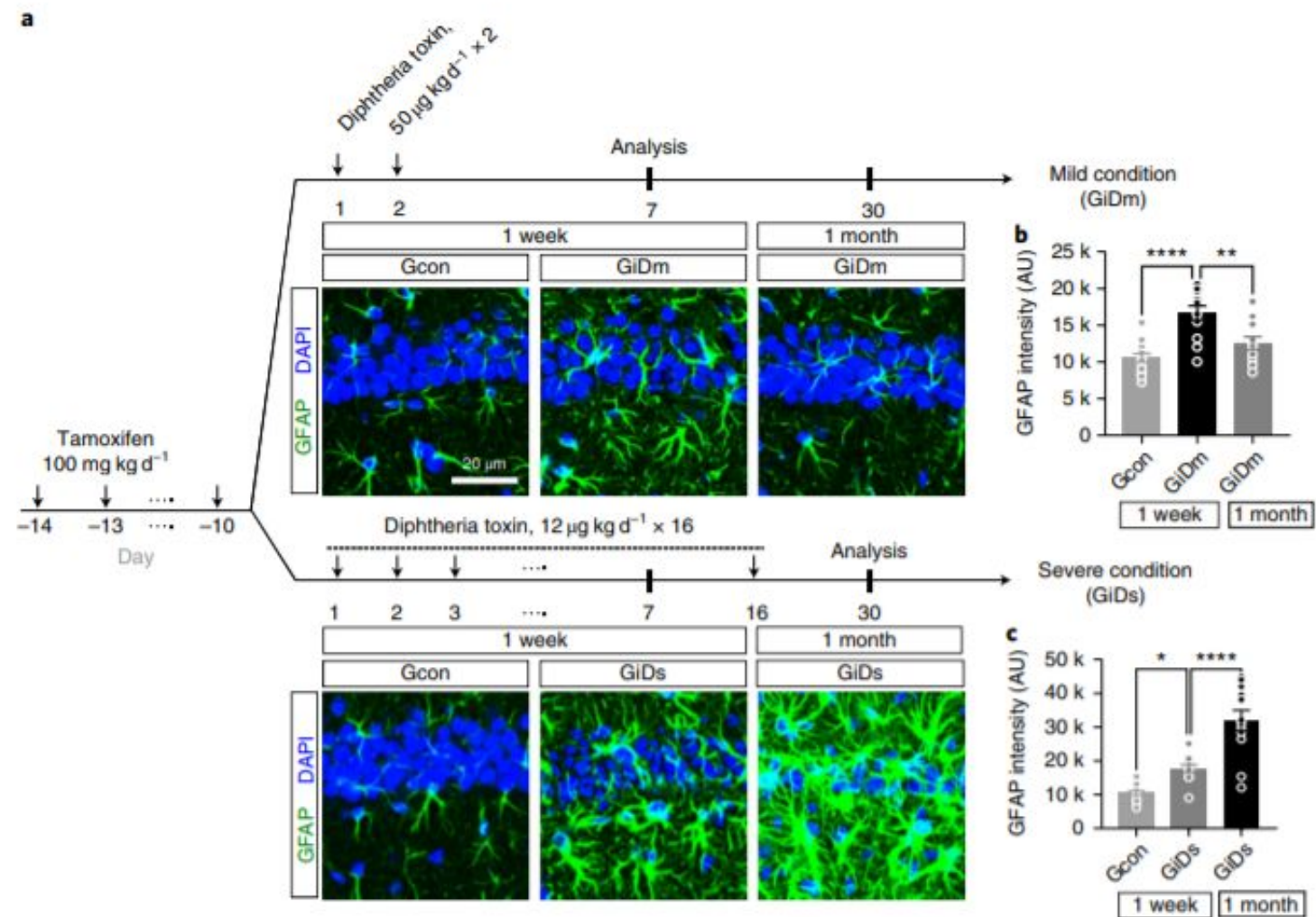


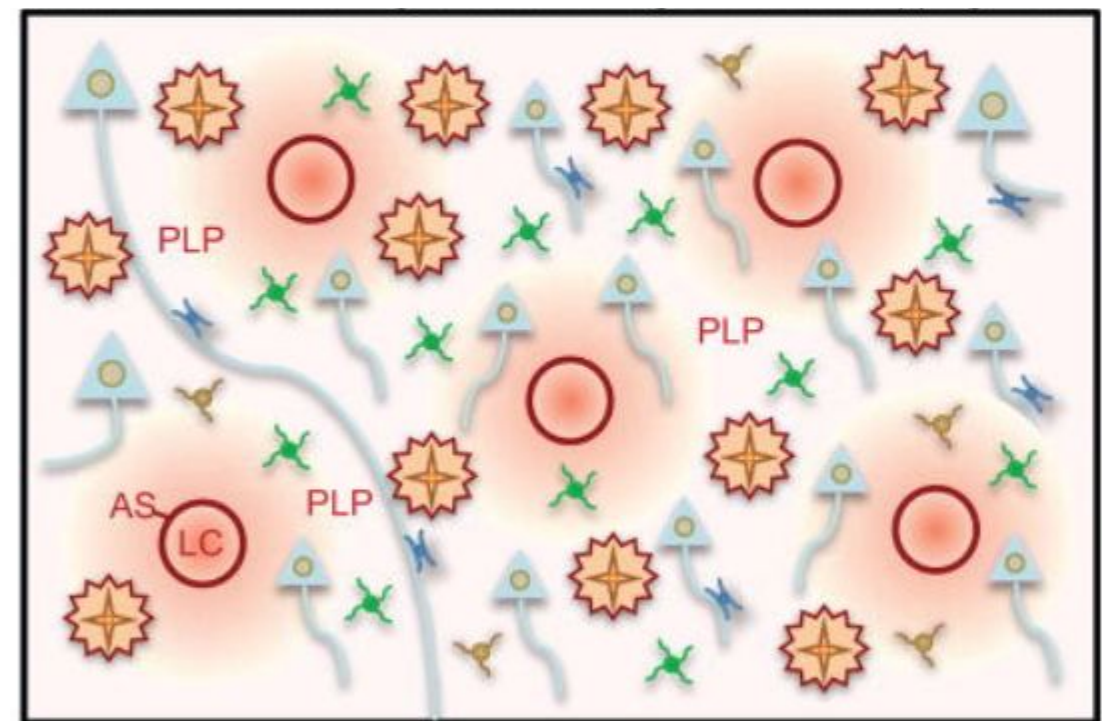
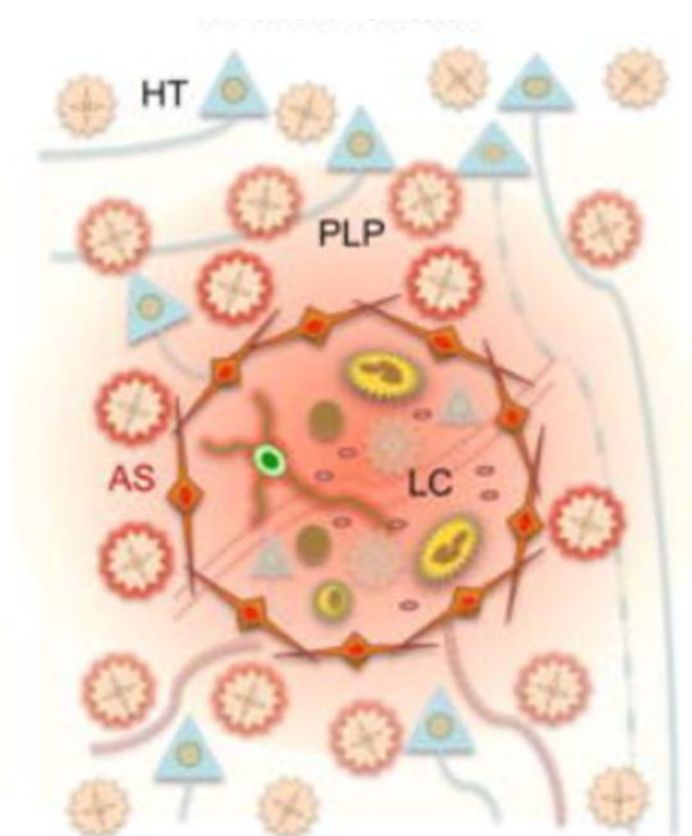




Alternative pathways of DT actions

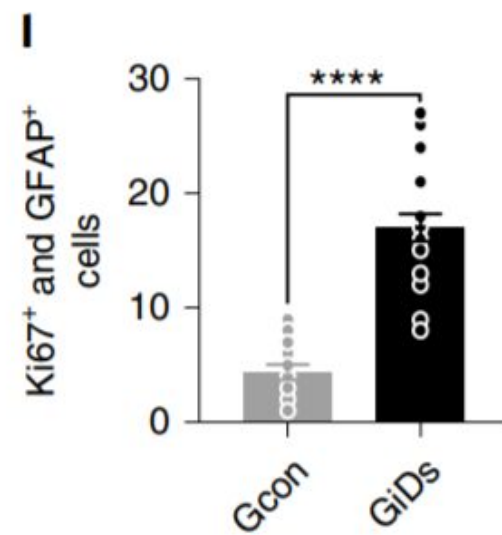
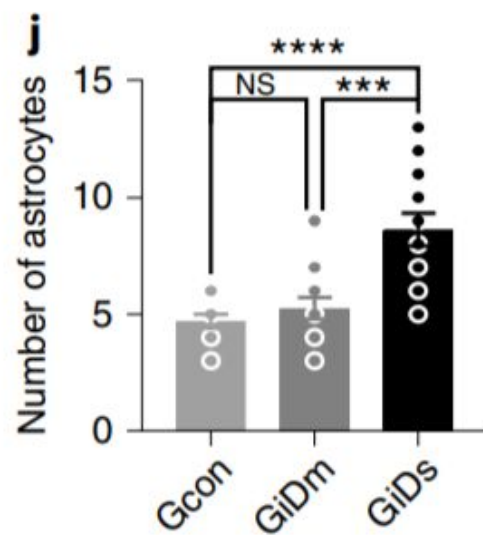
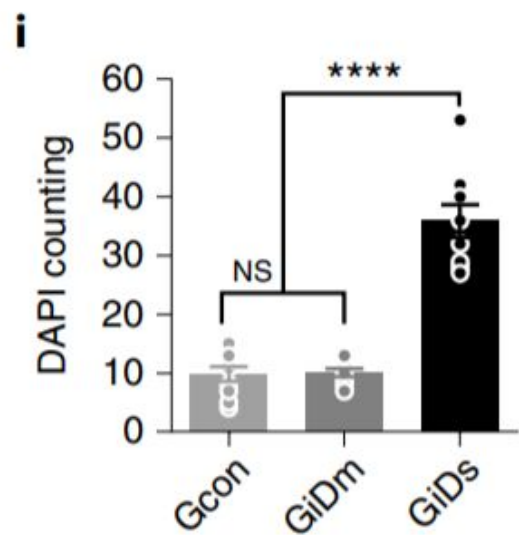
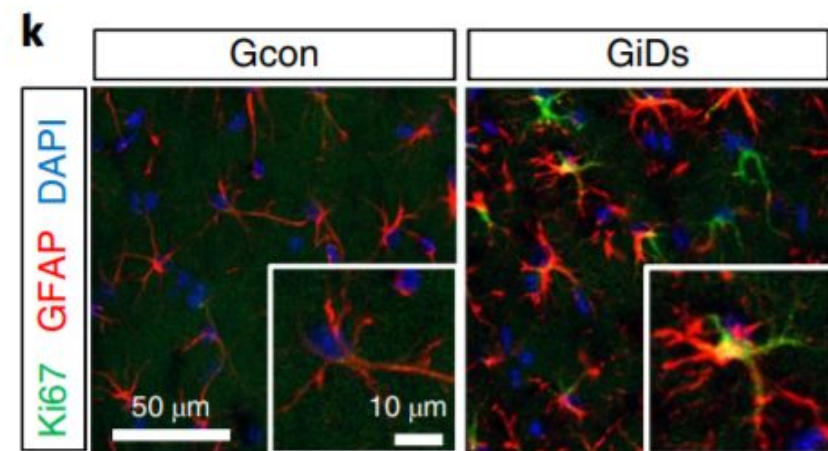
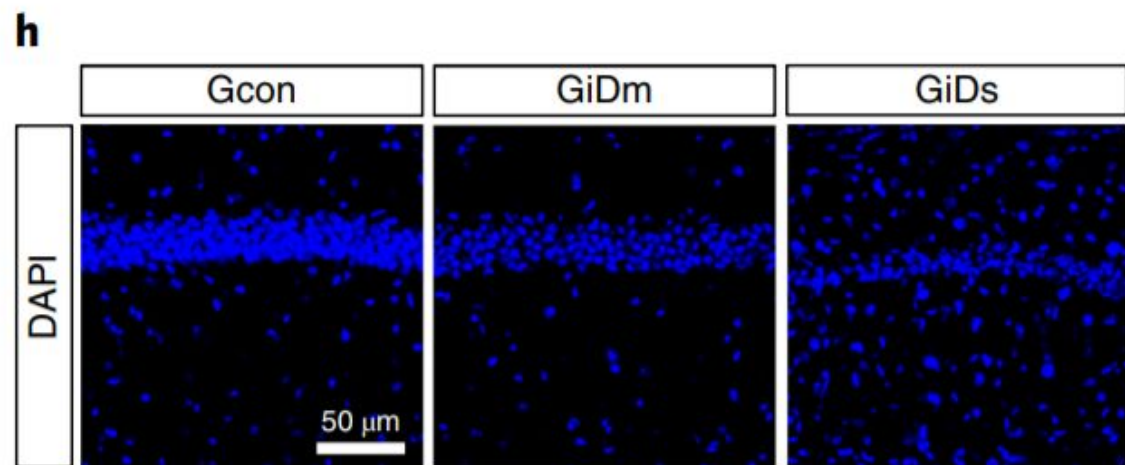


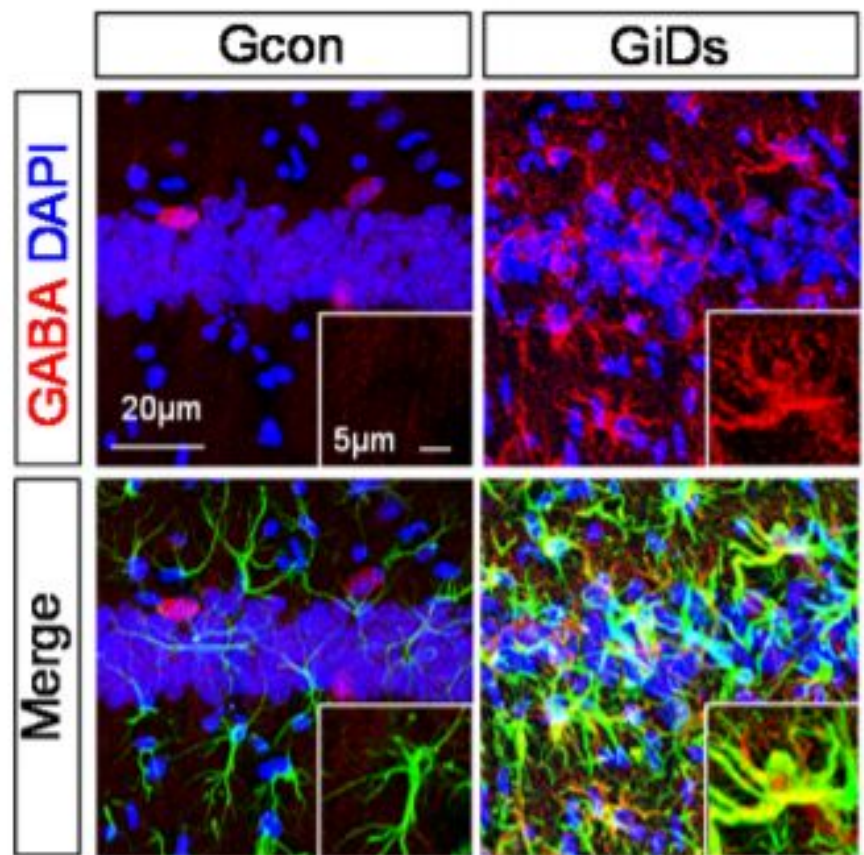




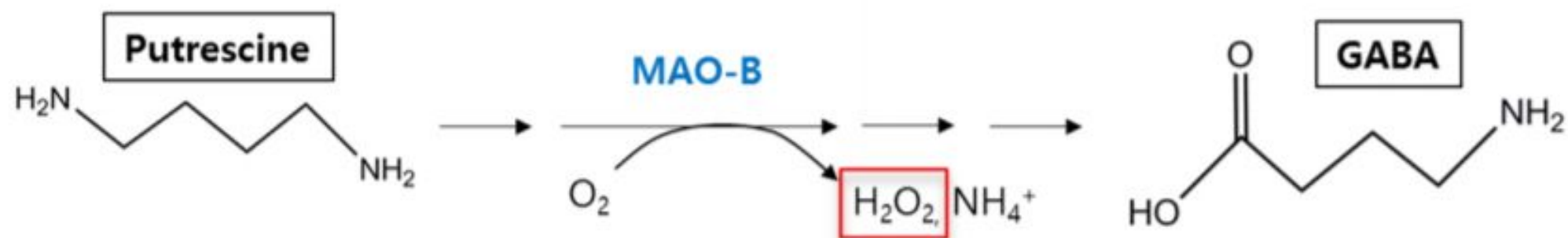
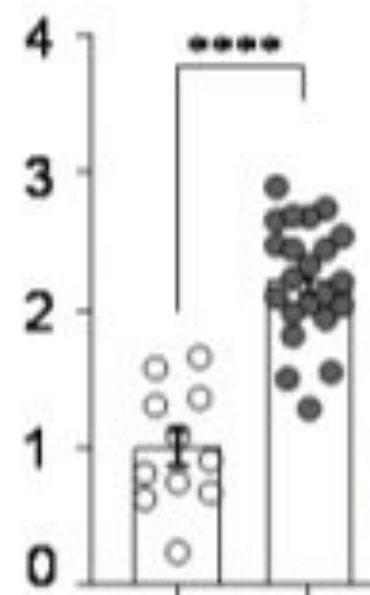
- | | | | | | |
|--|------------|--|--------------------|--|------------------------|
| | Astrocyte | | Reactive astrocyte | | Scar-forming astrocyte |
| | Neuron | | Microglia | | Reactive microglia |
| | Macrophage | | Platelet | | Blood vessel |
| | Neutrophil | | Lymphocyte | | |

Burda J. and Sofroniew M. 2016

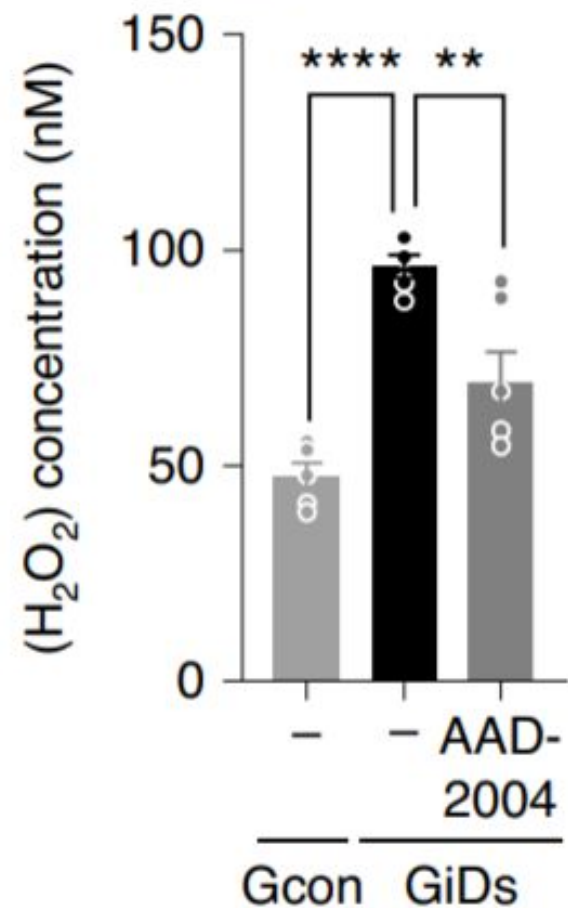
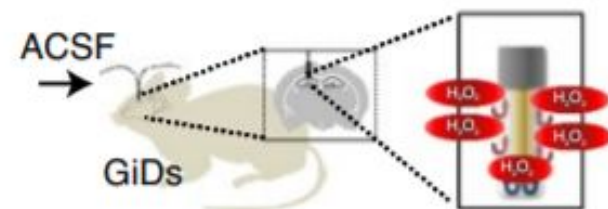
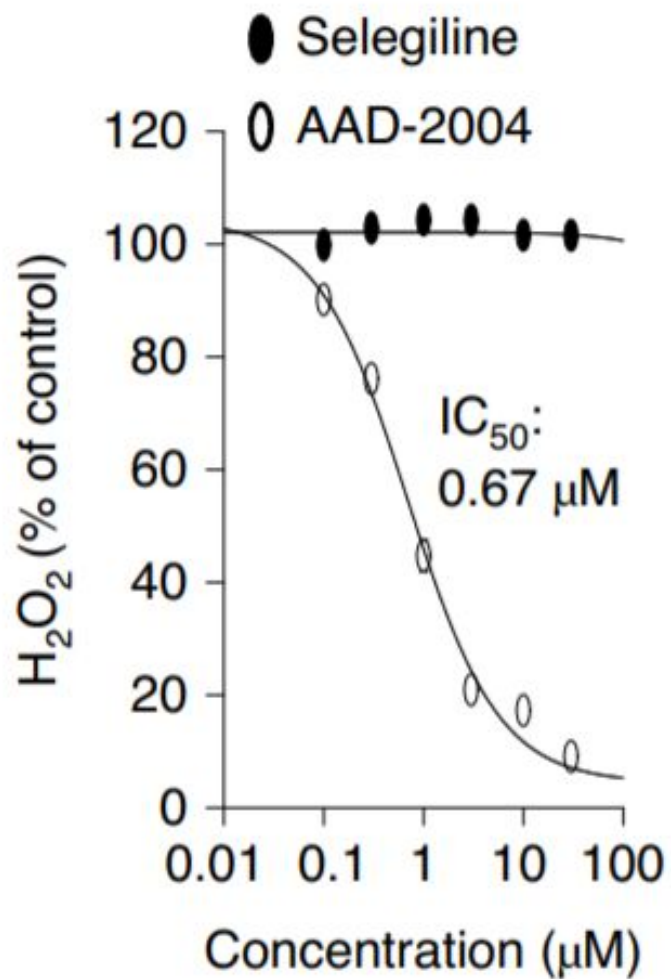
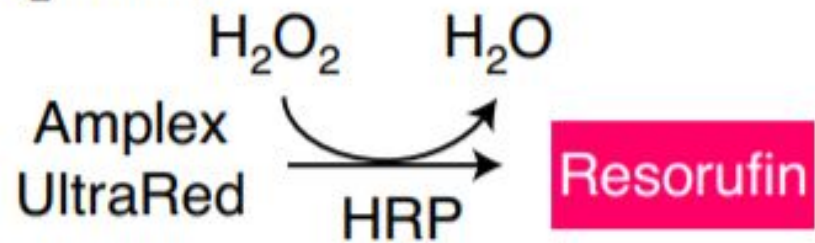


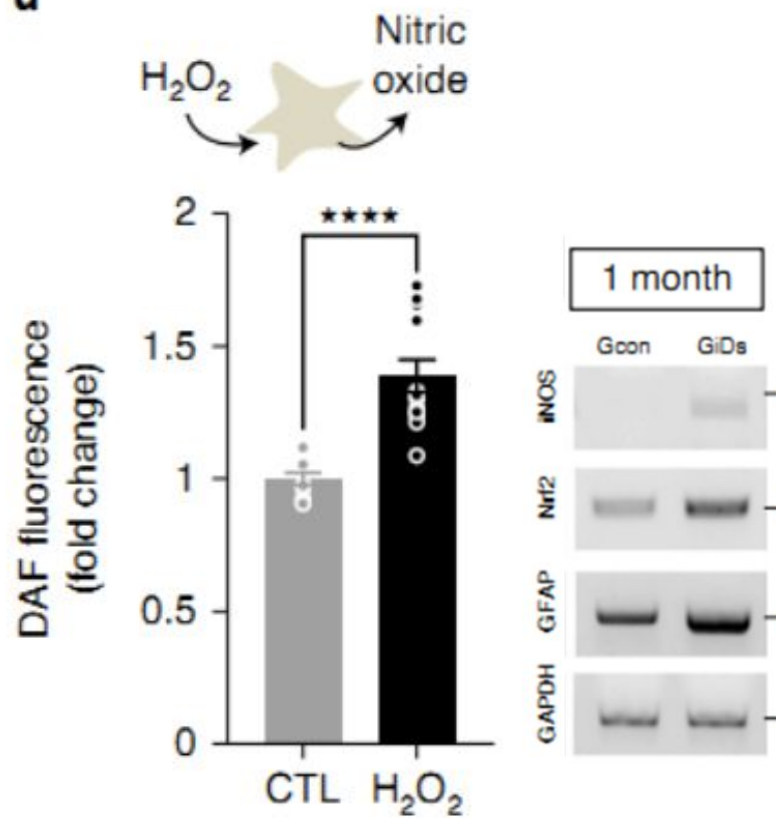
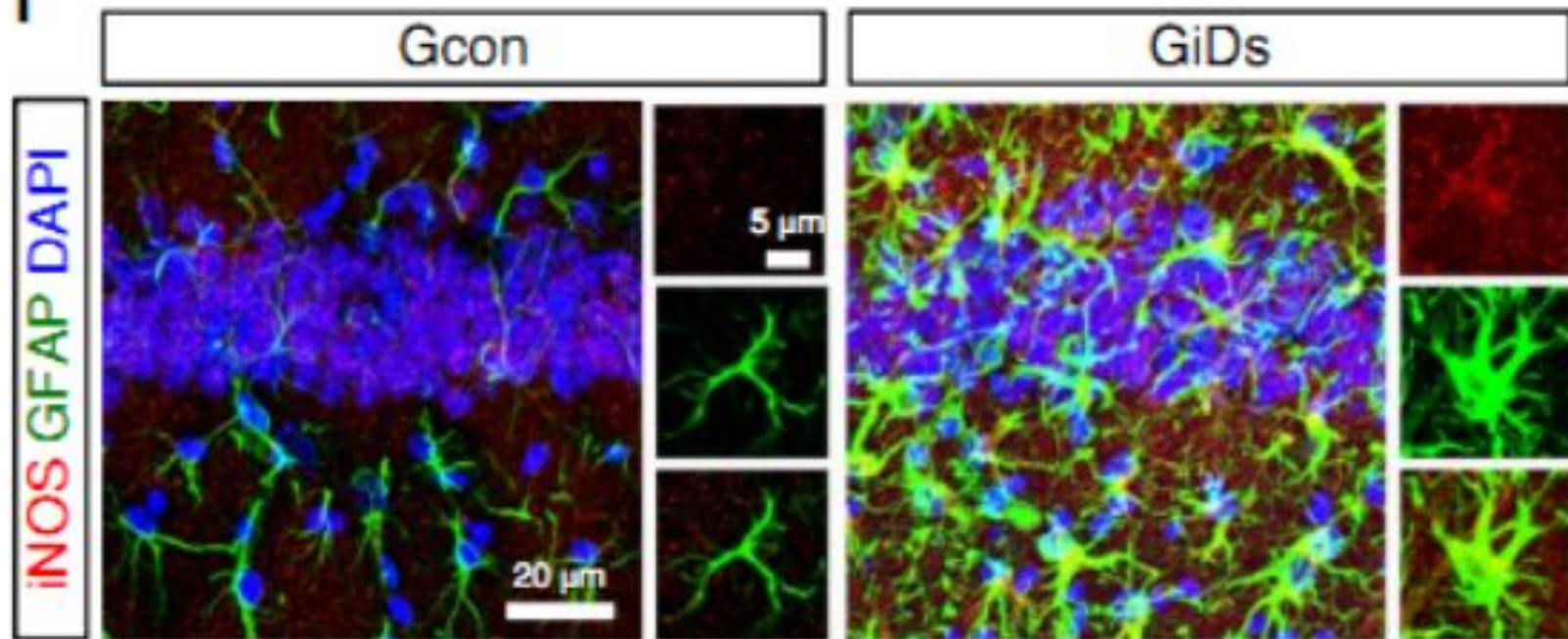


i
GABA in GFAP+
(Fold change)

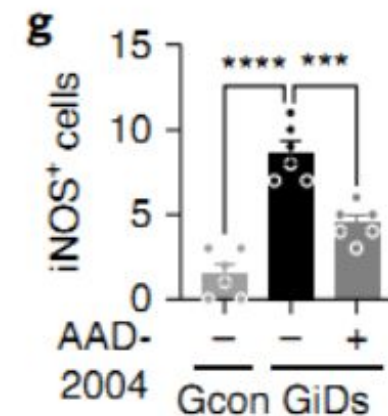
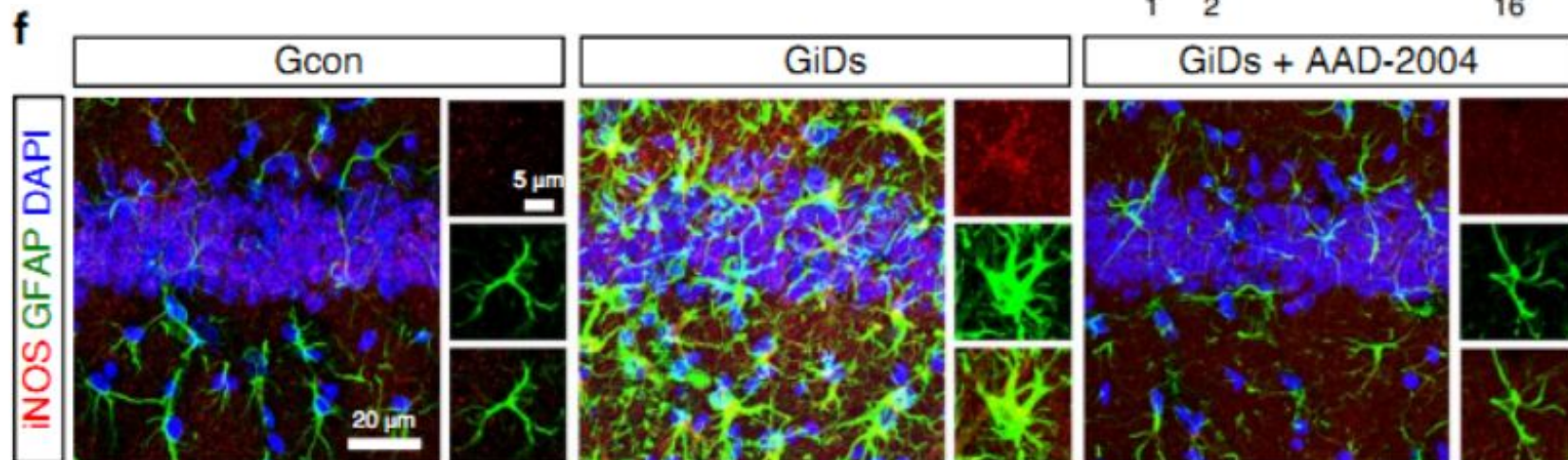
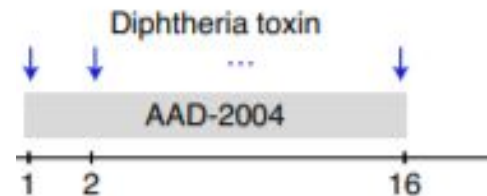


H₂O₂ assay

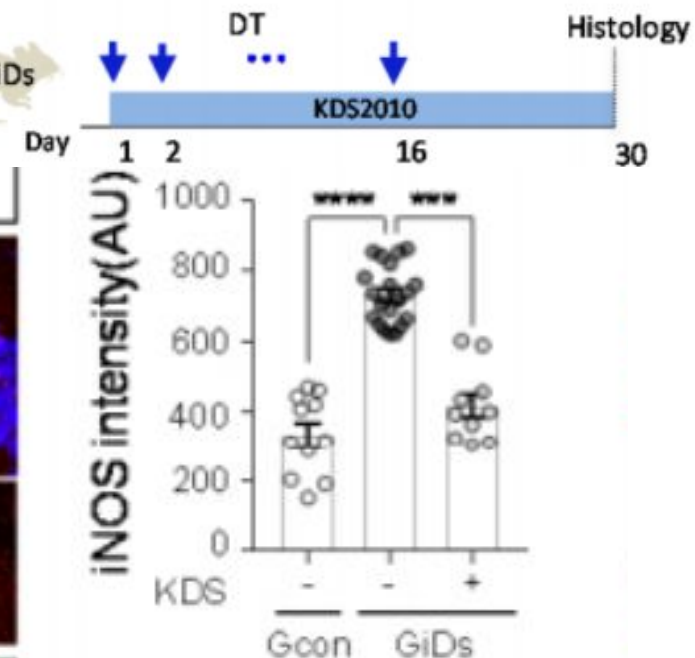
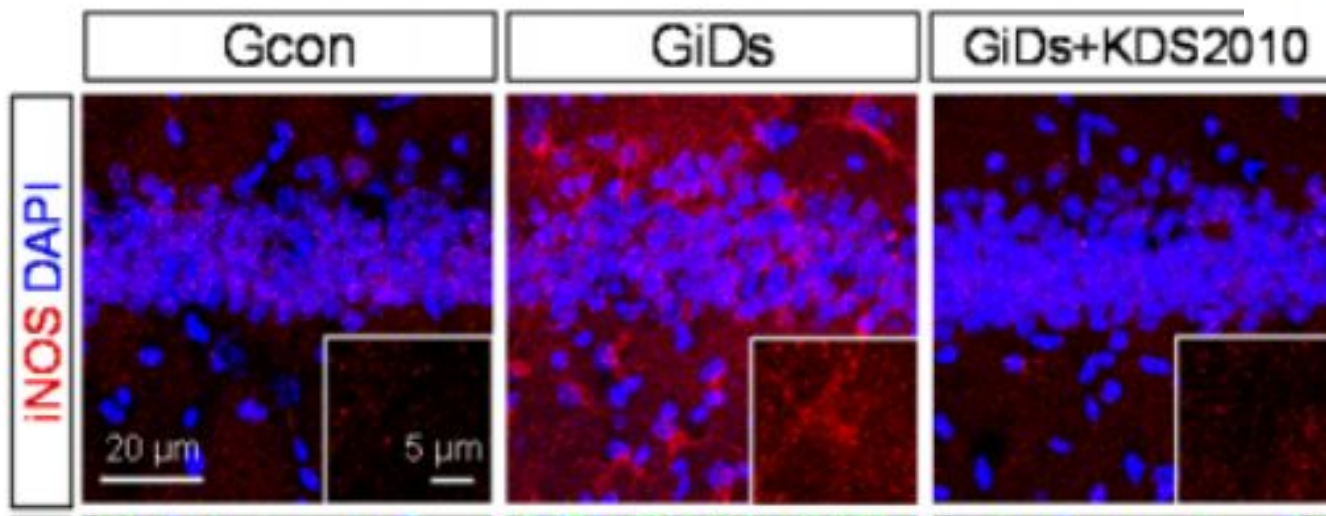
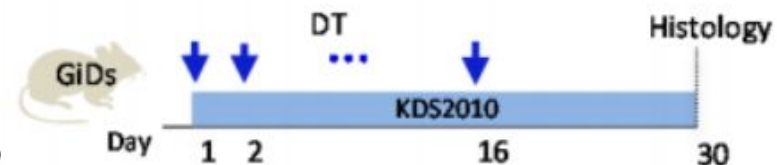


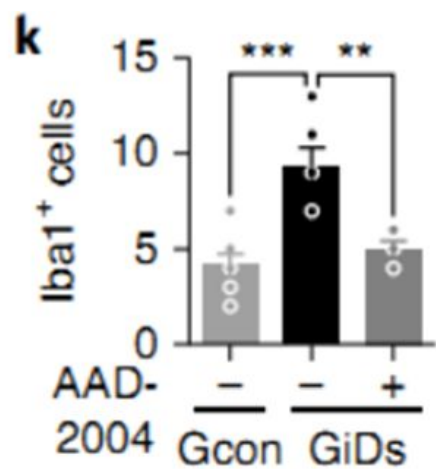
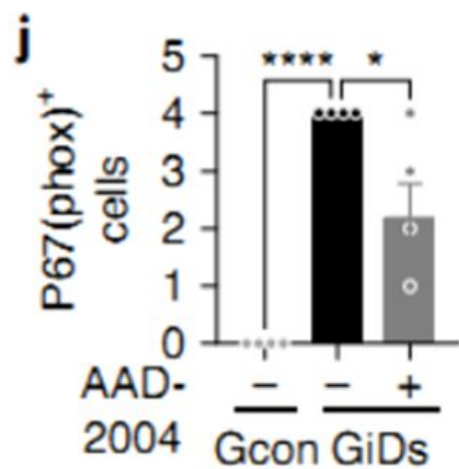
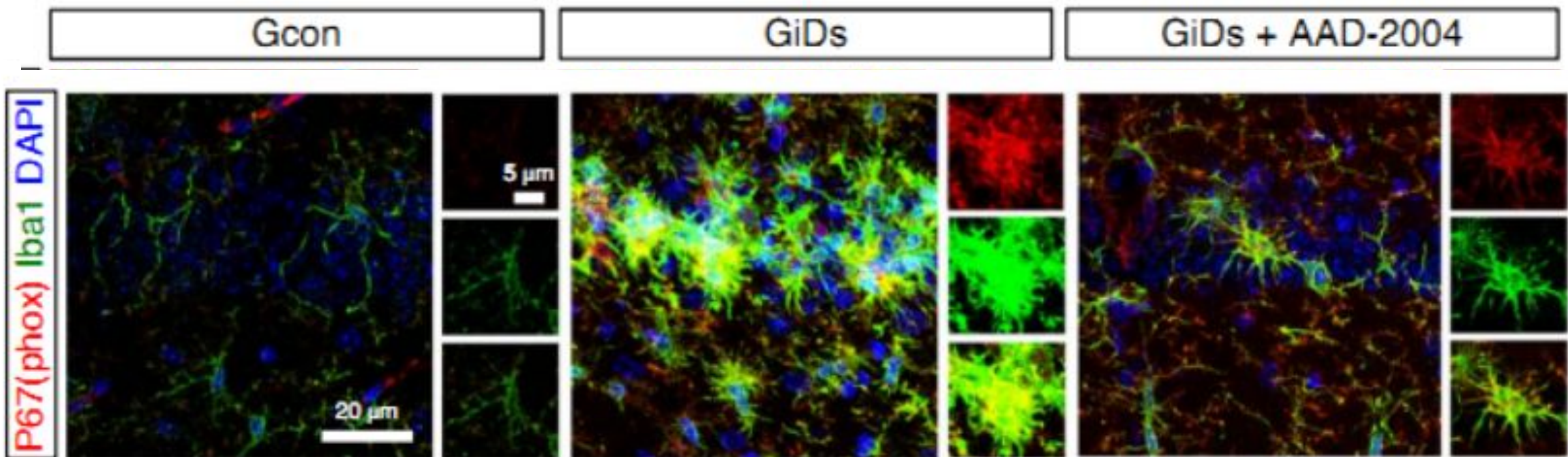
d**f**

ADD-2004 — H2O2

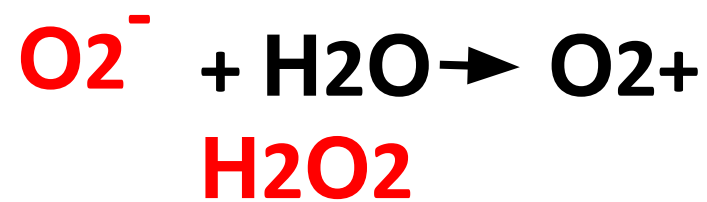


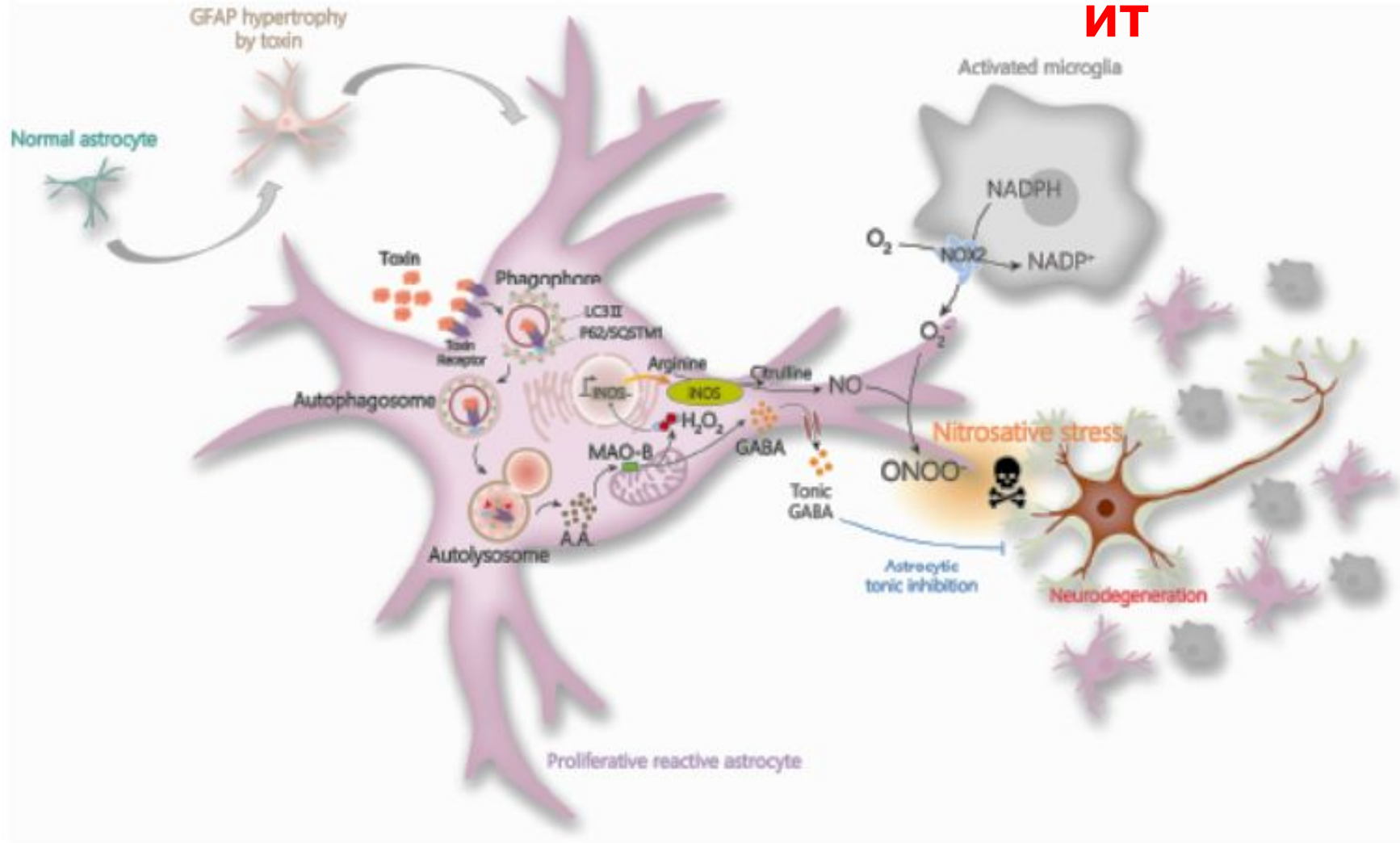
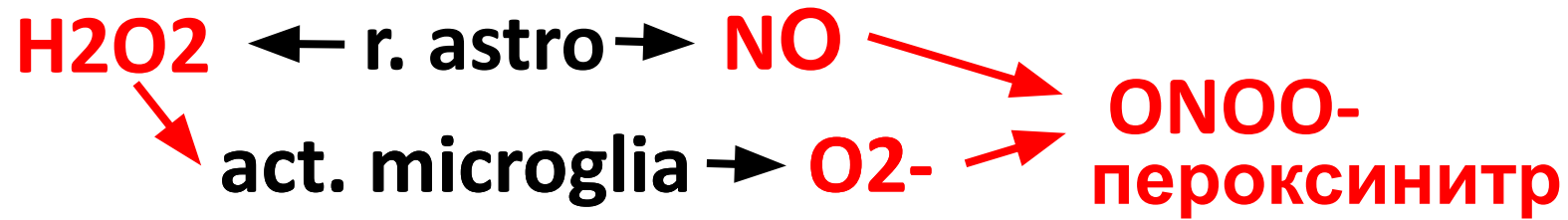
KDS2010 — MAO-B

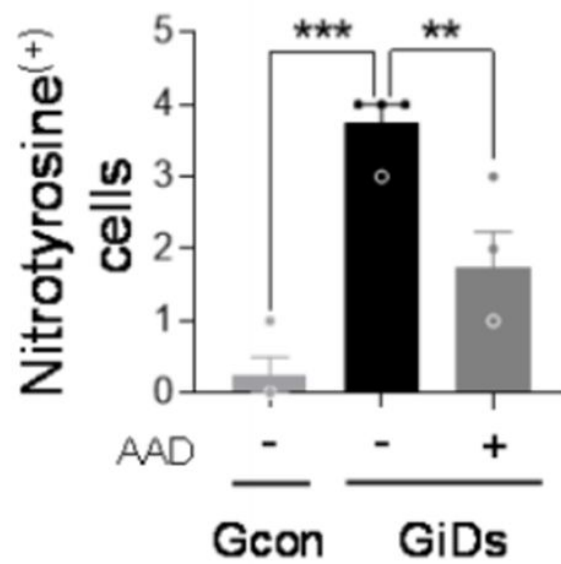
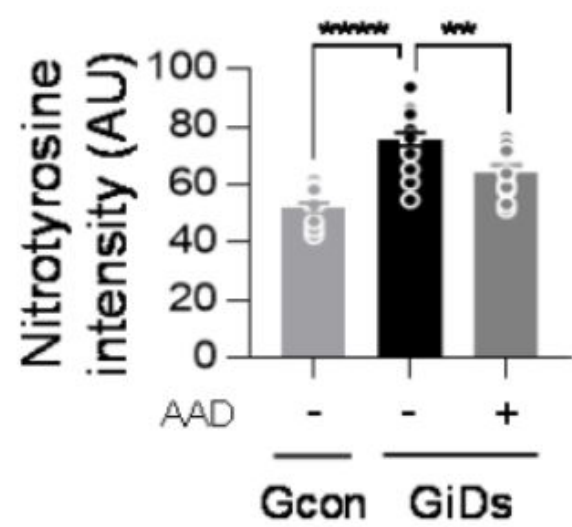
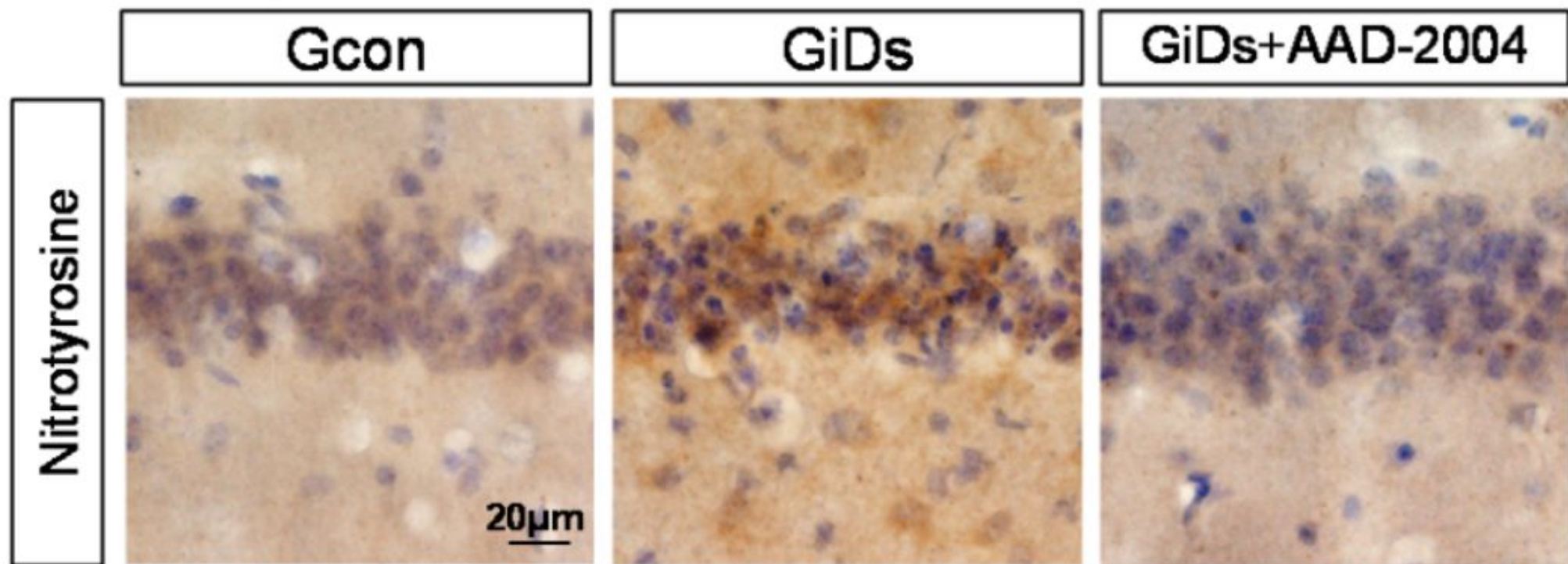


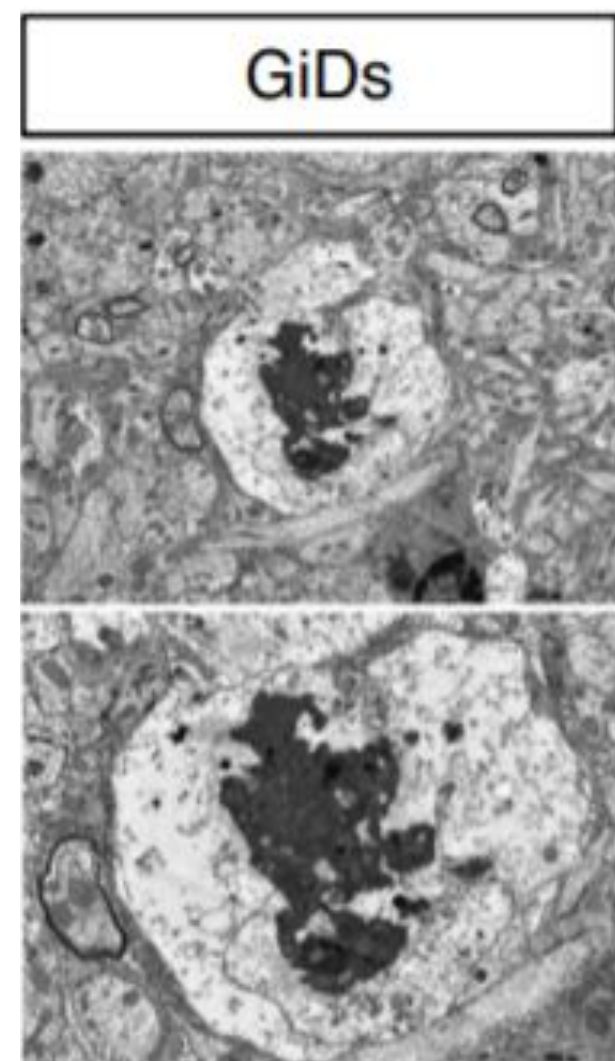
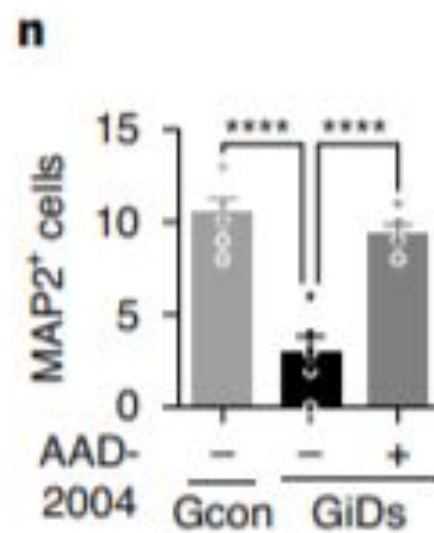
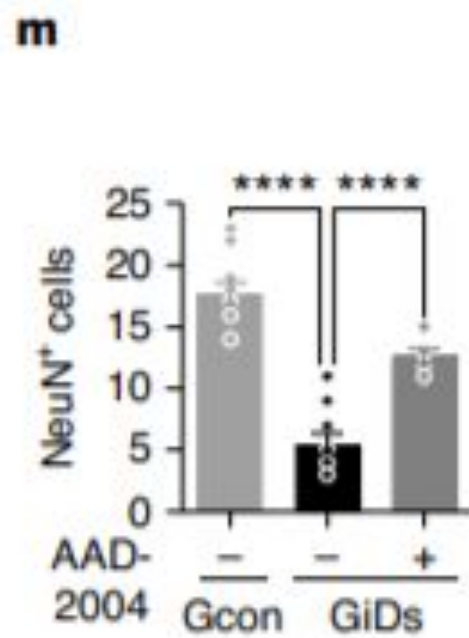
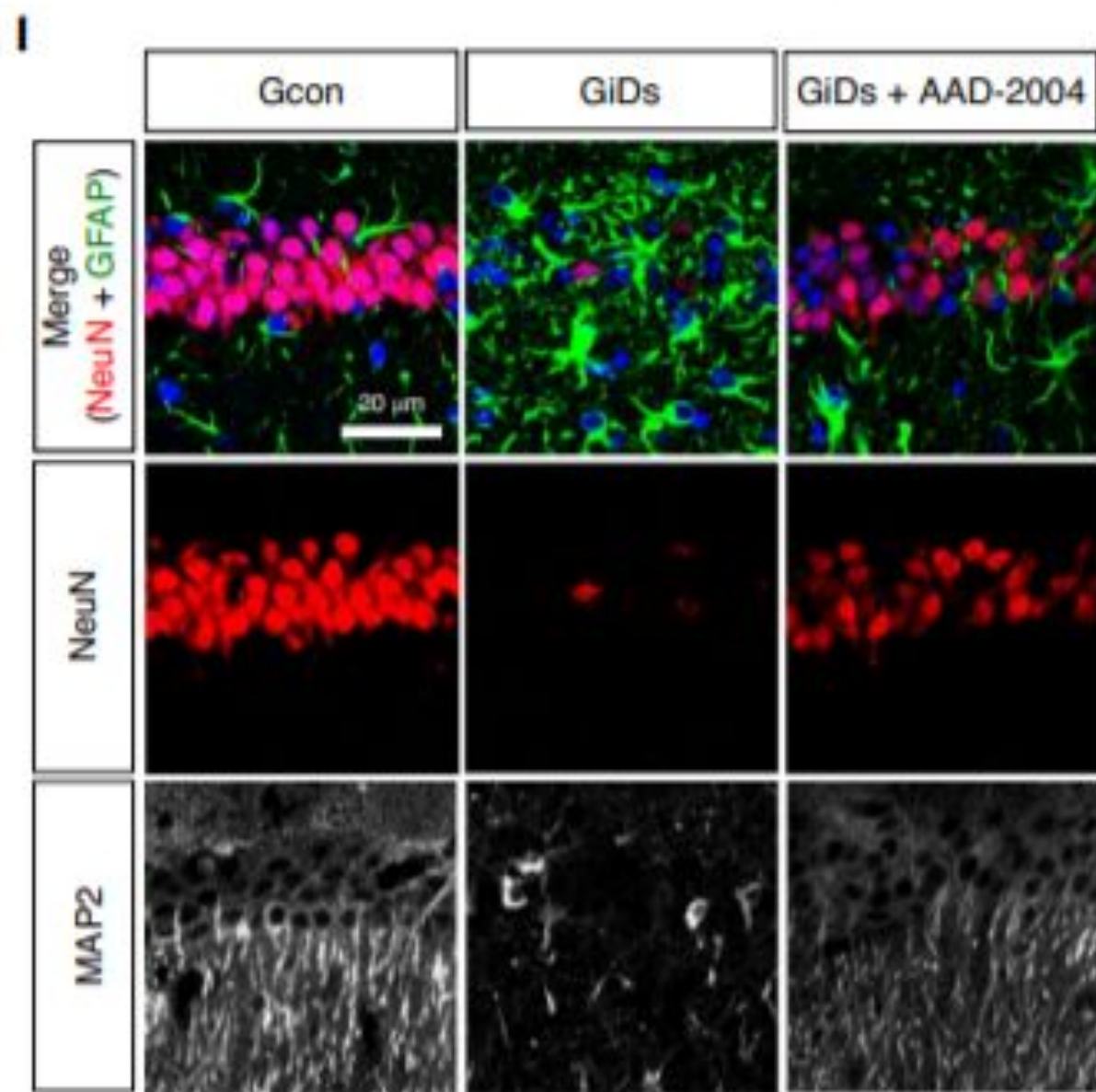


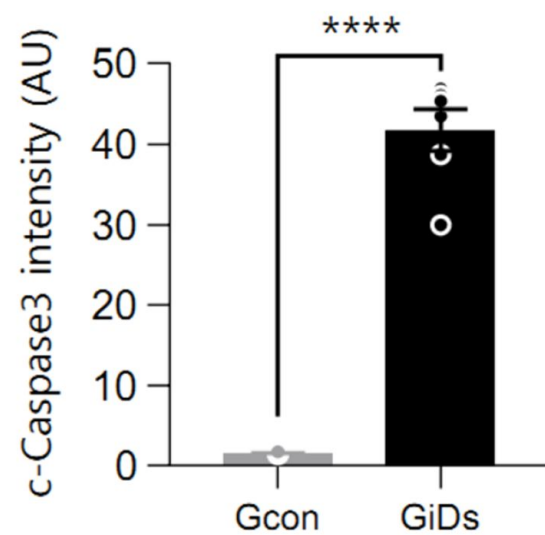
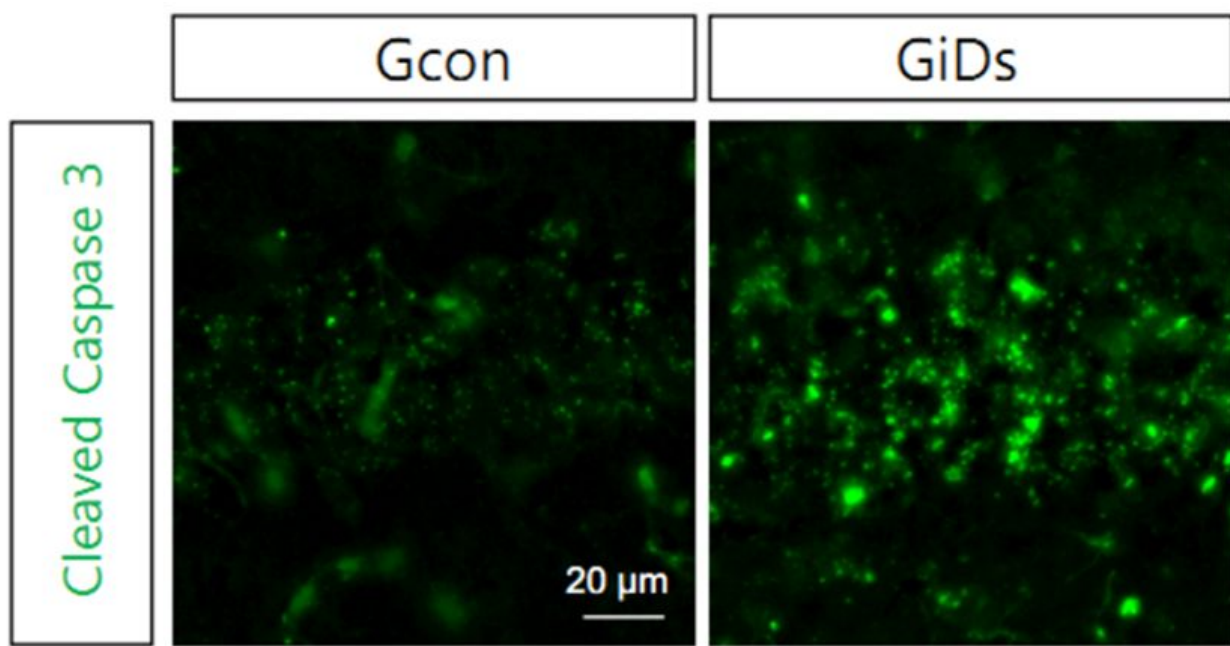
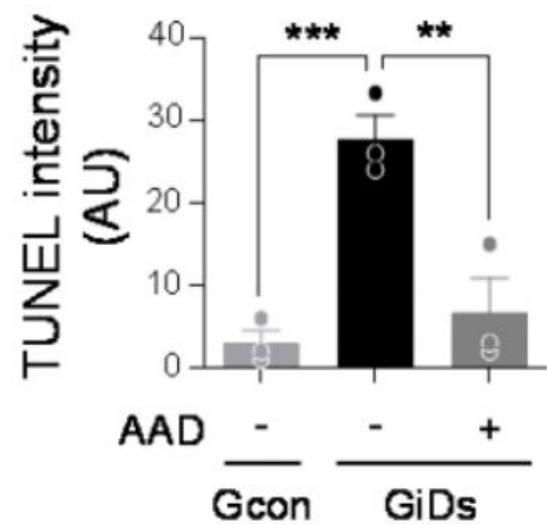
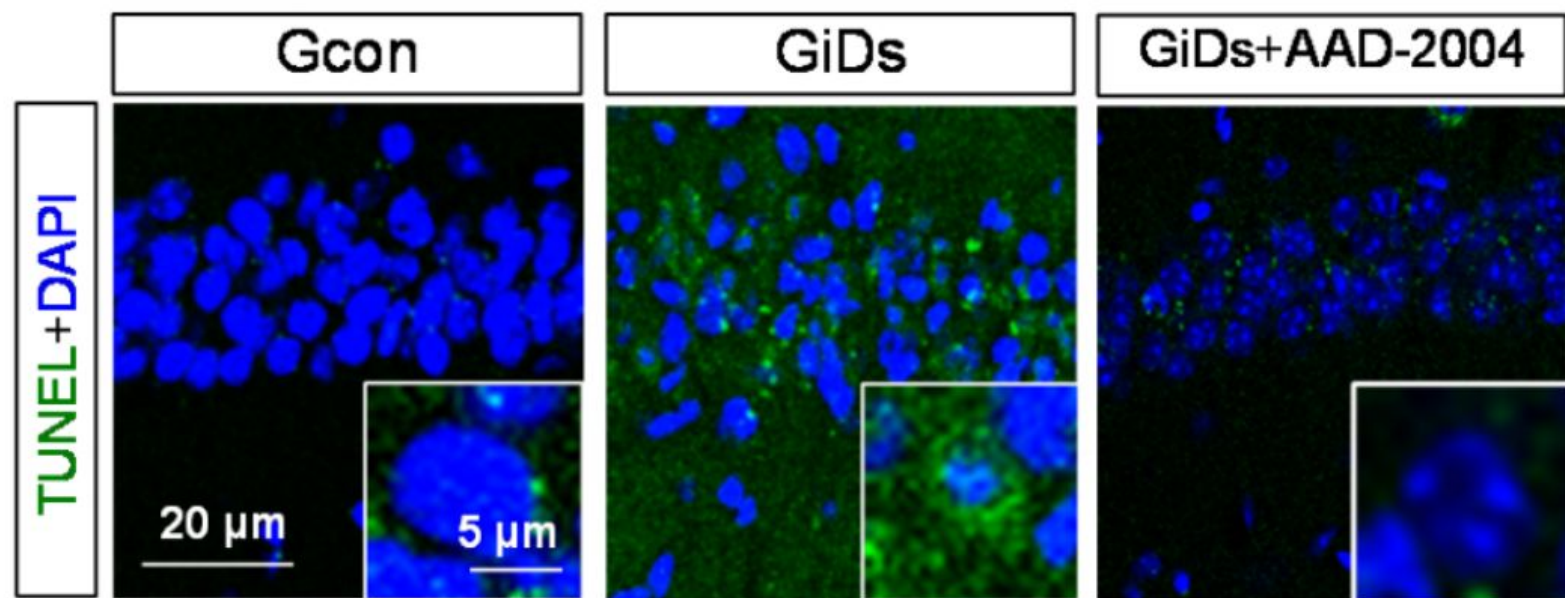
NADPH-
оксидаза-2

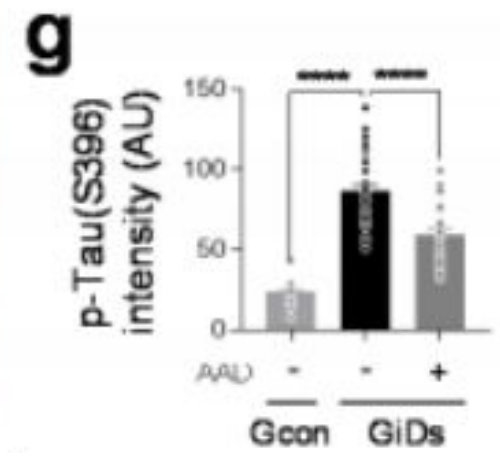
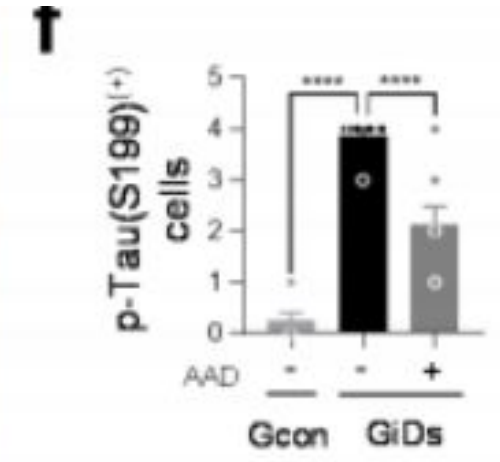
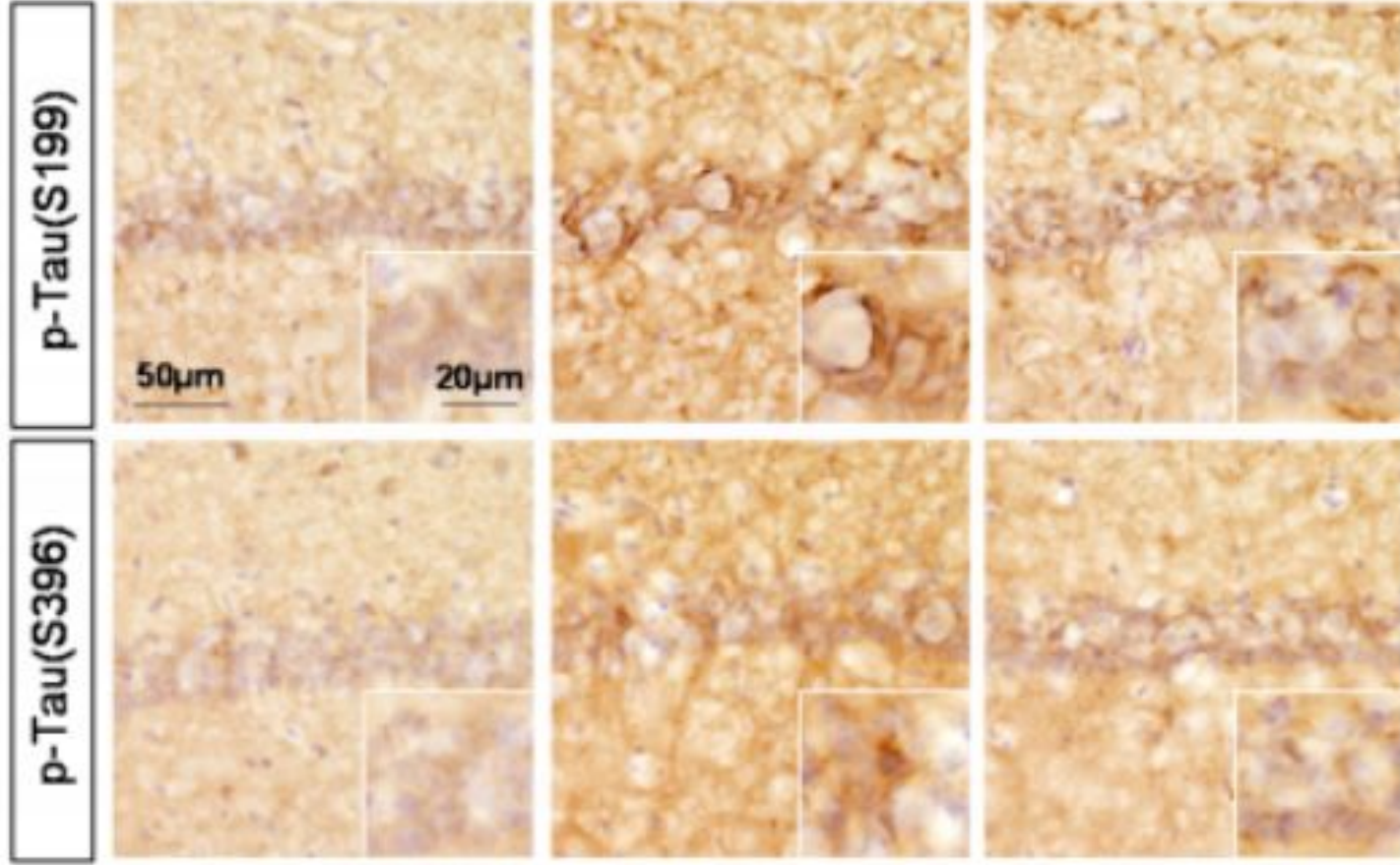




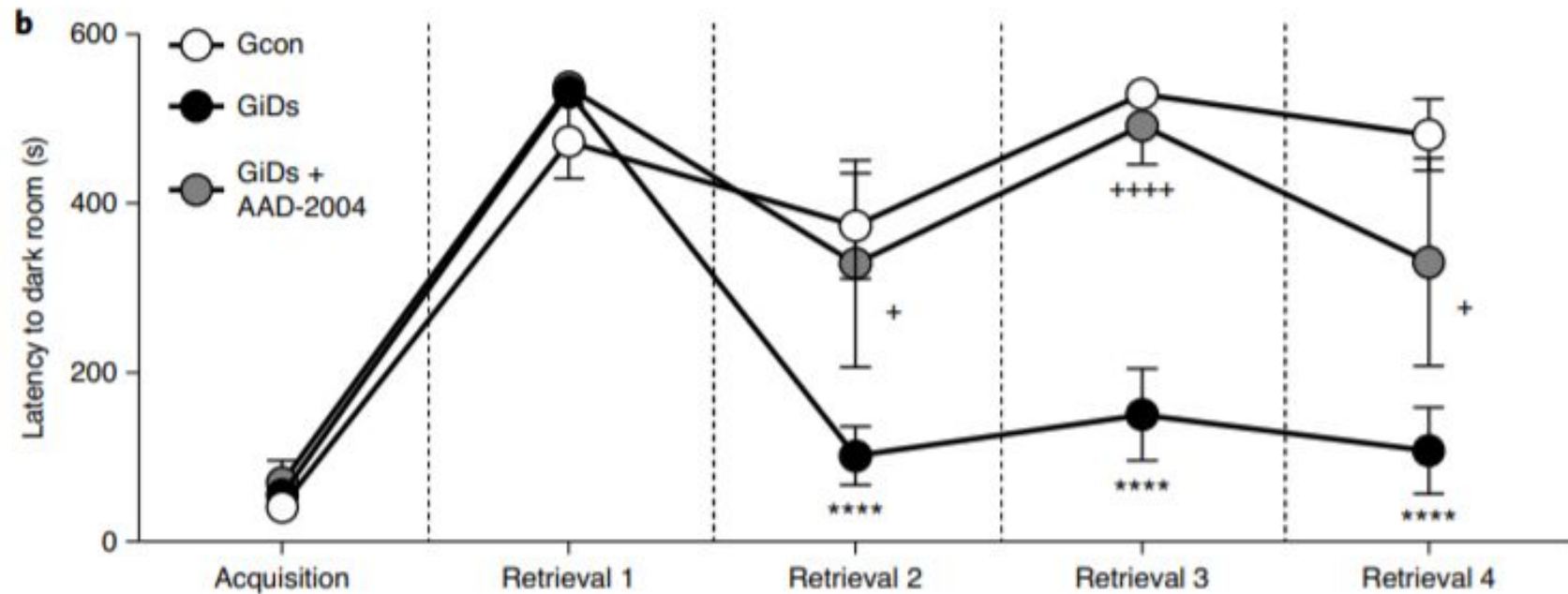
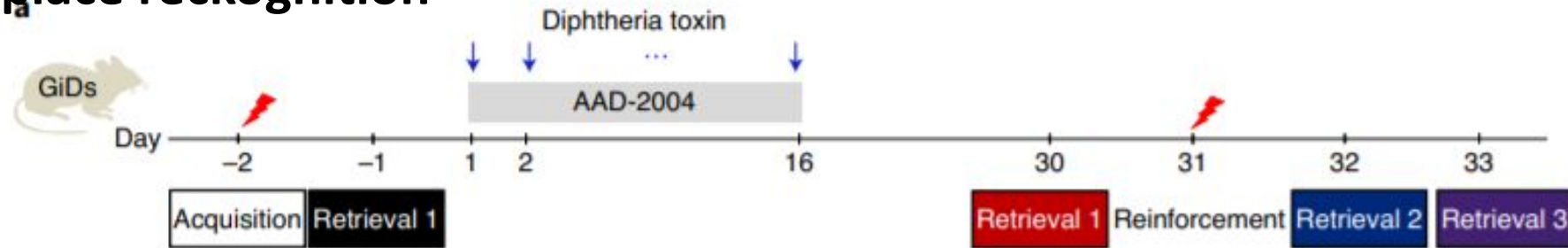


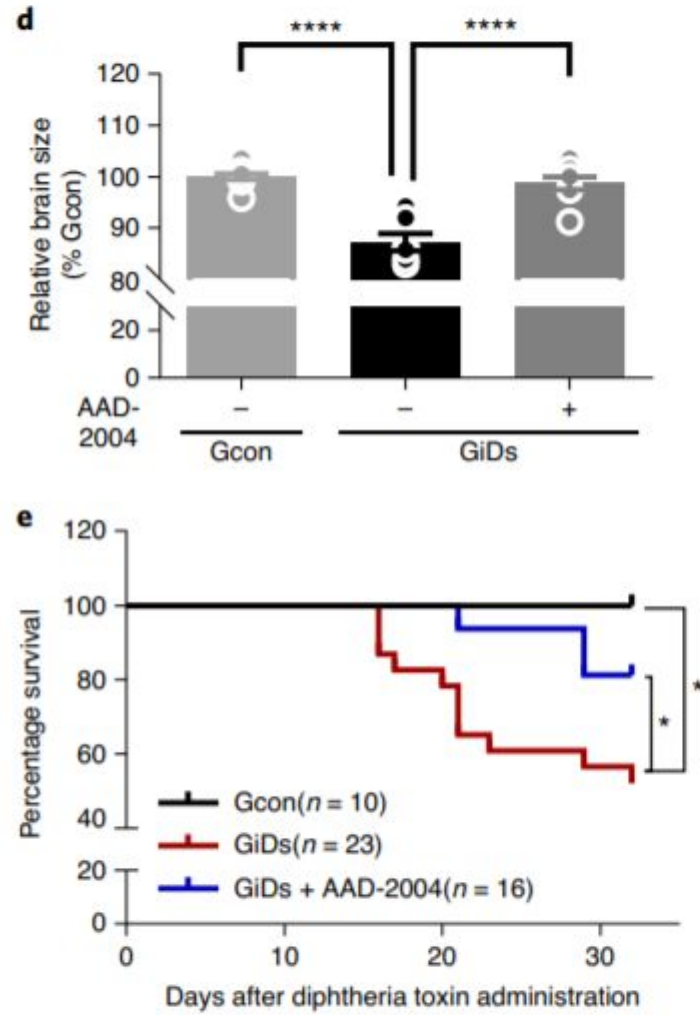
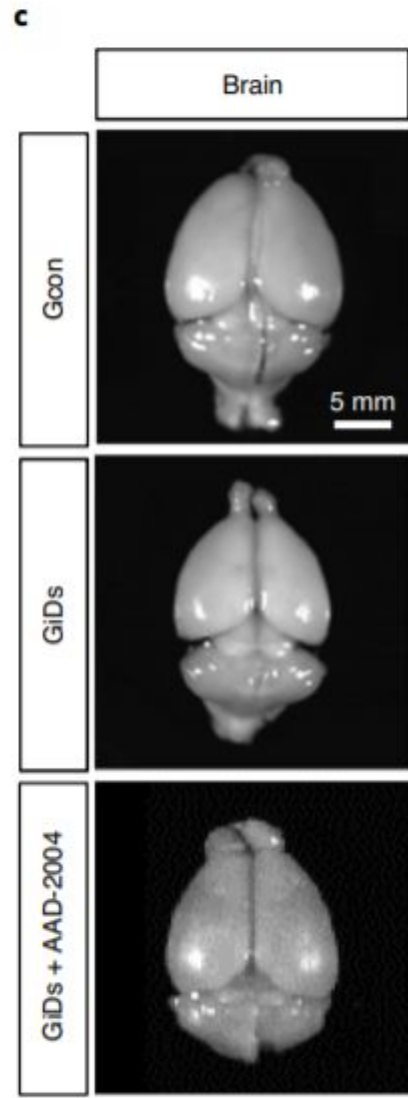




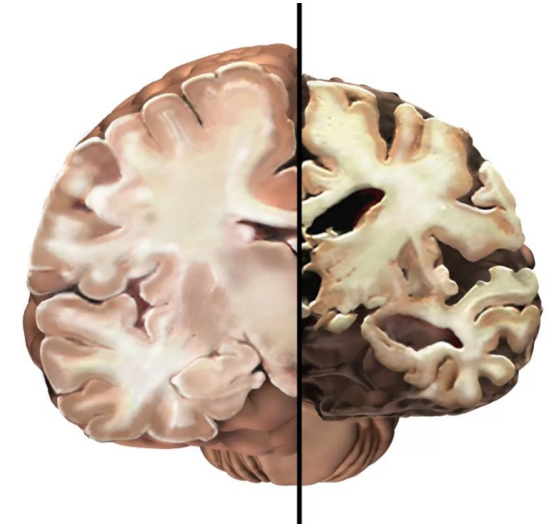
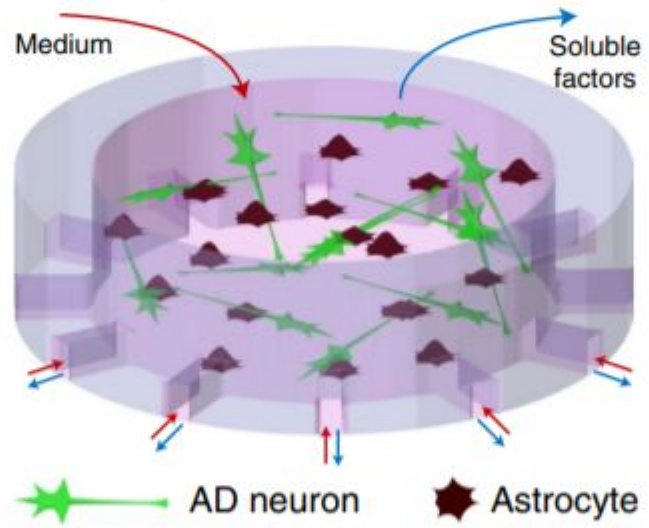


- пассивное избегание
- водный лабиринт Морриса
- novel place recognition



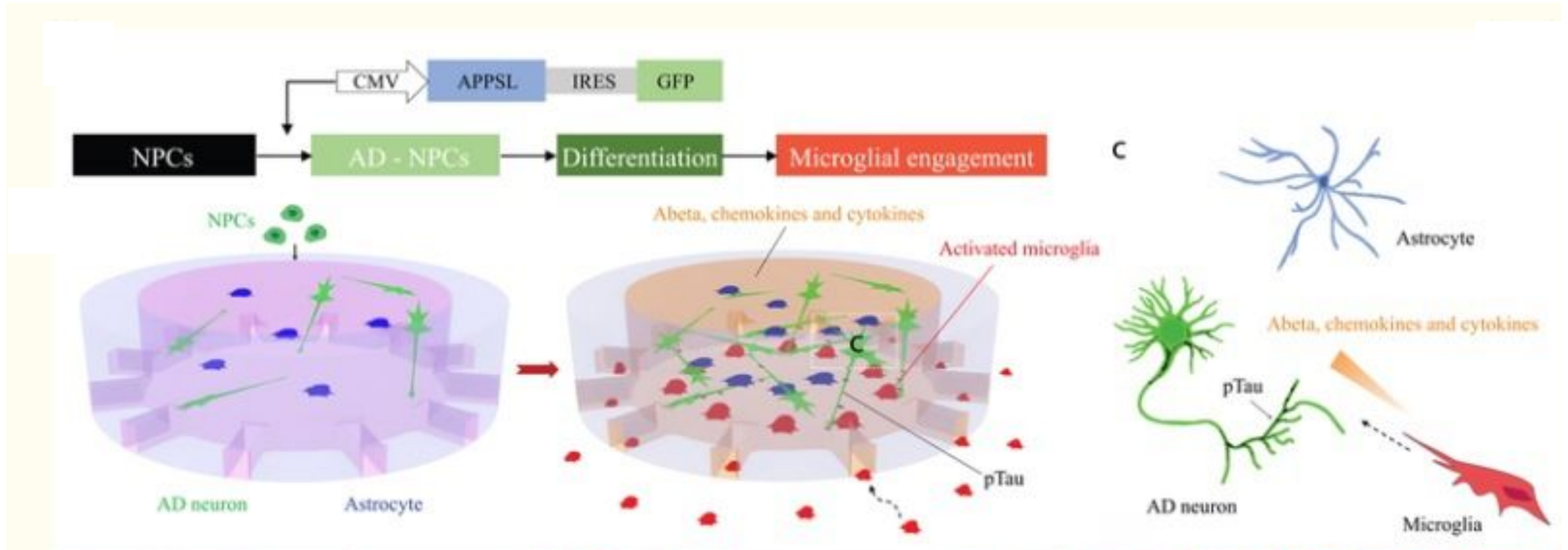


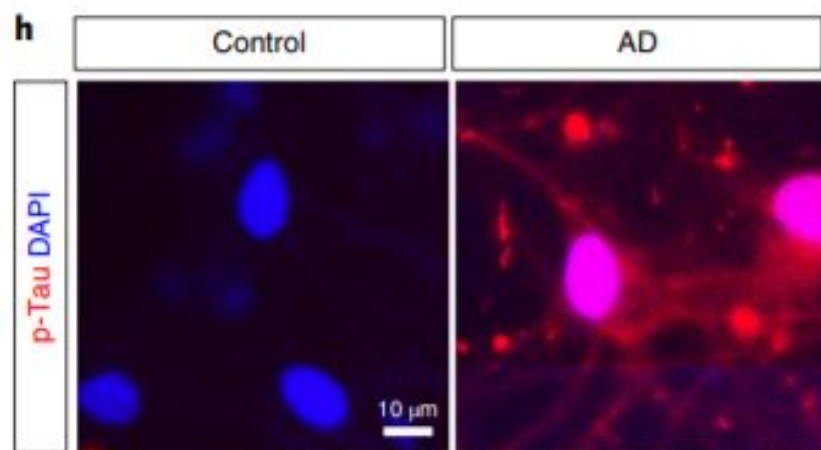
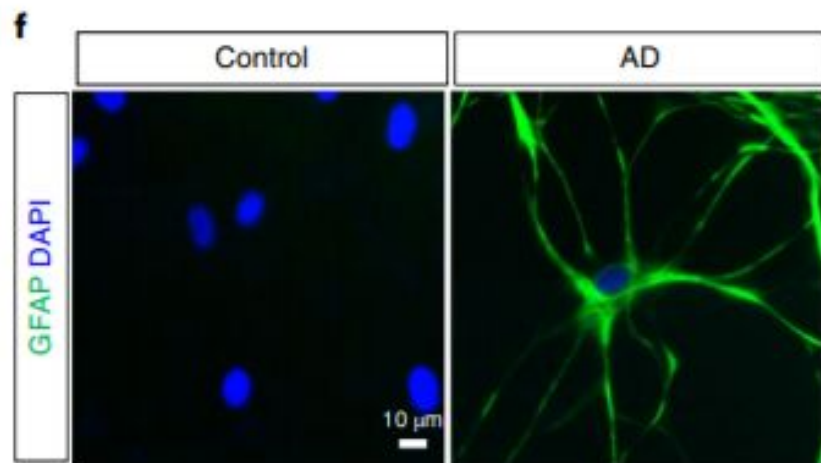
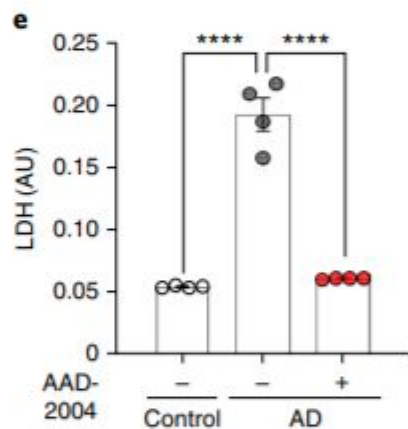
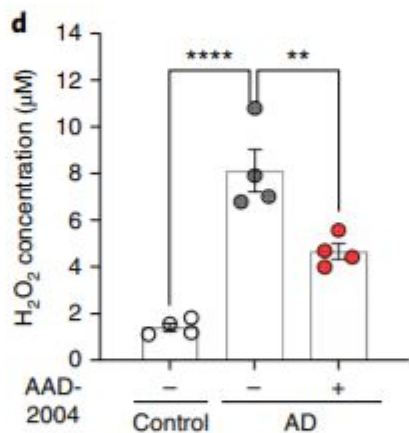
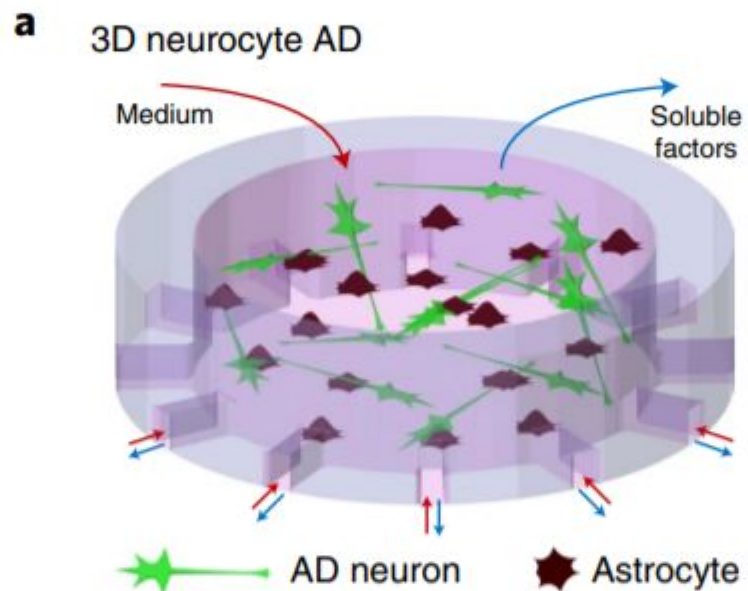
a 3D neurocyte AD



3D hNeuroGliAD

NPCs: APP (K670N/M671L, V717I)





ADD-2004



- H₂O₂
- GFAP
-

жизнеспособност

и

- **p-тау**



WT or APP/PS1

APP:

K670N/M671L («Swedish»)

1716V («Florida»)

V717I («London»)

PSEN1:

M146L

L286

ADD-2004

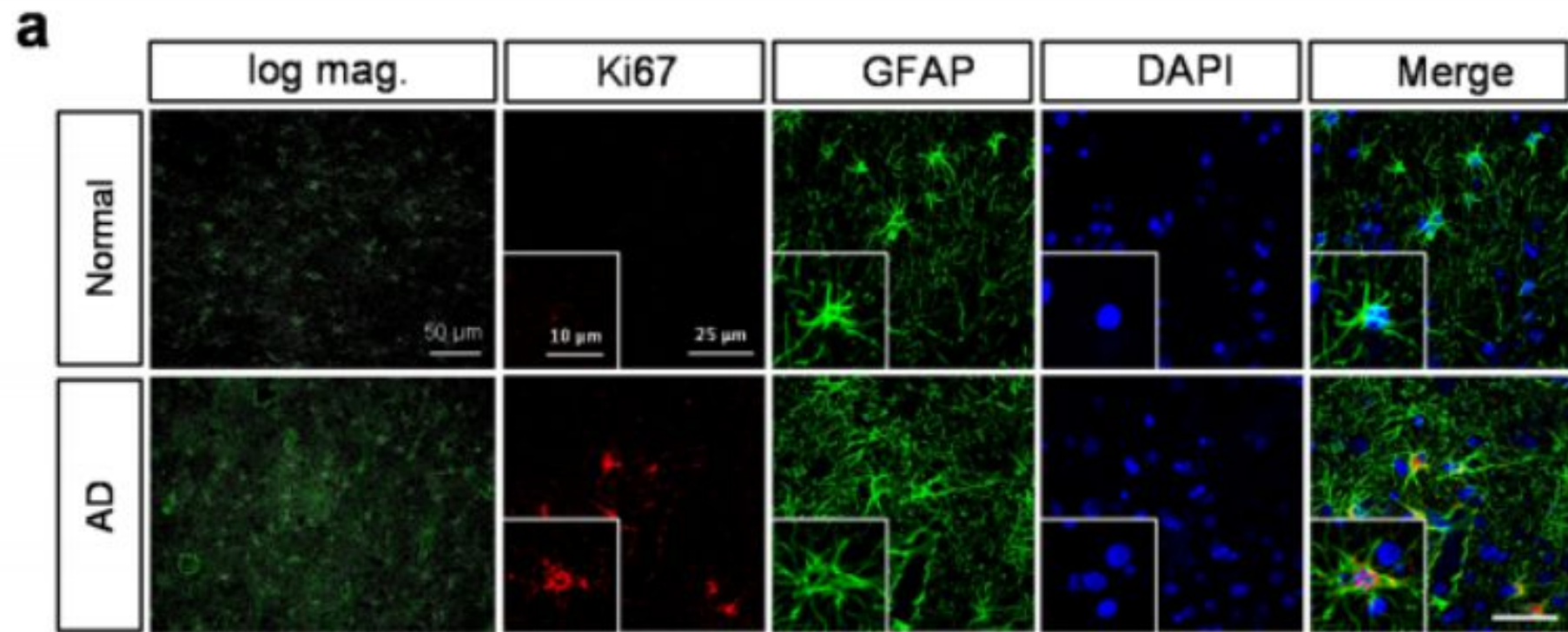
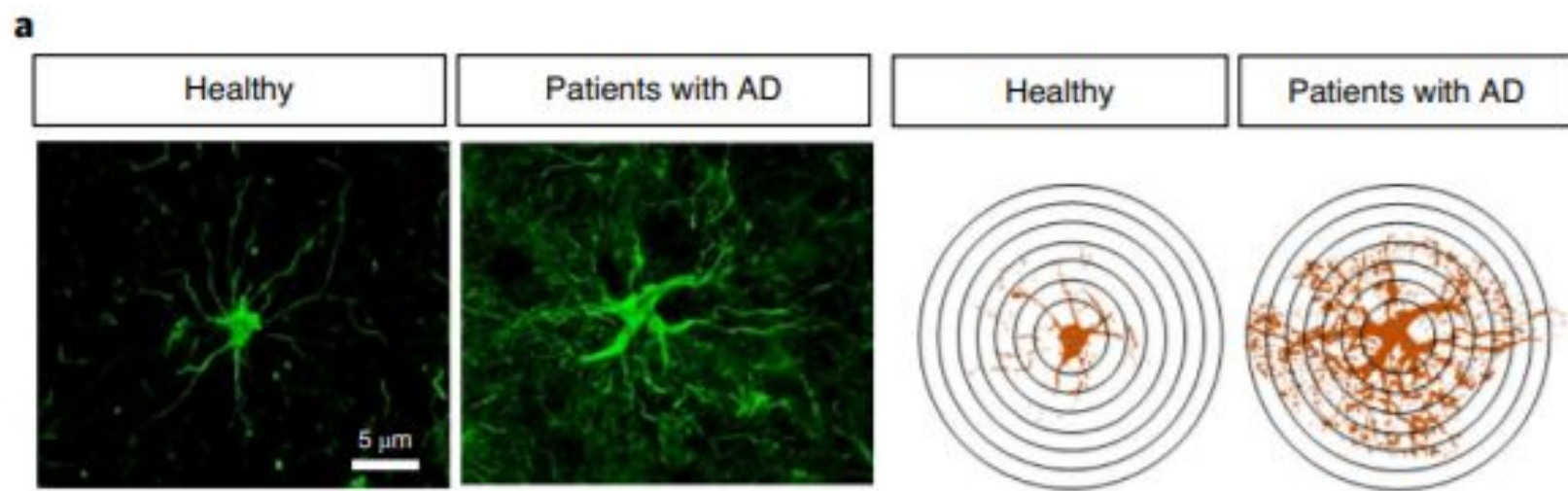
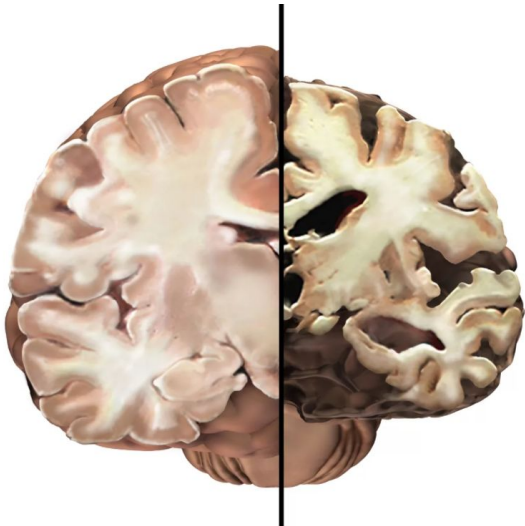


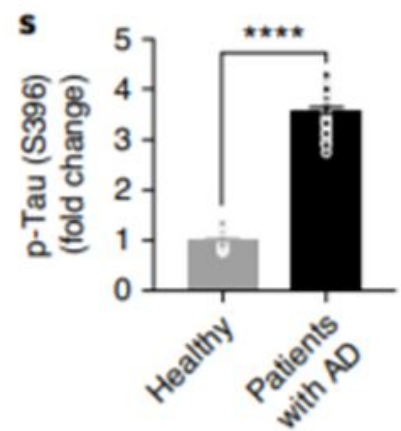
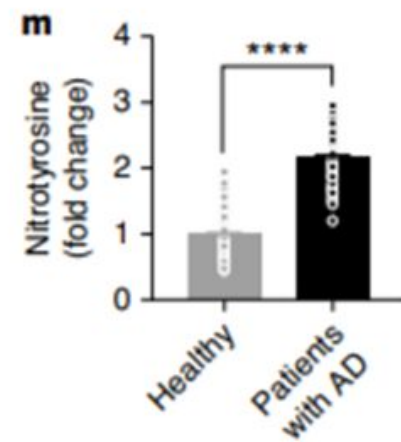
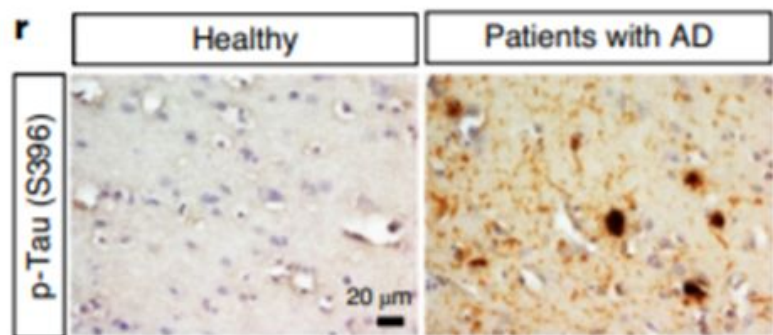
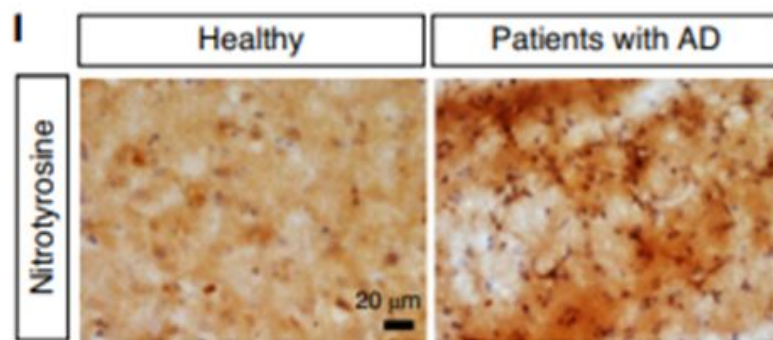
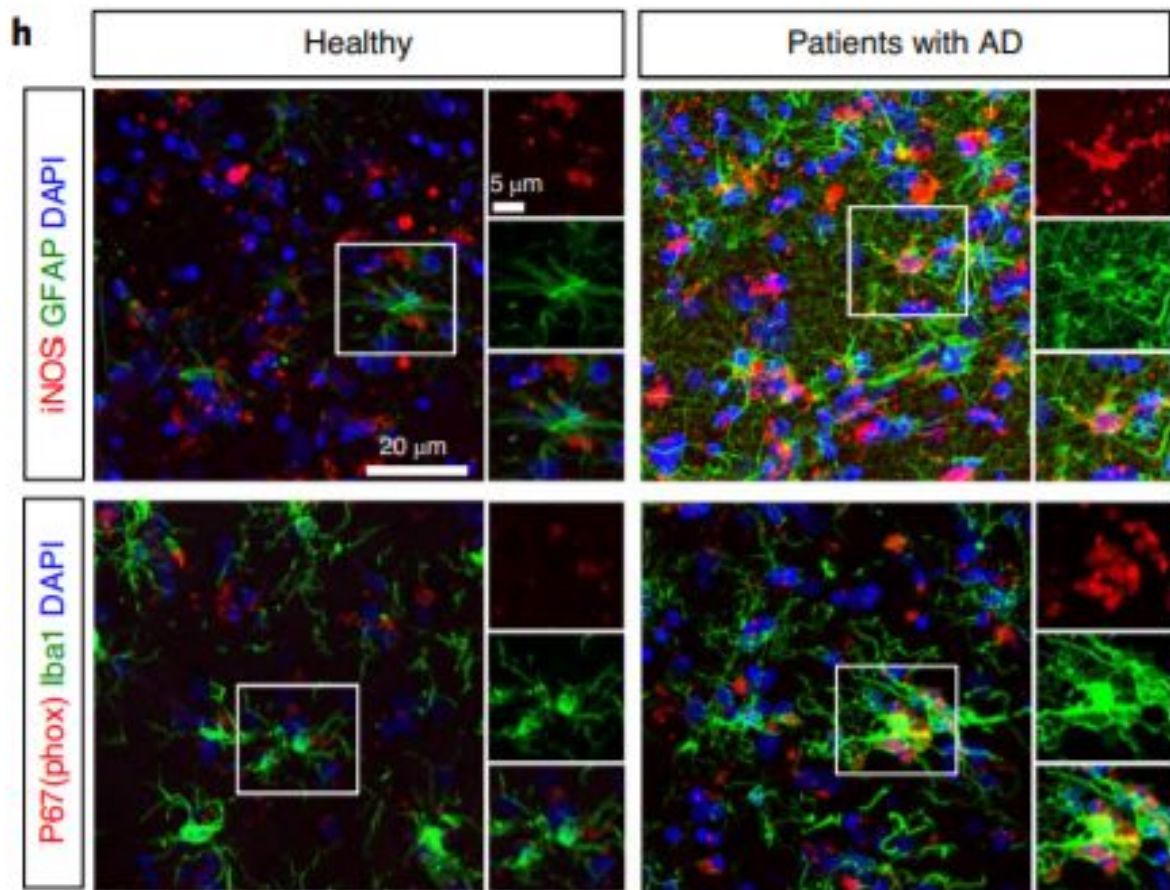
•  **H2O2**

• 

**пространственно
й**

памяти





Virus injection

AAV-GFAP104-GFP

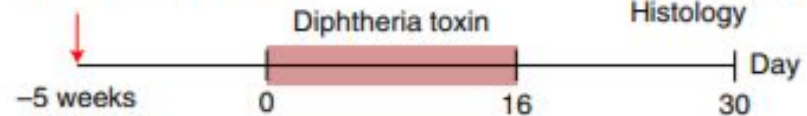
or

AAV-GFAP104-DTR-GFP

Behavior

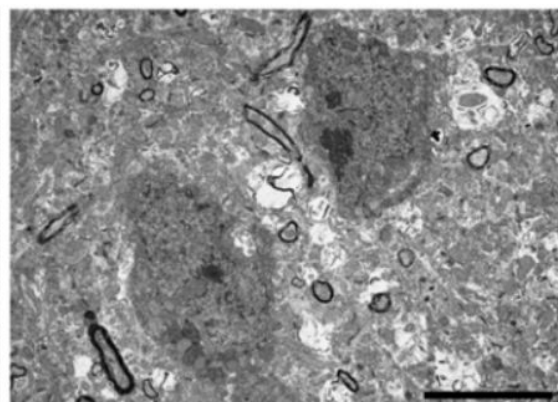
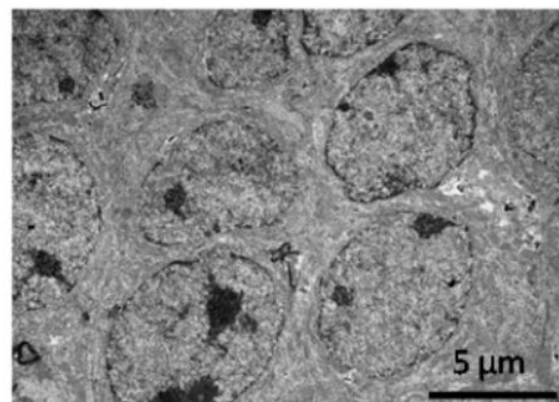
Electrophysiology

Histology



APP/PS1 + GFP

APP/PS1 + DTR



cleaved
caspase 3

NeuN

c-caspase 3
+ NeuN

WT+GFP

APP/PS1+GFP

APP/PS1+DTR

