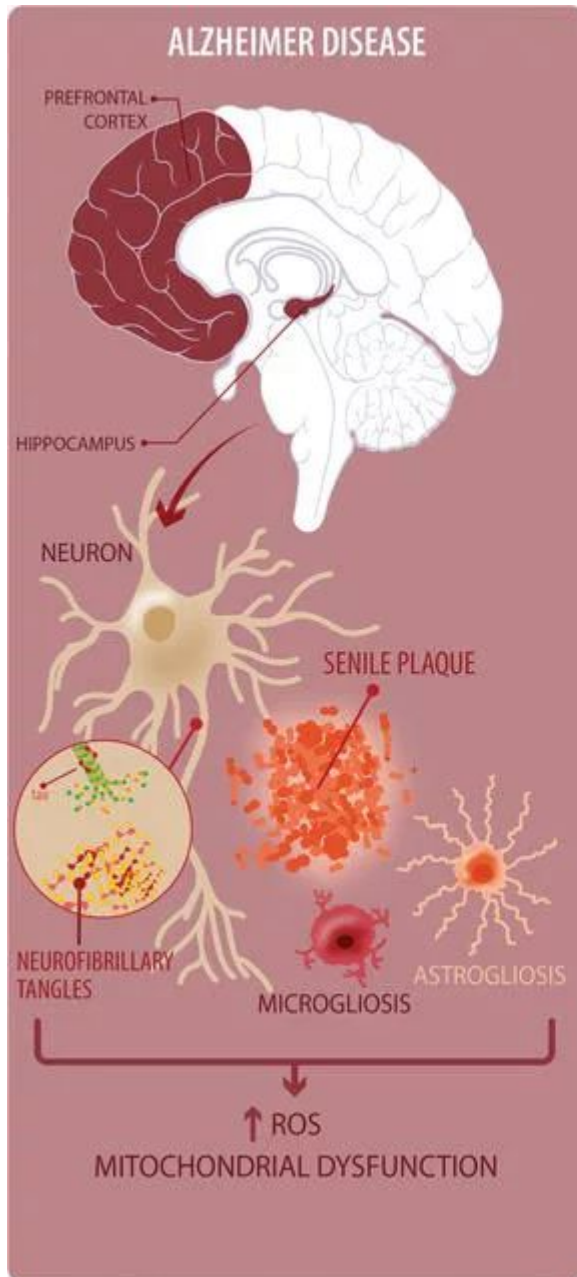




# Severe reactive astrocytes precipitate pathological hallmarks of Alzheimer's disease via $\text{H}_2\text{O}_2^-$ production

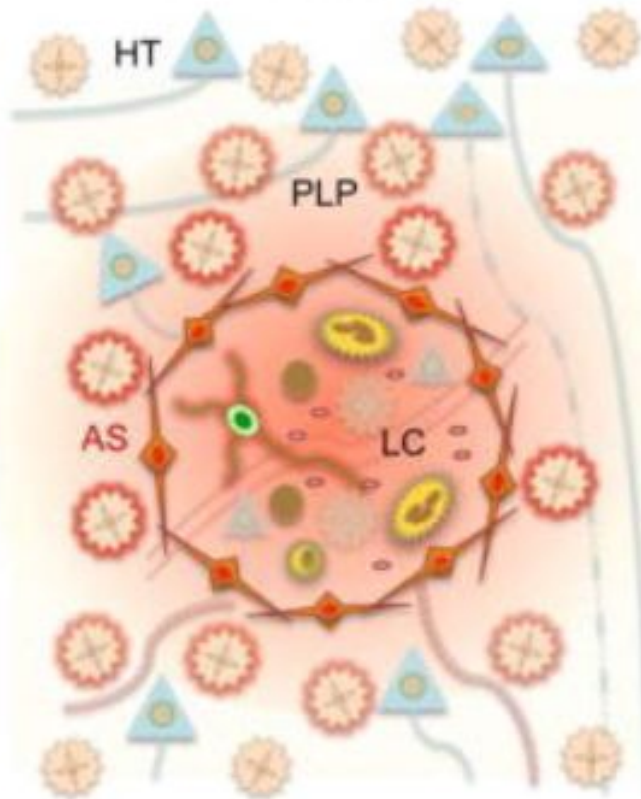
Heejung Chun <sup>1,2,3</sup>, Hyeonjoo Im<sup>3</sup>, You Jung Kang<sup>4</sup>, Yunha Kim<sup>3</sup>, Jin Hee Shin<sup>5</sup>, Woojin Won<sup>1,6</sup>, Jiwoon Lim<sup>1</sup>, Yeonha Ju<sup>1,7,8</sup>, Yongmin Mason Park<sup>1,7,8</sup>, Sunpil Kim<sup>1,6</sup>, Seung Eun Lee<sup>9</sup>, Jaekwang Lee<sup>2</sup>, Junsung Woo<sup>2</sup>, Yujin Hwang<sup>3</sup>, Hyesun Cho<sup>3,10</sup>, Seonmi Jo <sup>2,11</sup>, Jong-Hyun Park <sup>12</sup>, Daesoo Kim <sup>11</sup>, Doo Yeon Kim <sup>13</sup>, Jeong-Sun Seo<sup>10,14</sup>, Byoung Joo Gwag<sup>5</sup>, Young Soo Kim <sup>15</sup>, Ki Duk Park<sup>8,12,16</sup>, Bong-Kiun Kaang <sup>17</sup>, Hansang Cho<sup>4,18,19</sup>, Hoon Ryu <sup>3,20</sup>  and C. Justin Lee <sup>1,2,6,7</sup> 



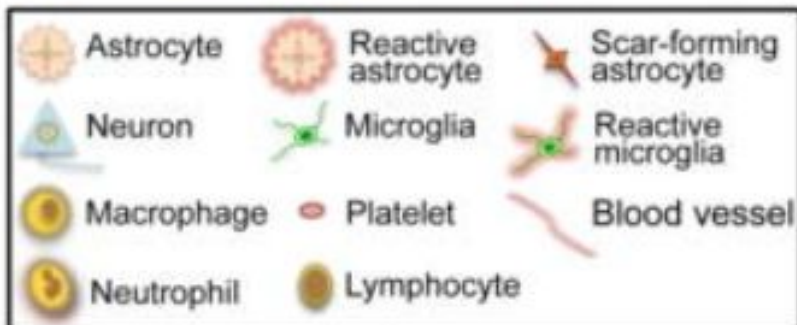
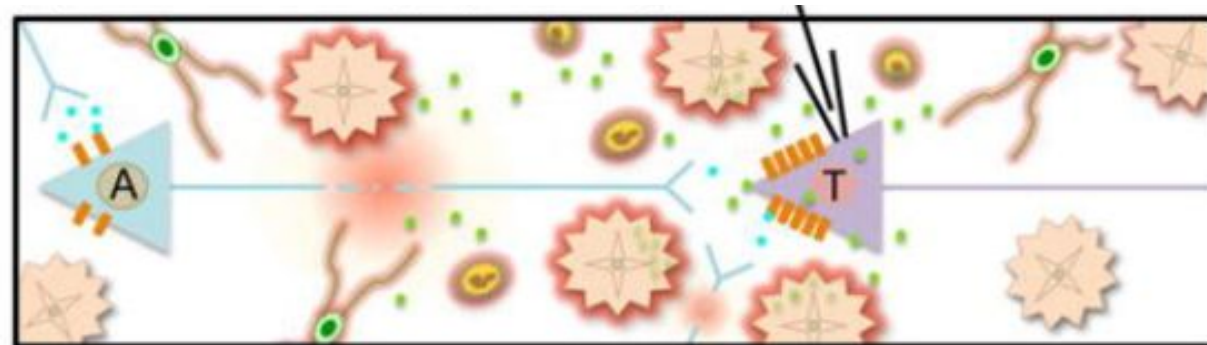
## AD:

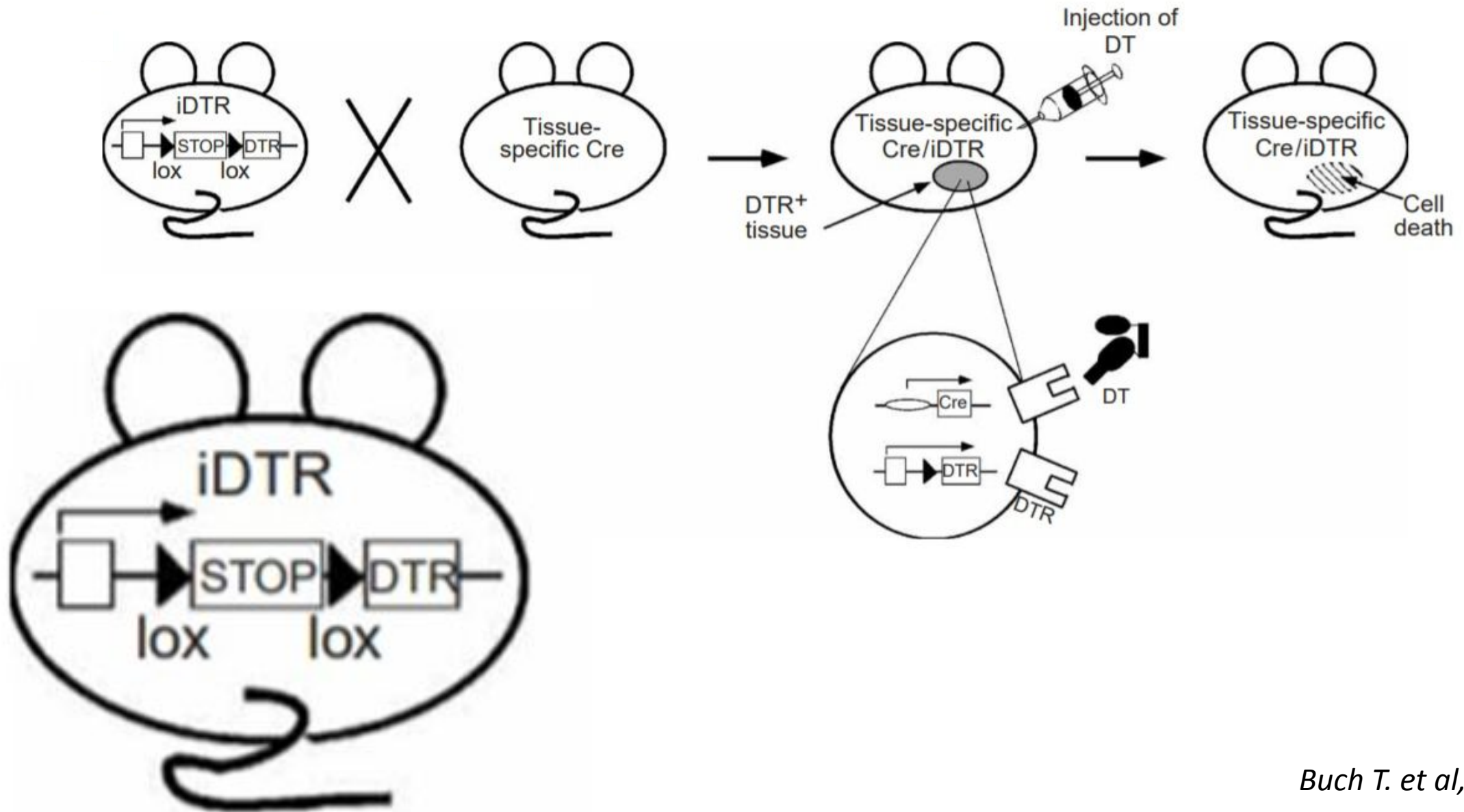
- Накопление  $\beta$ A и p-тау
- Мультиклеточный глиальный ответ;  
нейровоспаление
  - реактивный астроглиоз
  - активация микроглии
- Нейродегенерация

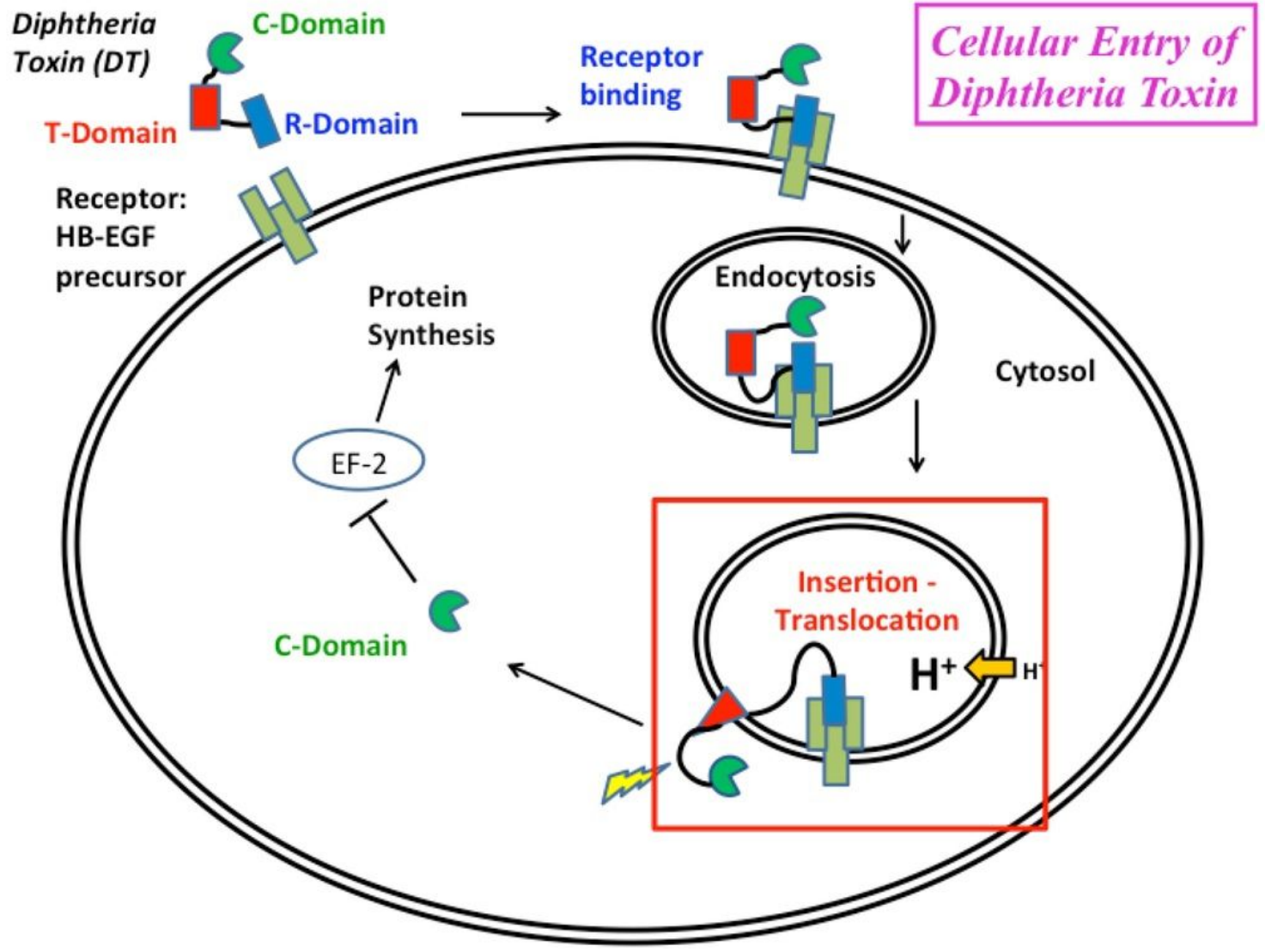
Focal lesion with scar formation

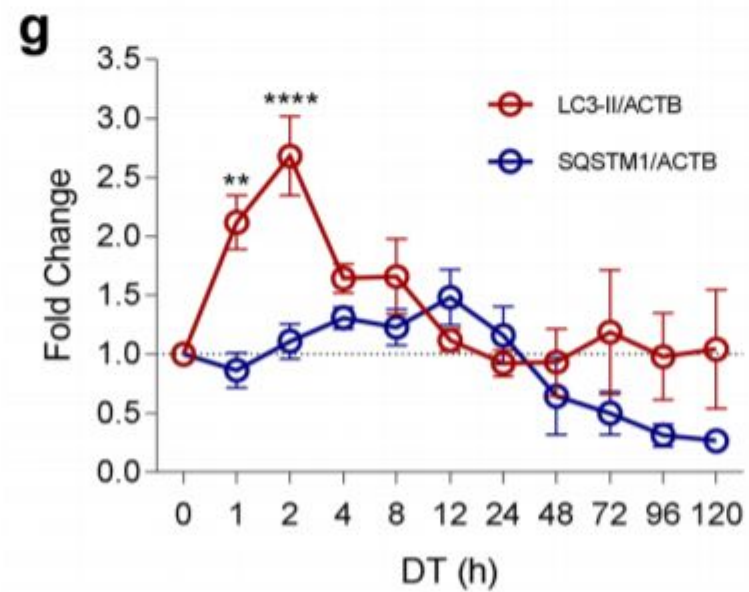
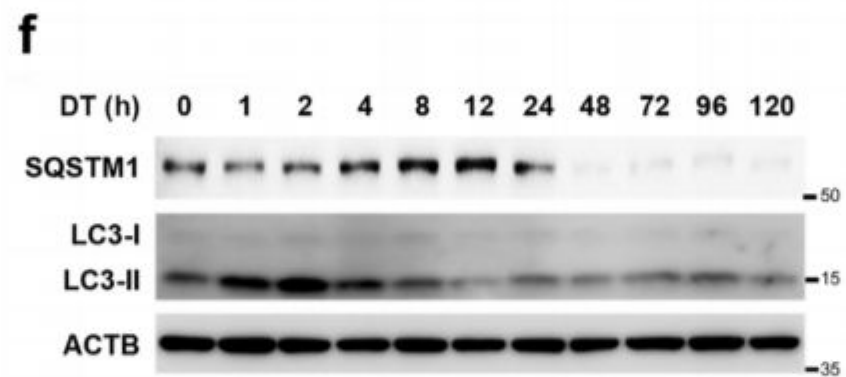
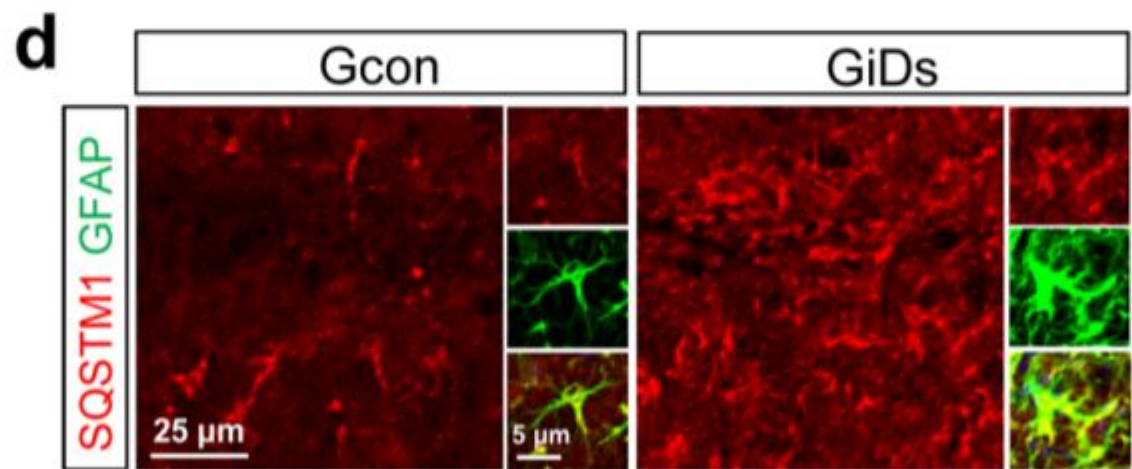
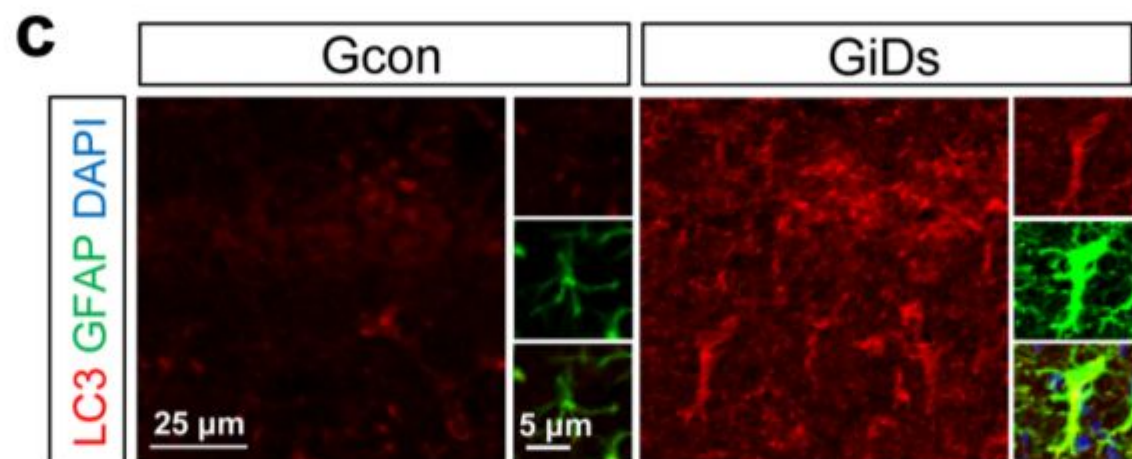


- Изоляция очага поражения
  - механический барьер
  - «химический» барьер
- Регуляция воспаления
- Регуляция проницаемости ГЭБ
- Посттравматическое ремоделирование нервной цепи
- Стимуляция регенерации

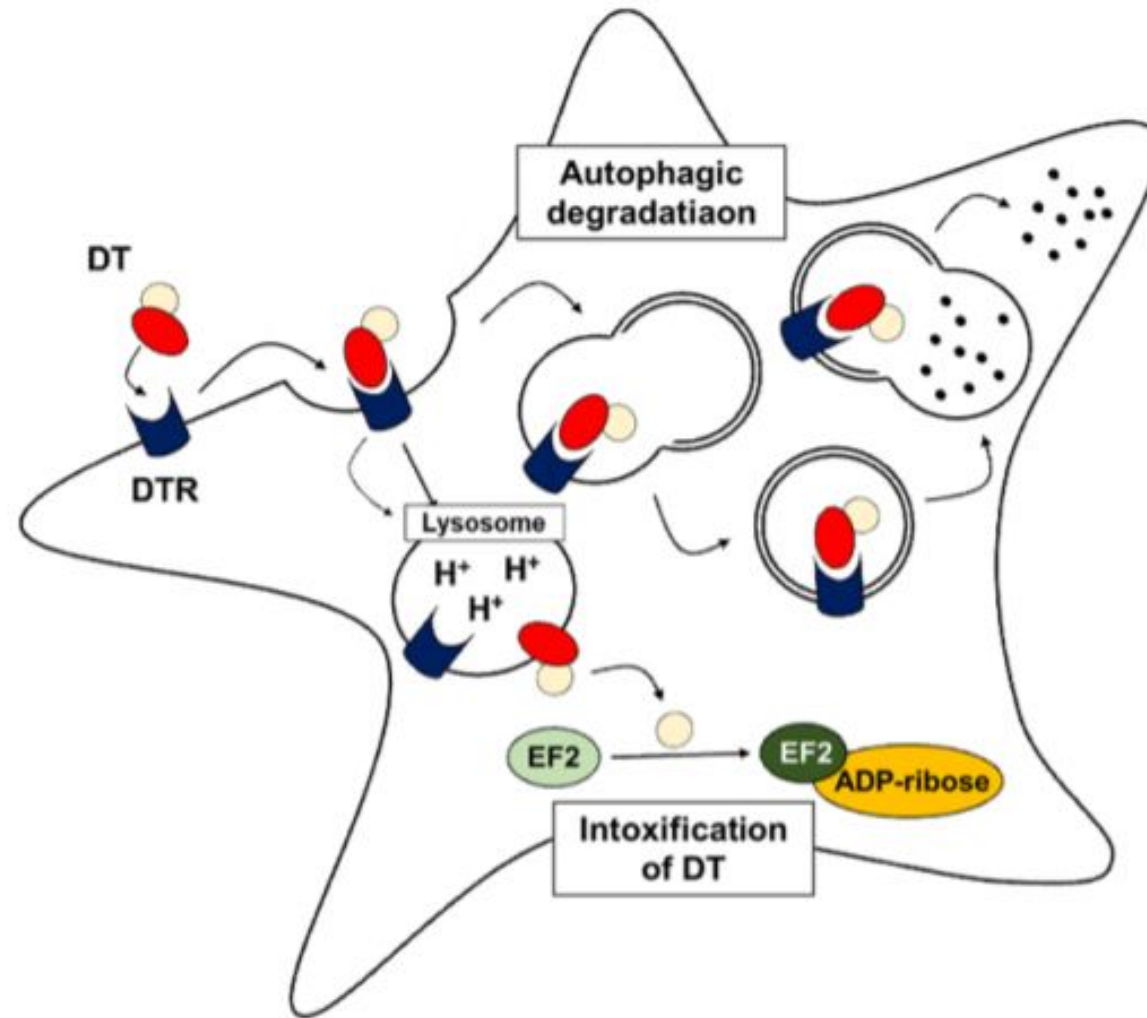


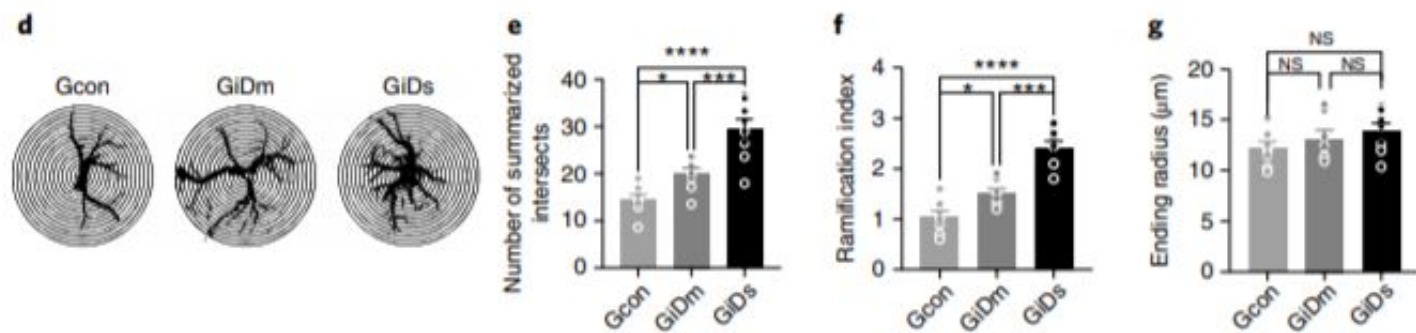
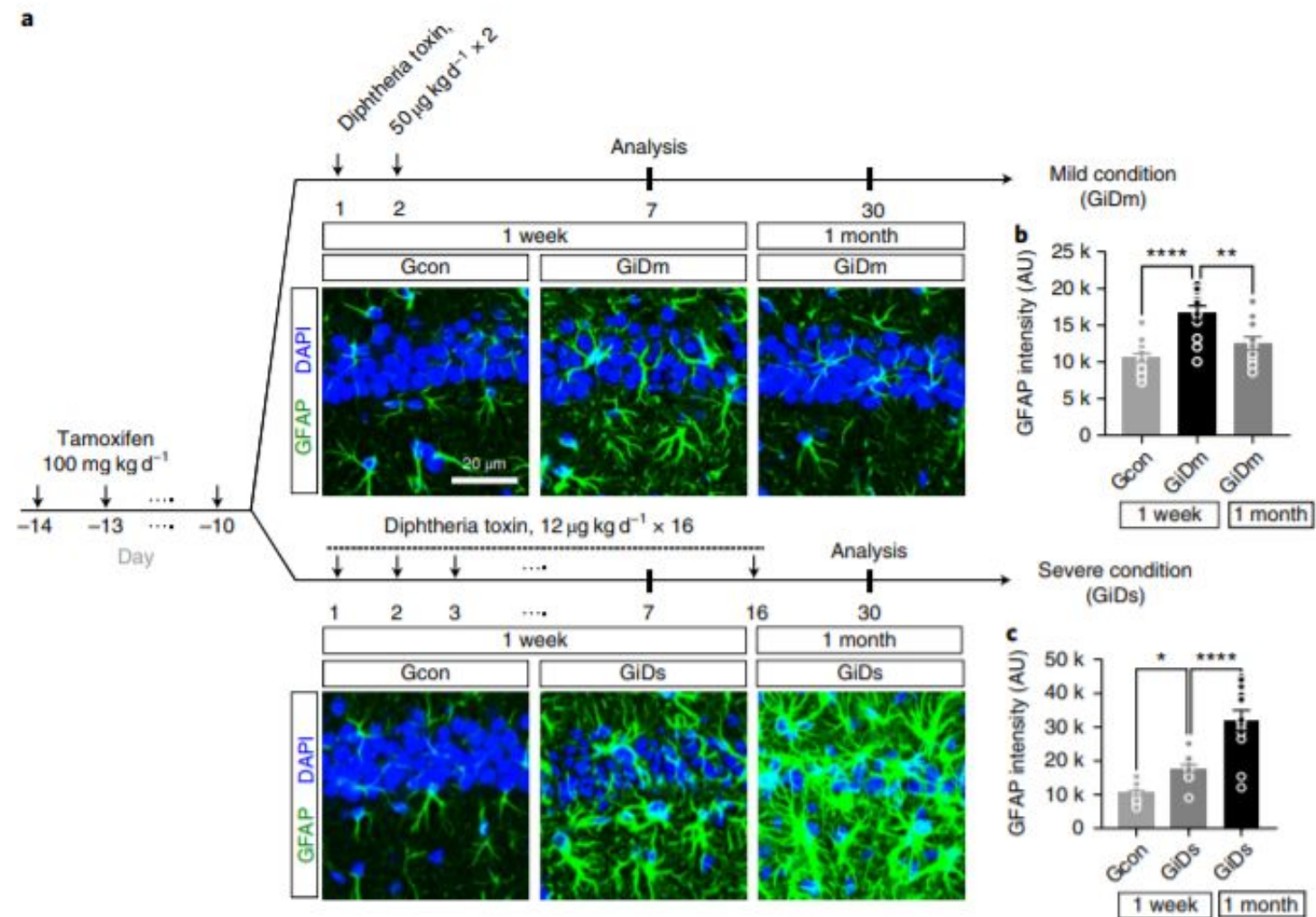




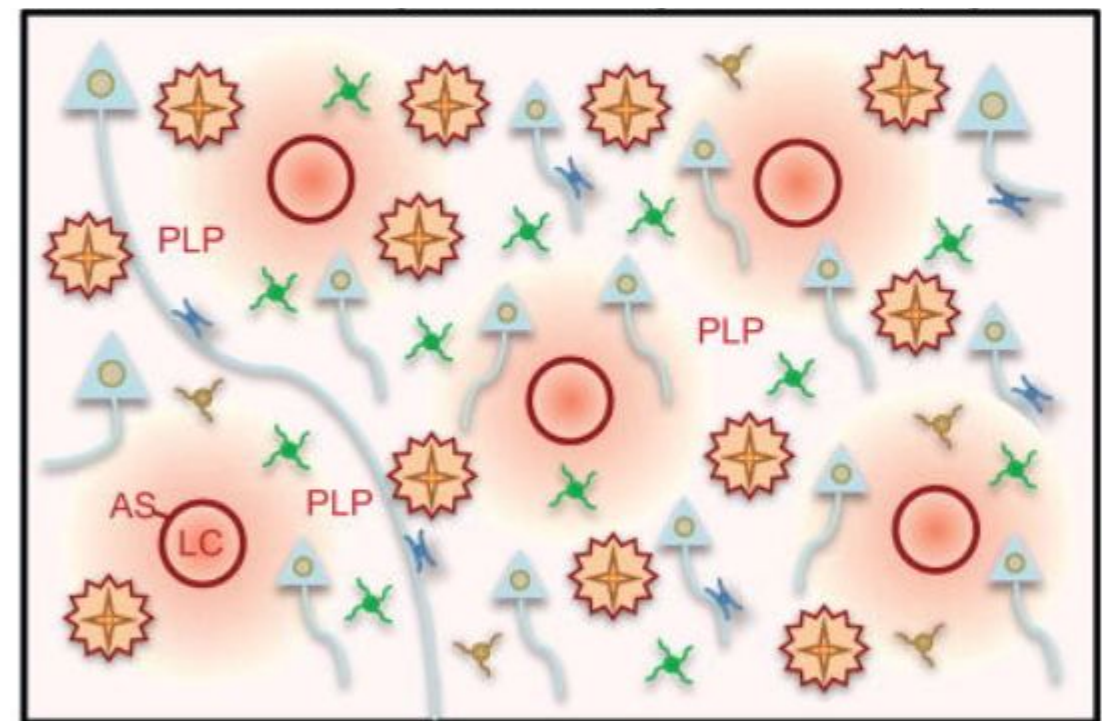
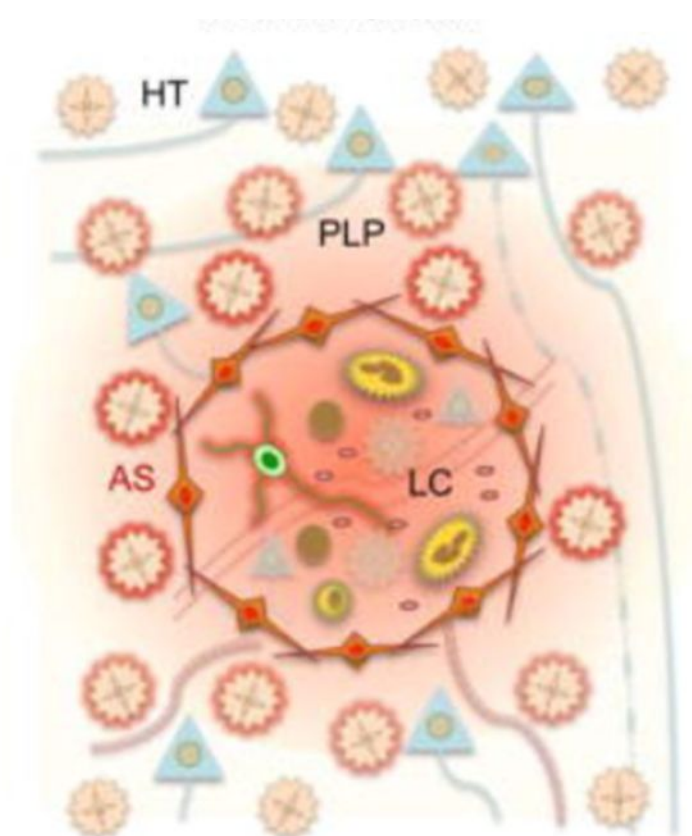


## Alternative pathways of DT actions



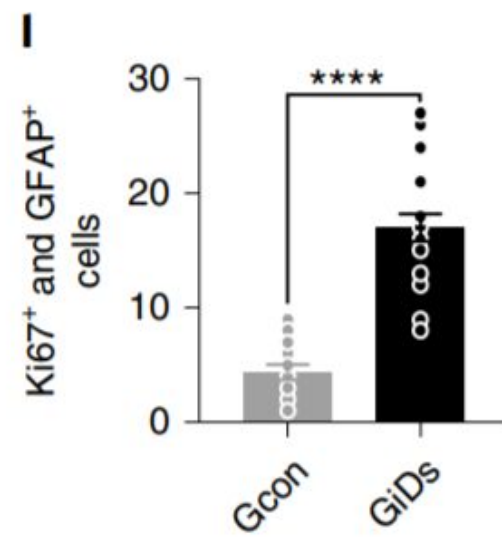
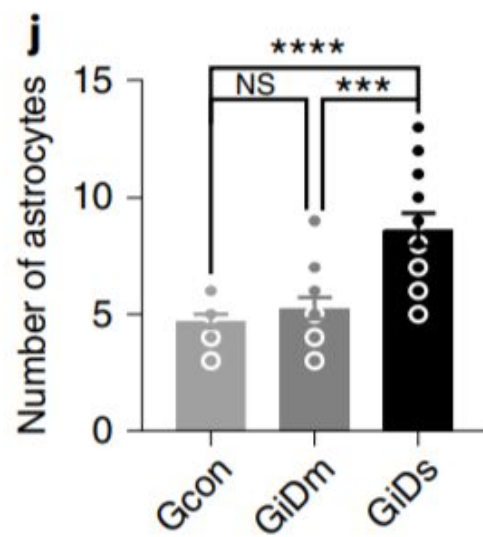
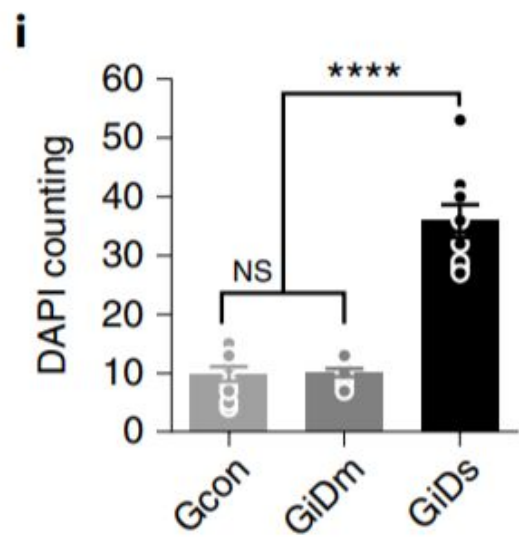
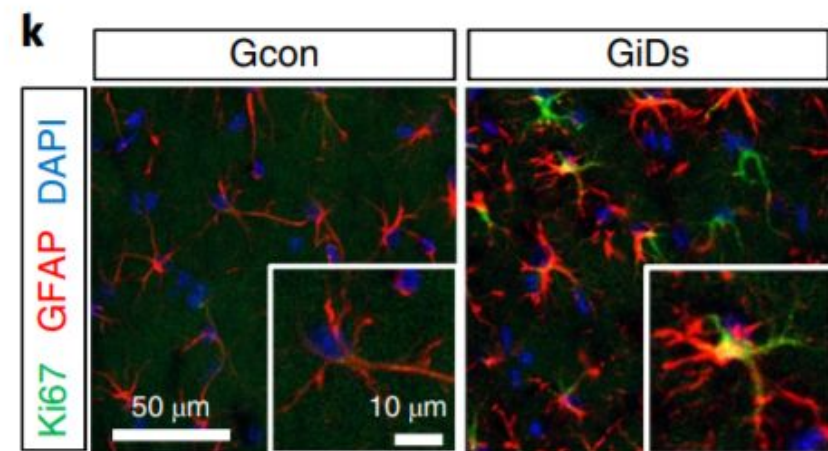
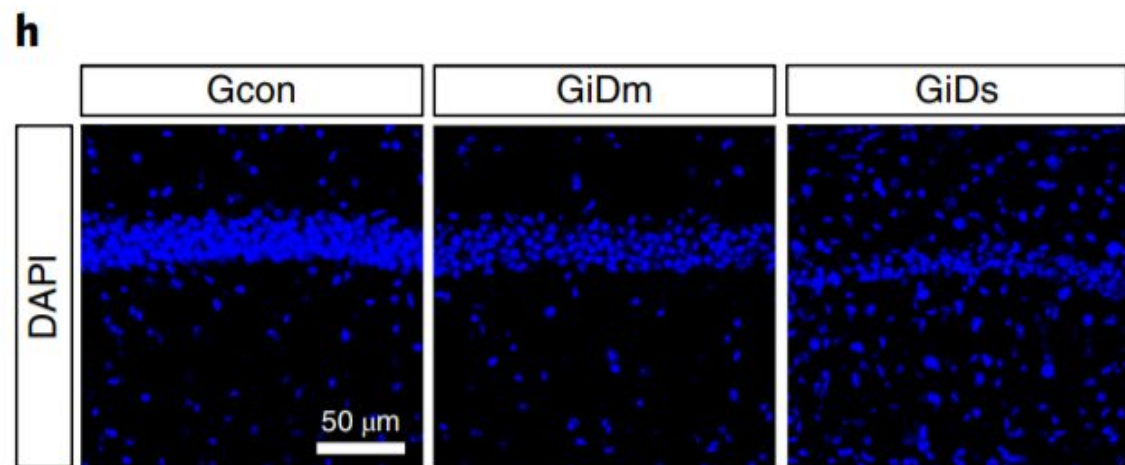


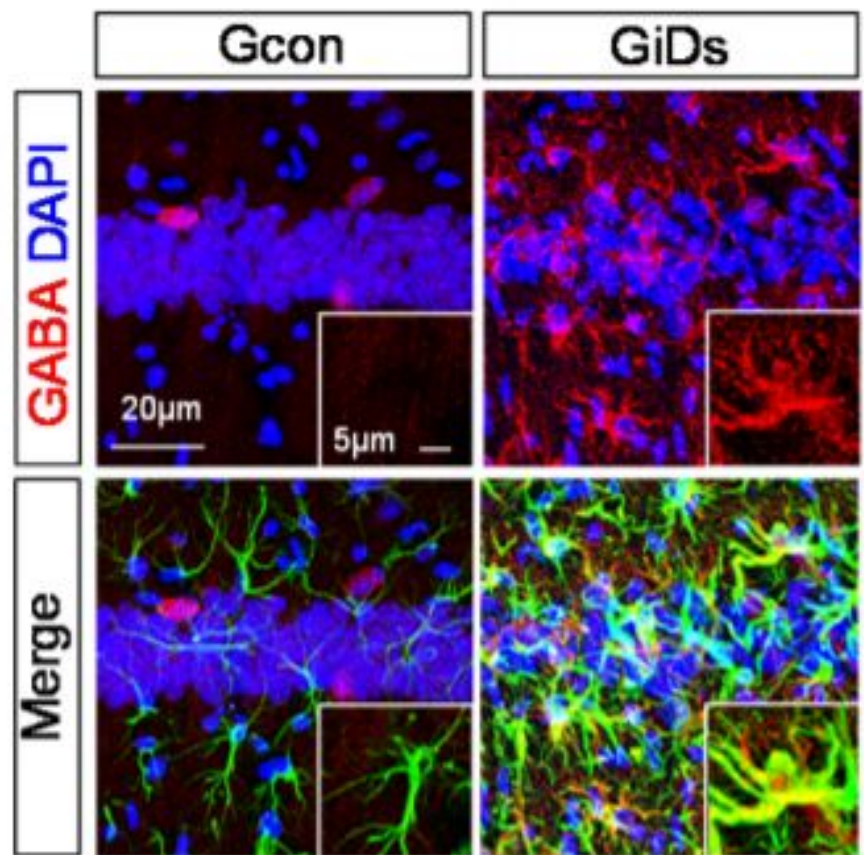




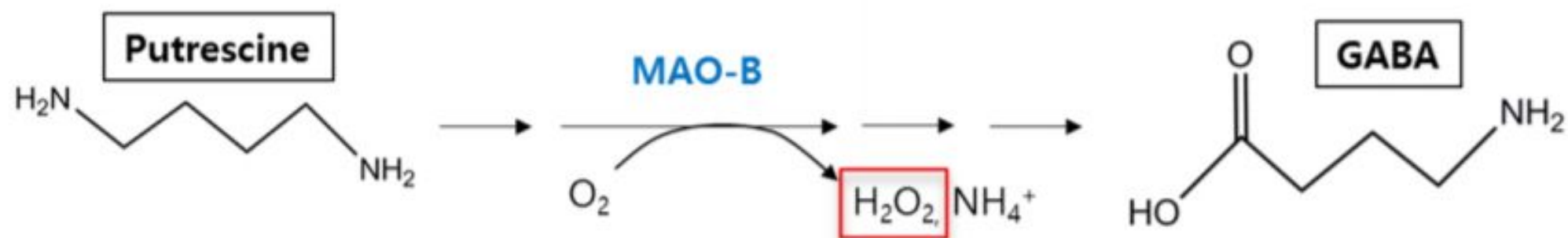
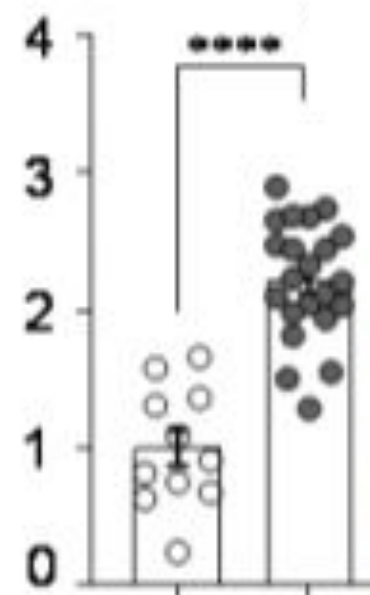
- |  |            |  |                    |  |                        |
|--|------------|--|--------------------|--|------------------------|
|  | Astrocyte  |  | Reactive astrocyte |  | Scar-forming astrocyte |
|  | Neuron     |  | Microglia          |  | Reactive microglia     |
|  | Macrophage | 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

*Burda J. and Sofroniew M. 2016*

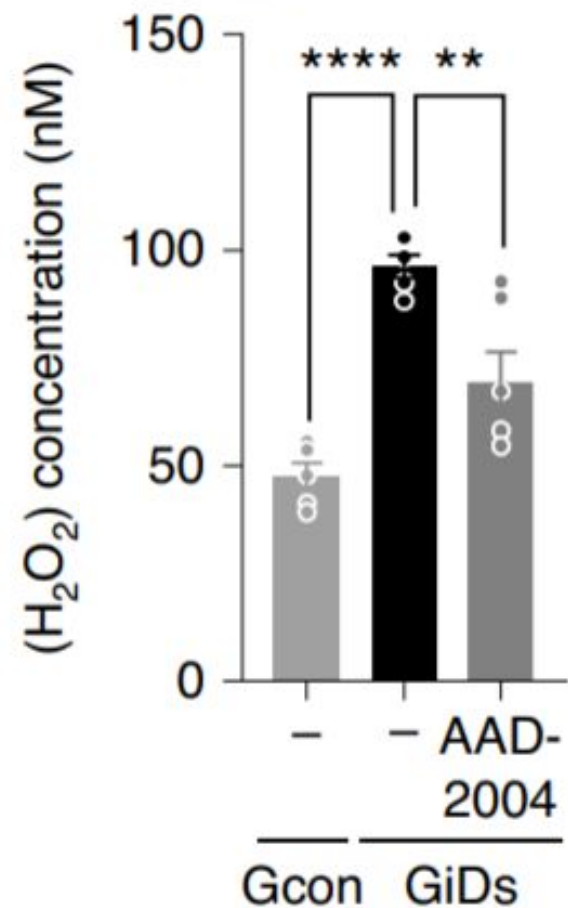
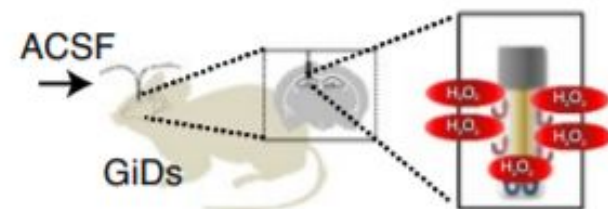
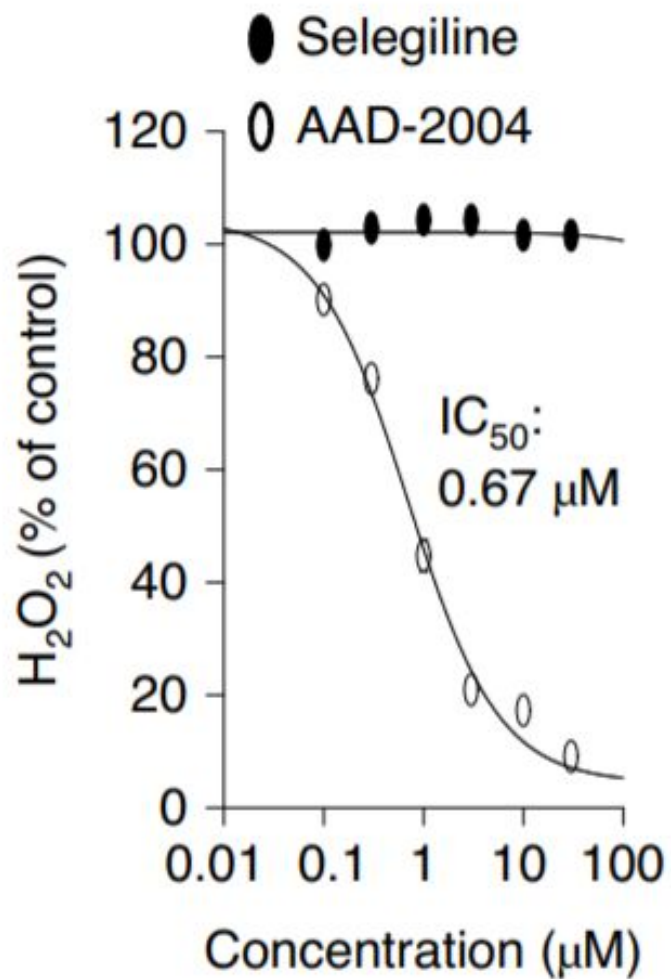
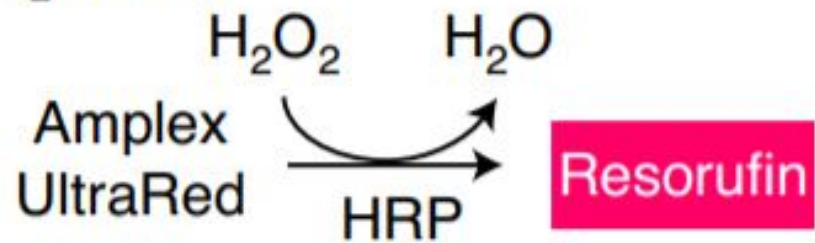


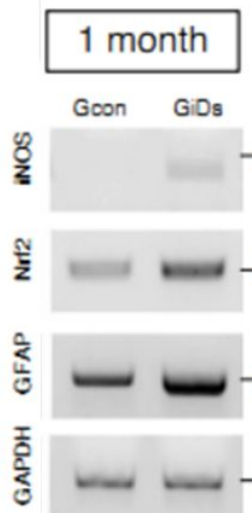
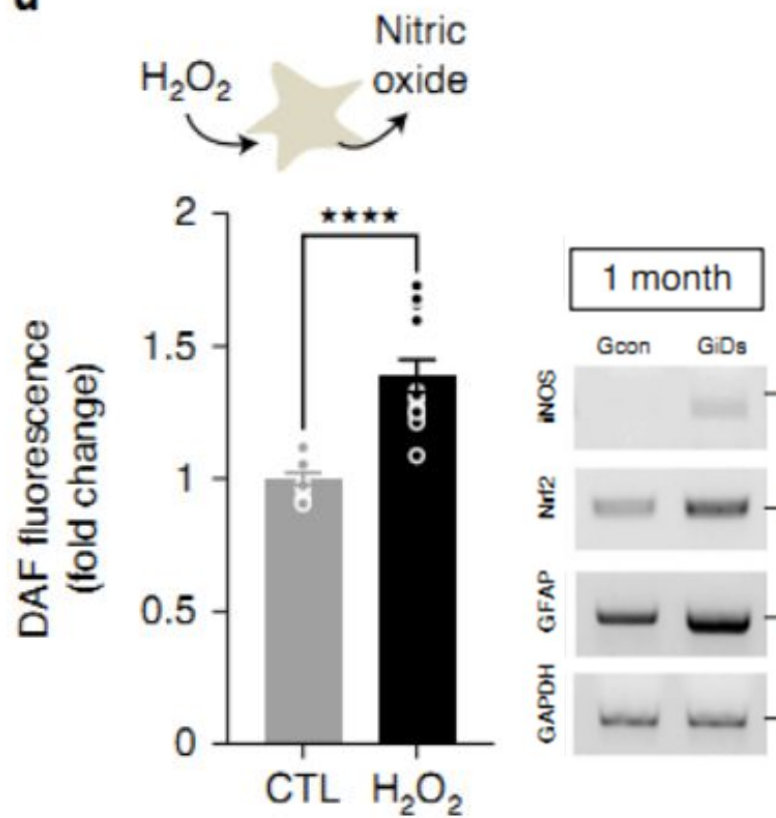
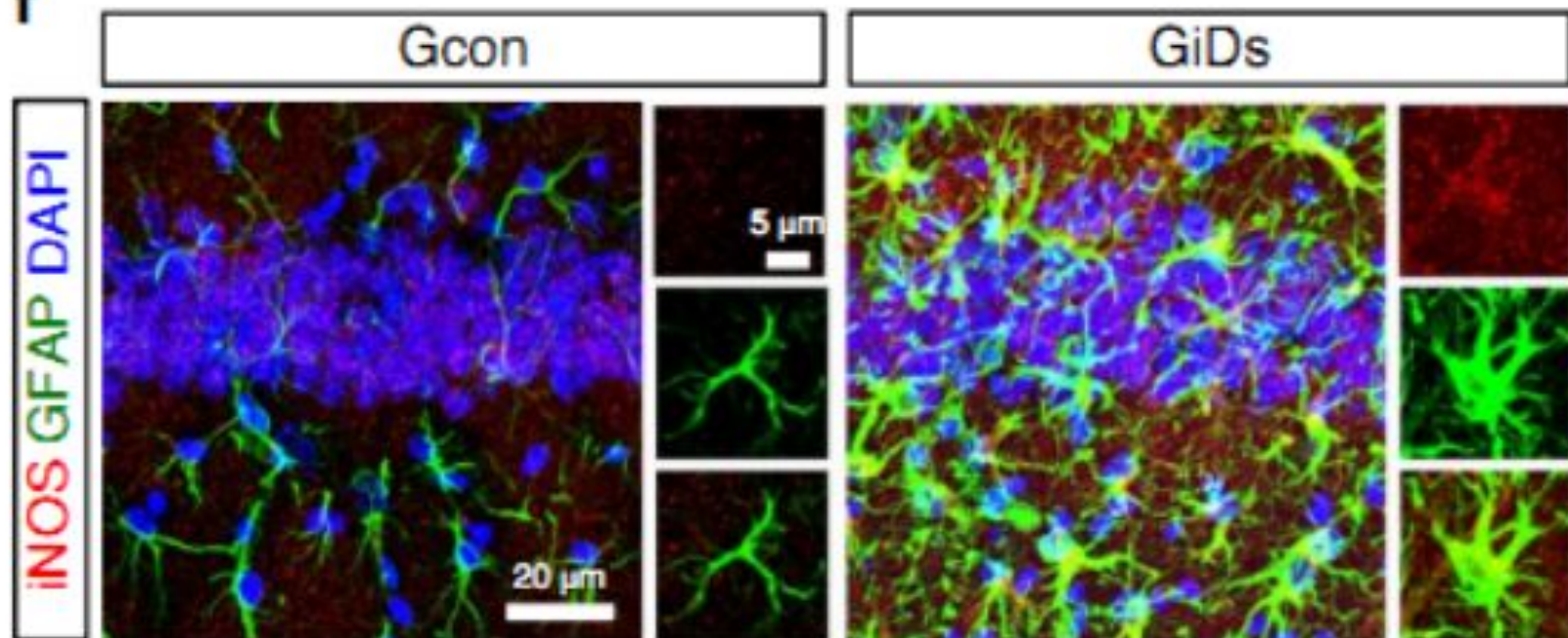


**i**  
GABA in GFAP+  
(Fold change)

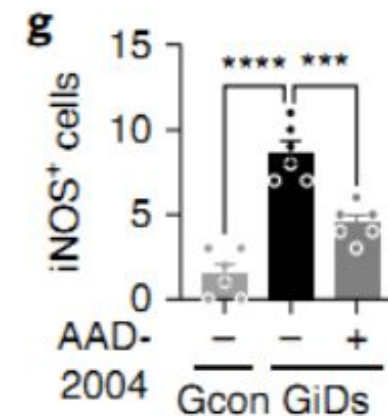
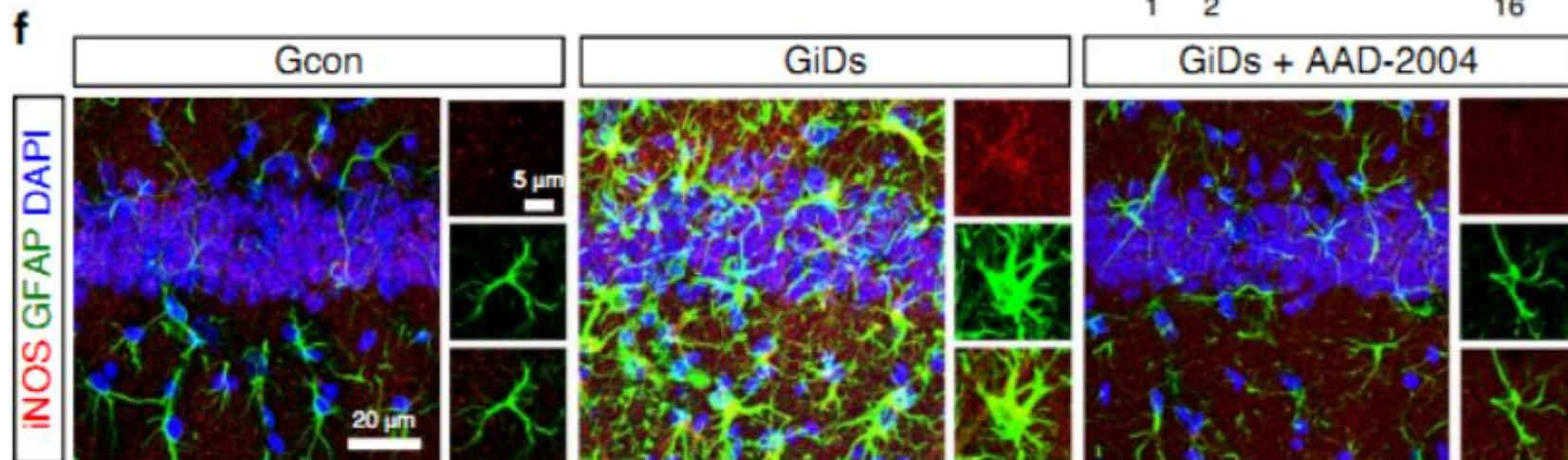
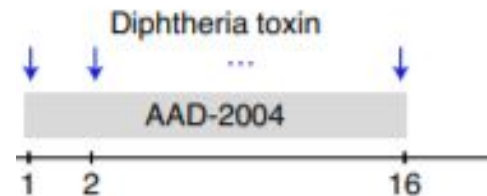


H<sub>2</sub>O<sub>2</sub> assay

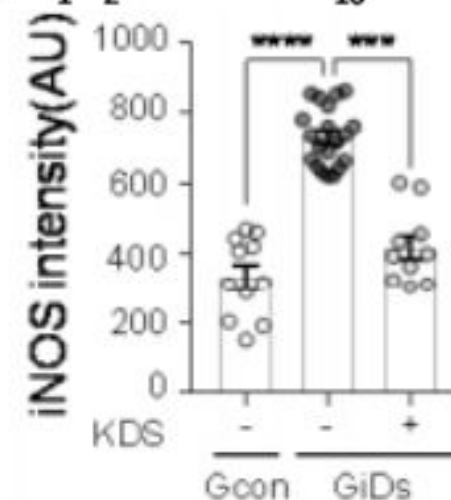
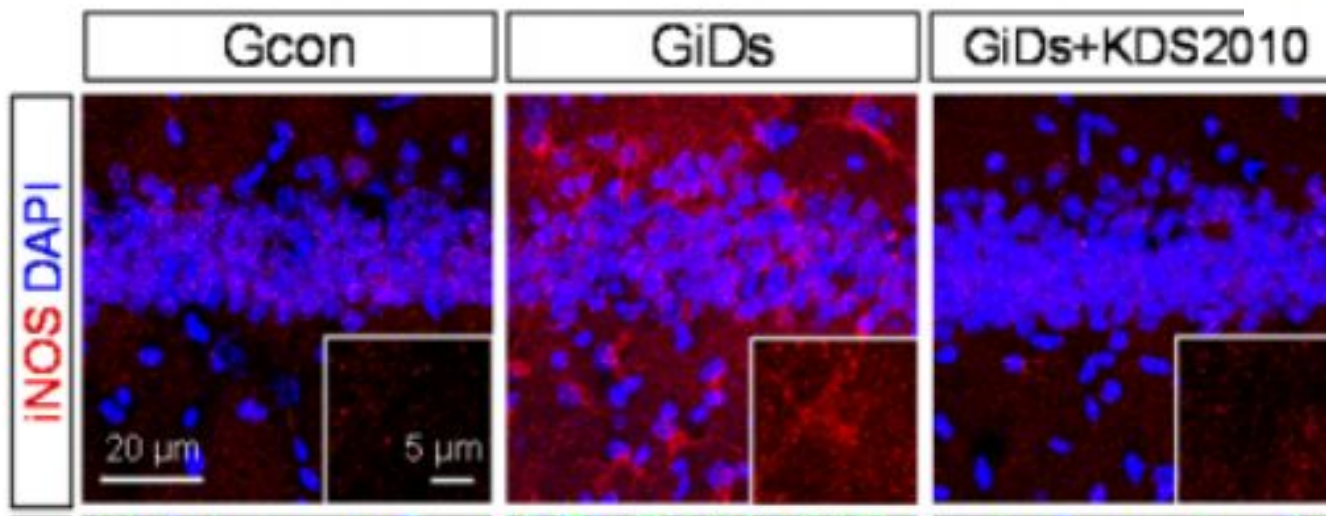
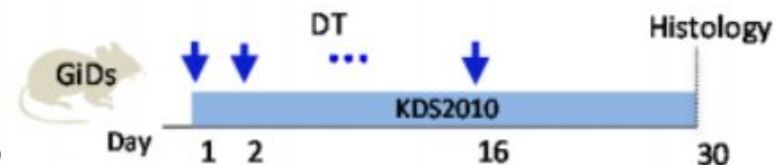


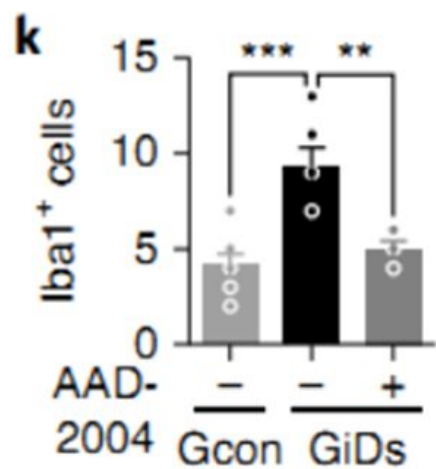
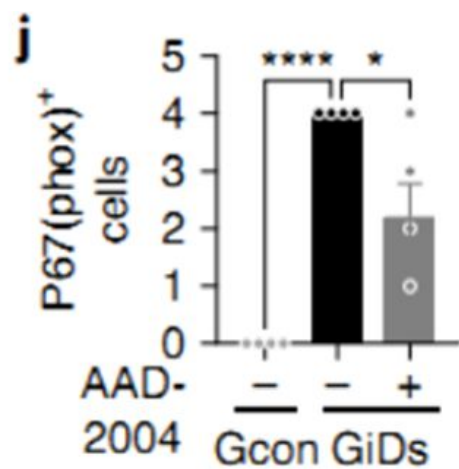
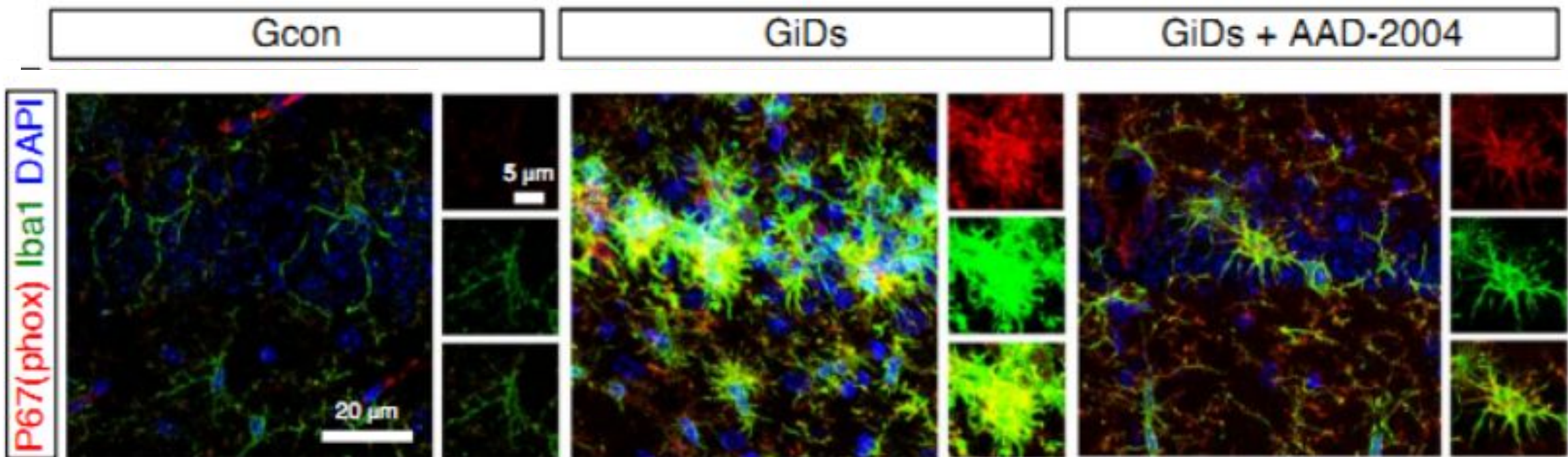
**d****f**

# ADD-2004 — H2O2

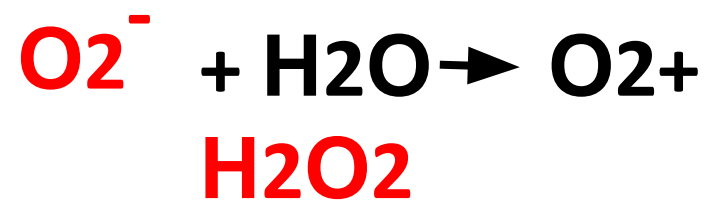


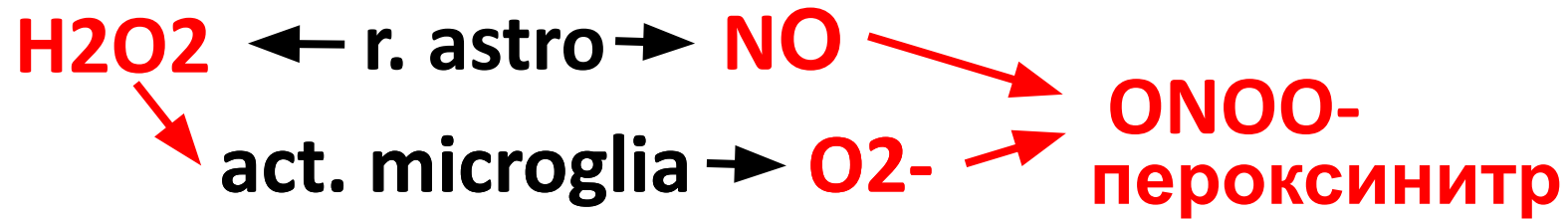
# KDS2010 — MAO-B



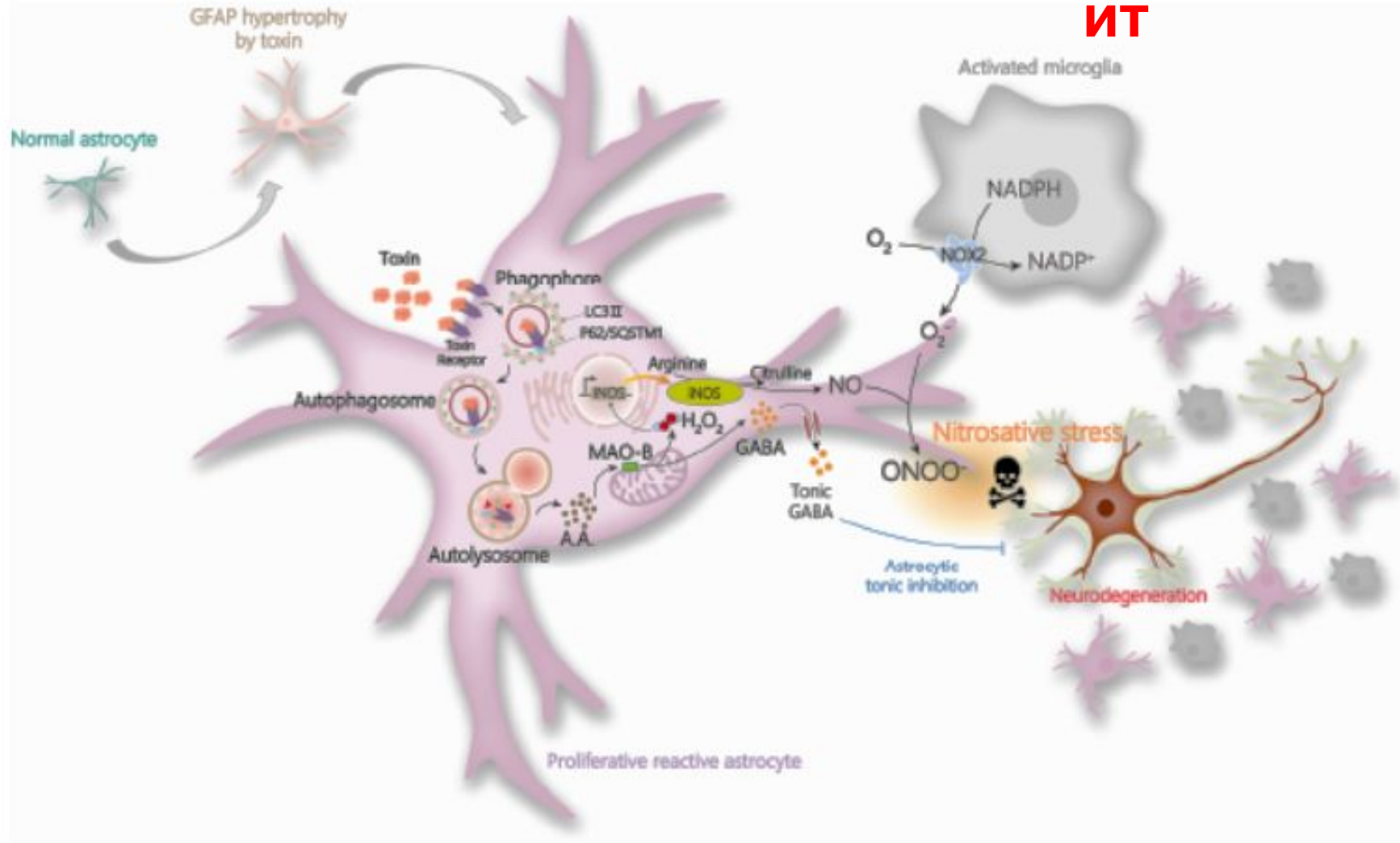


NADPH-  
оксидаза-2

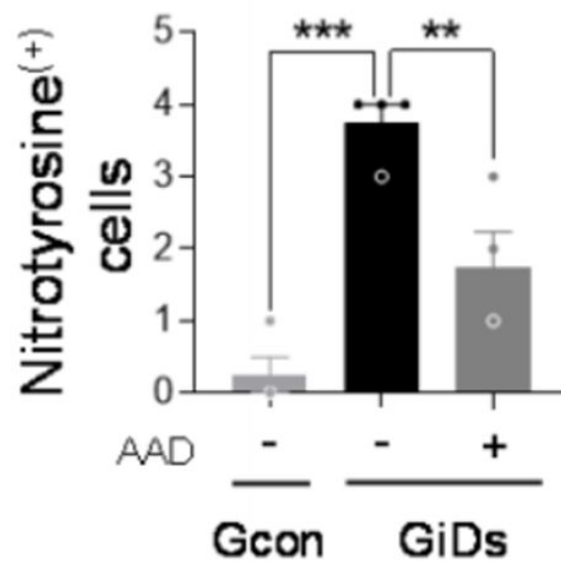
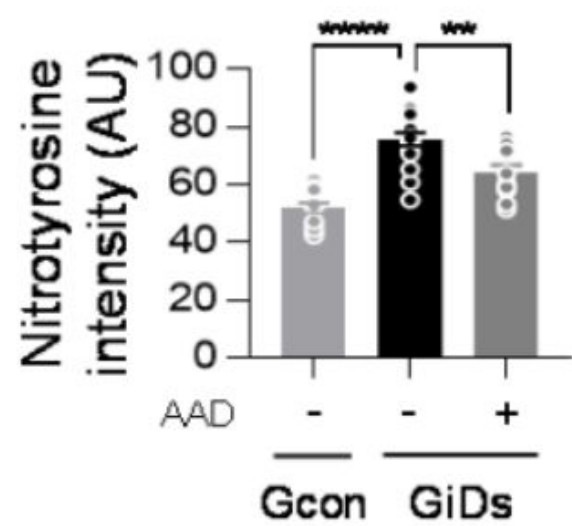
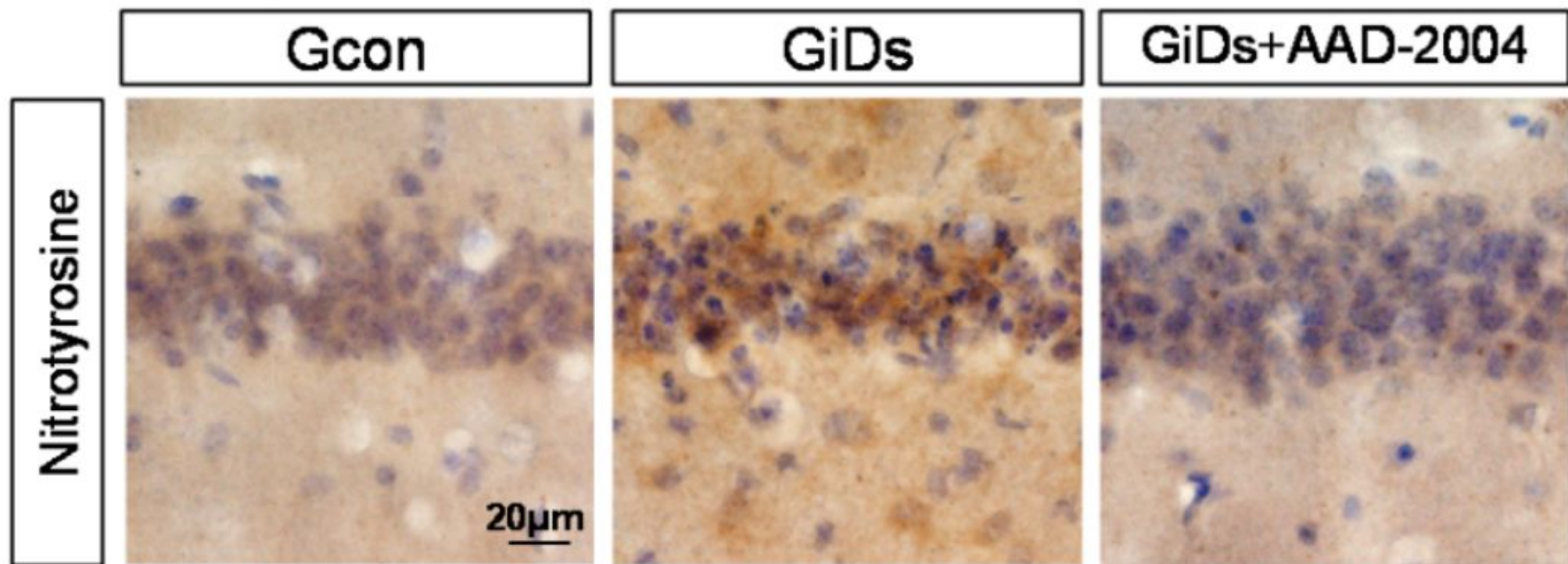


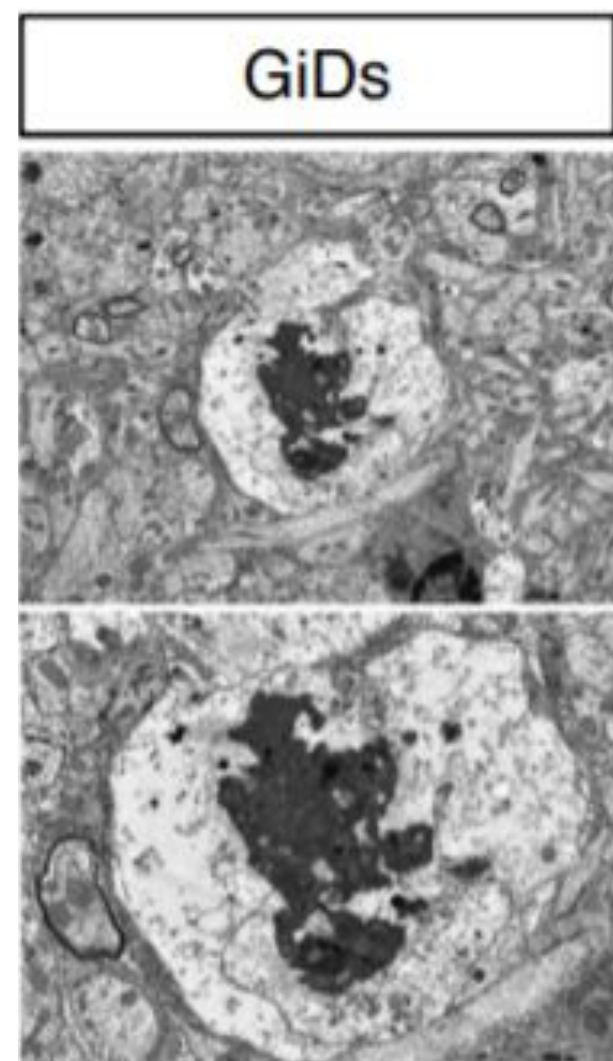
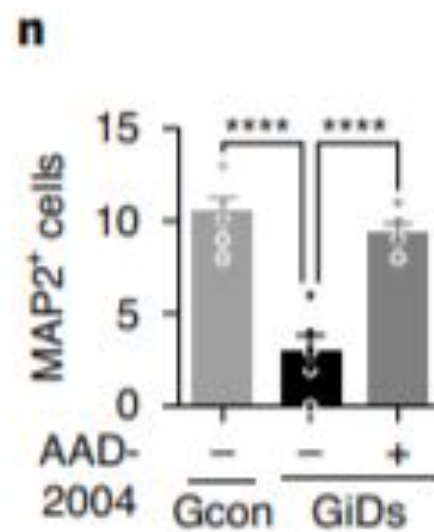
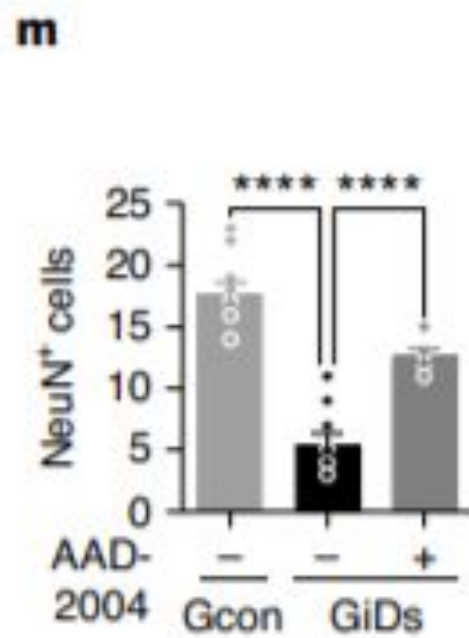
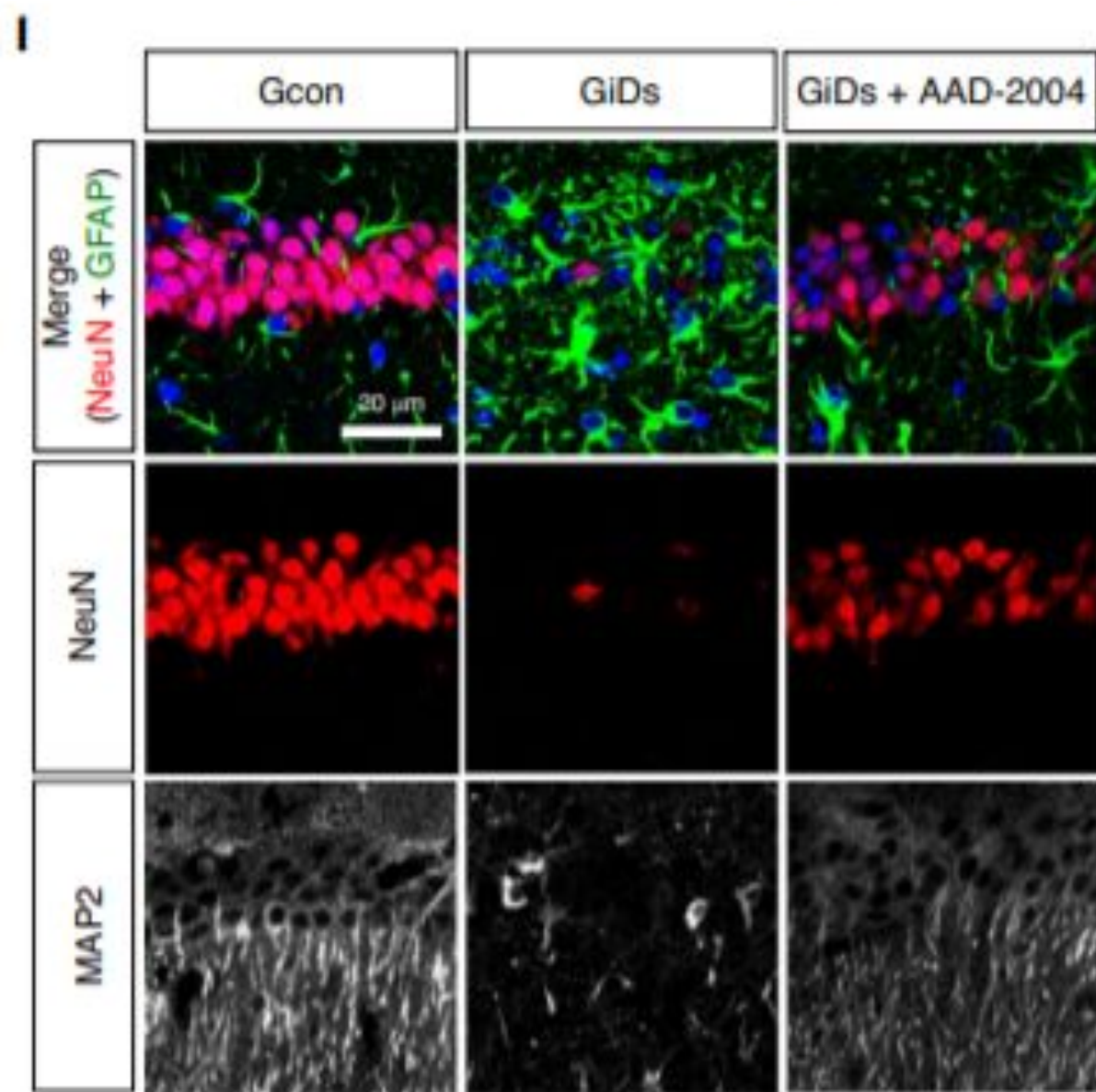


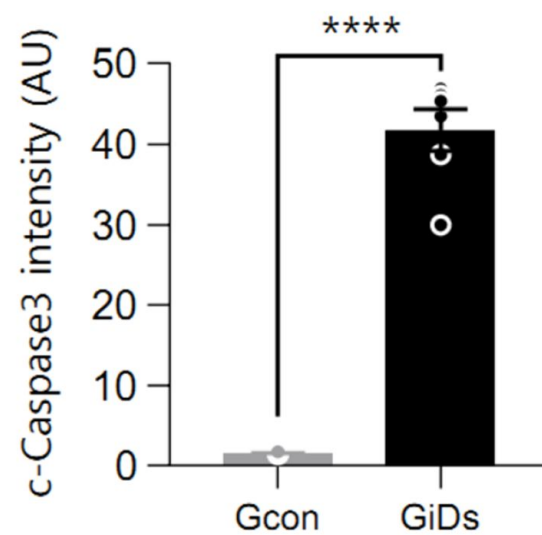
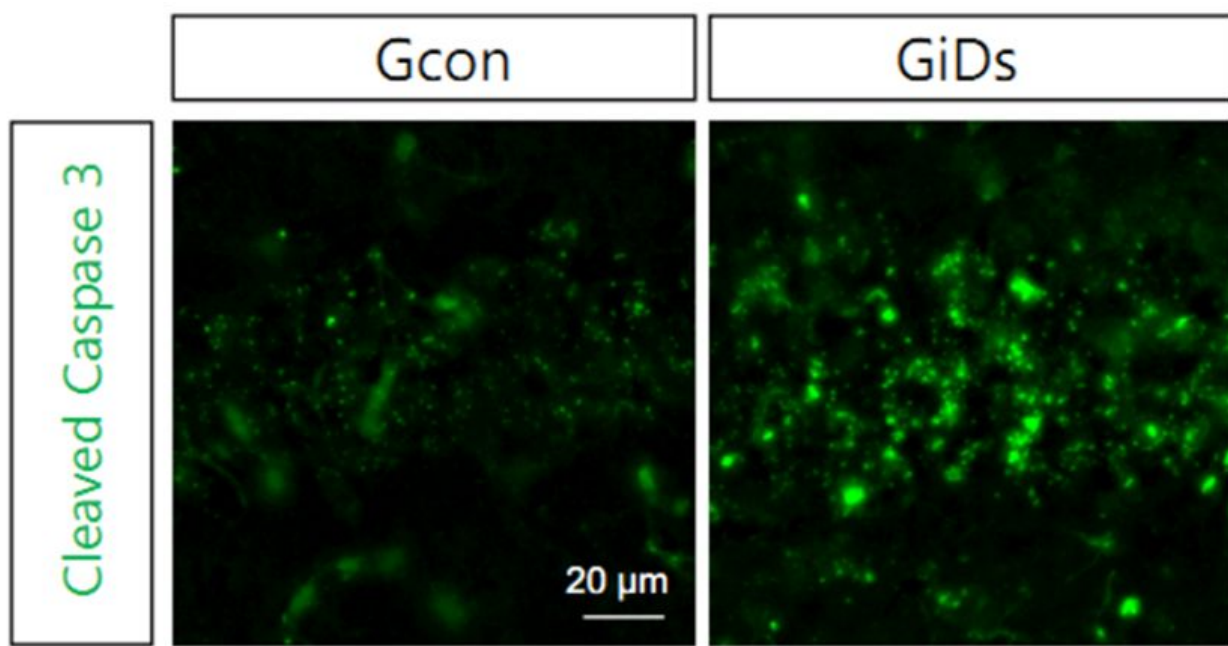
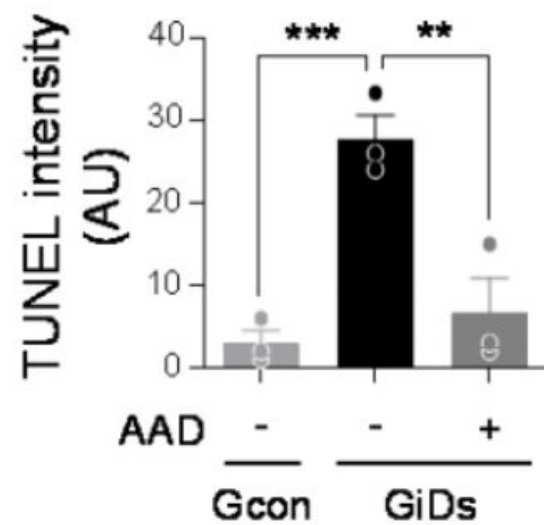
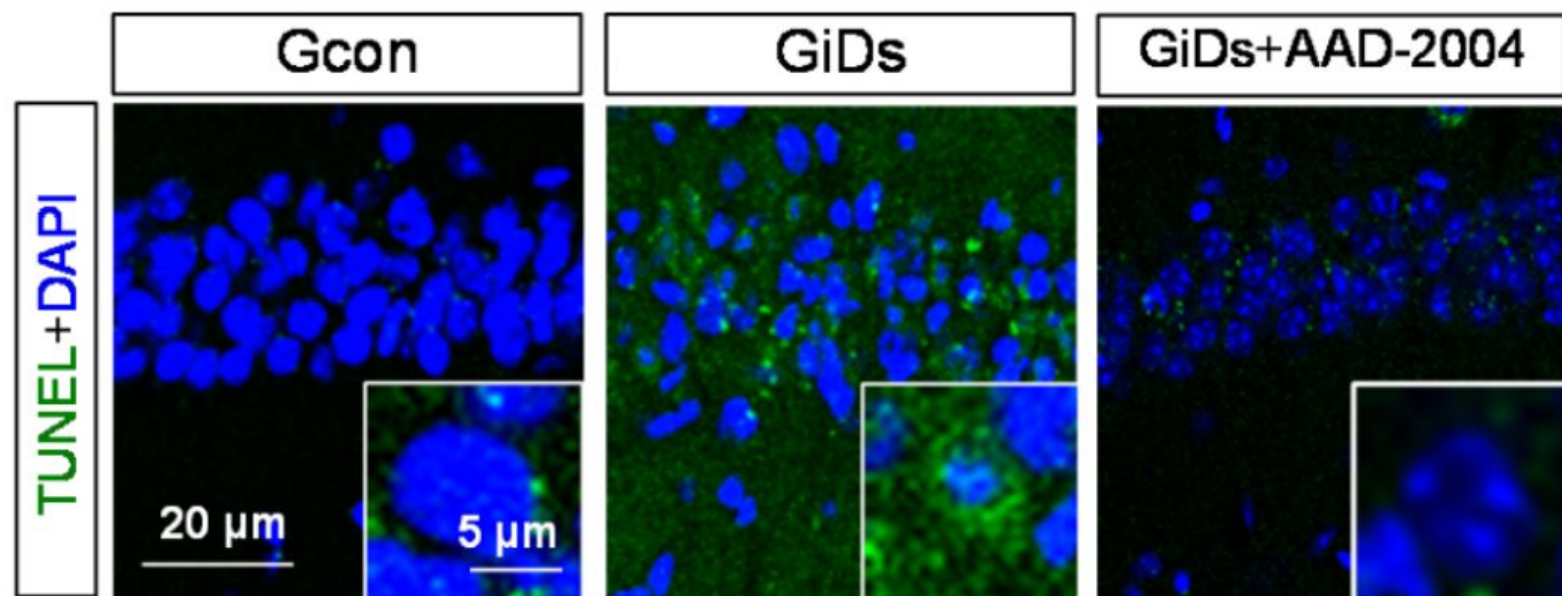
ИТ

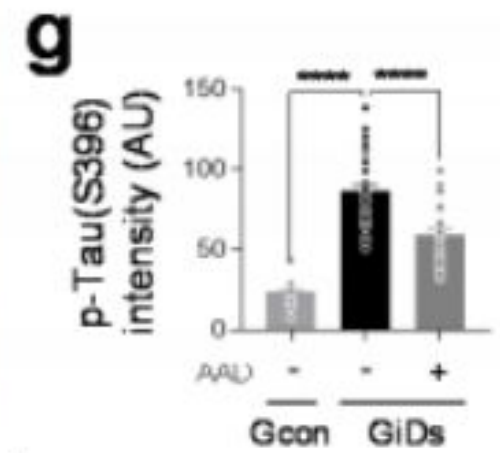
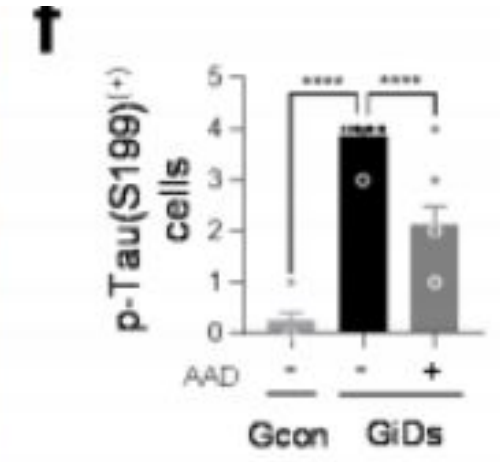
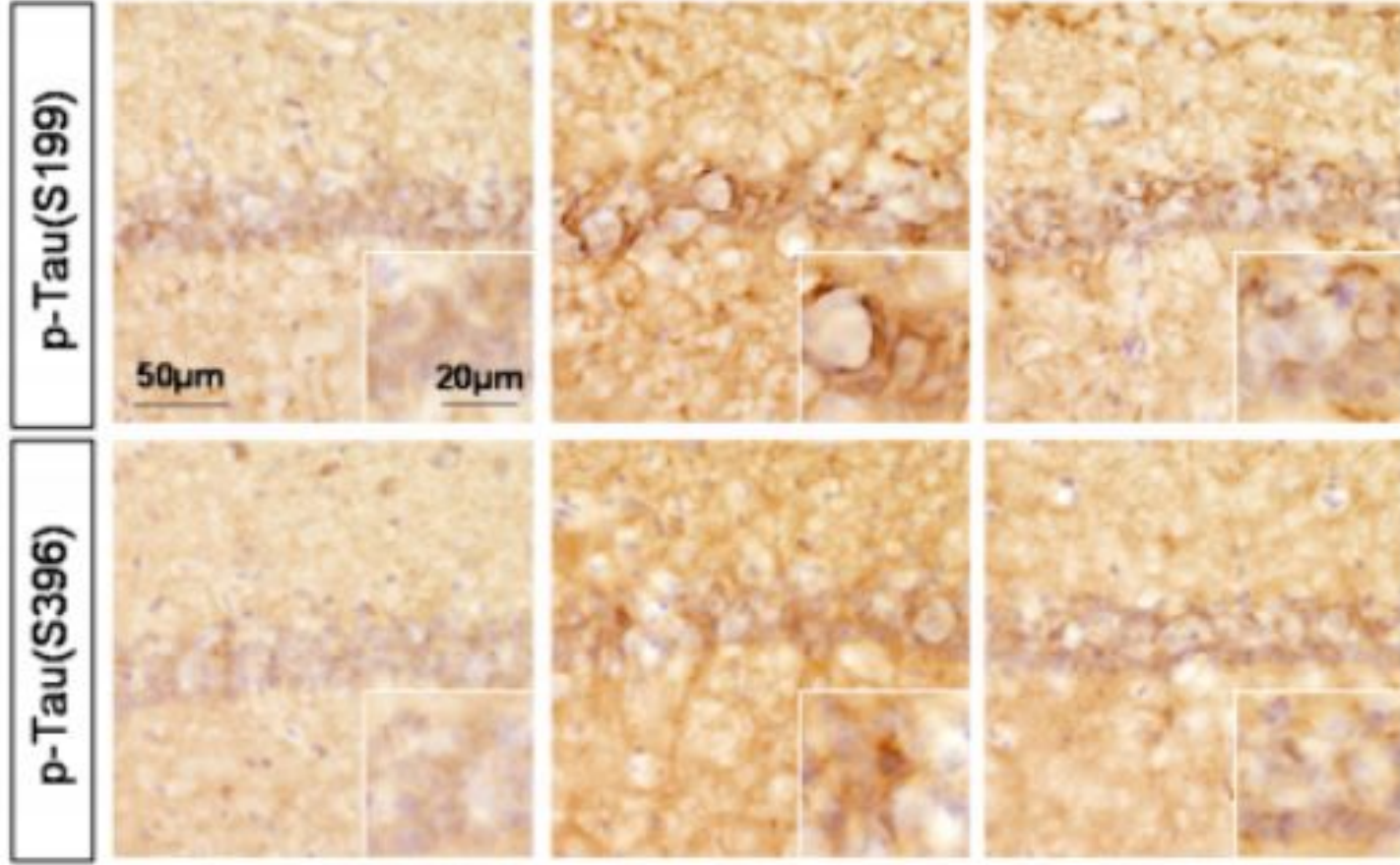




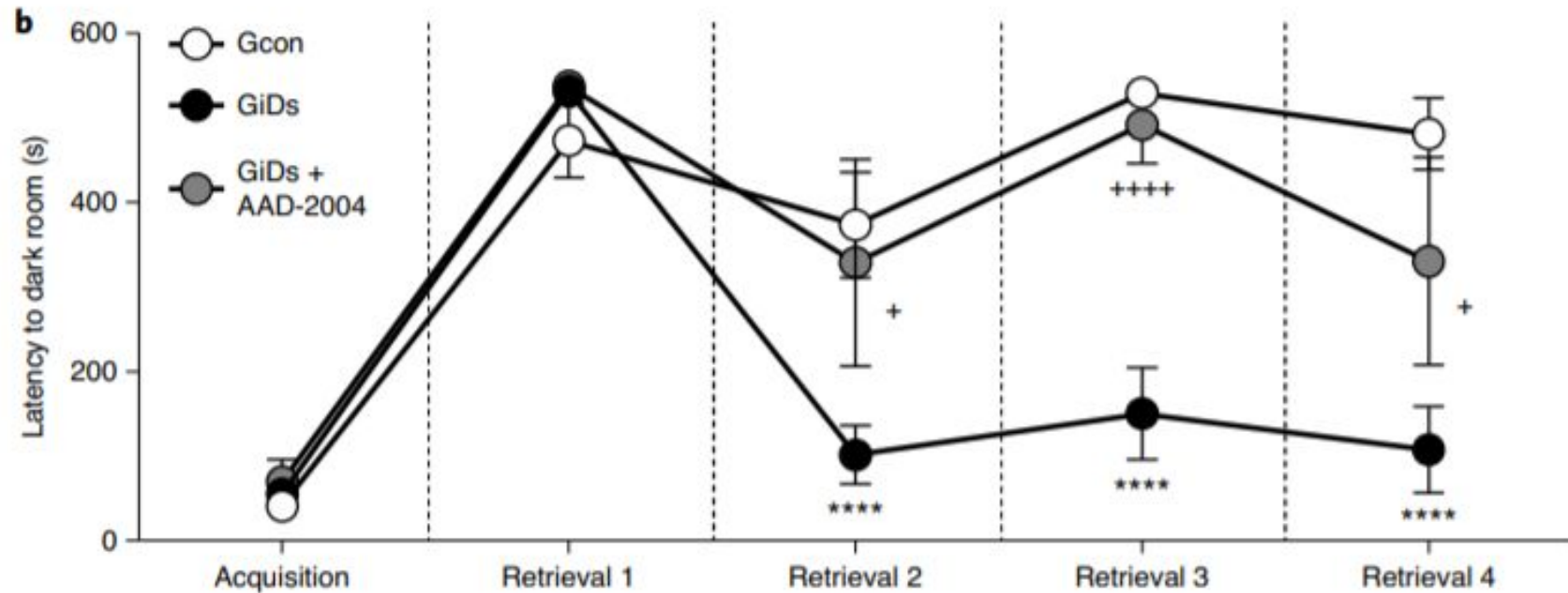
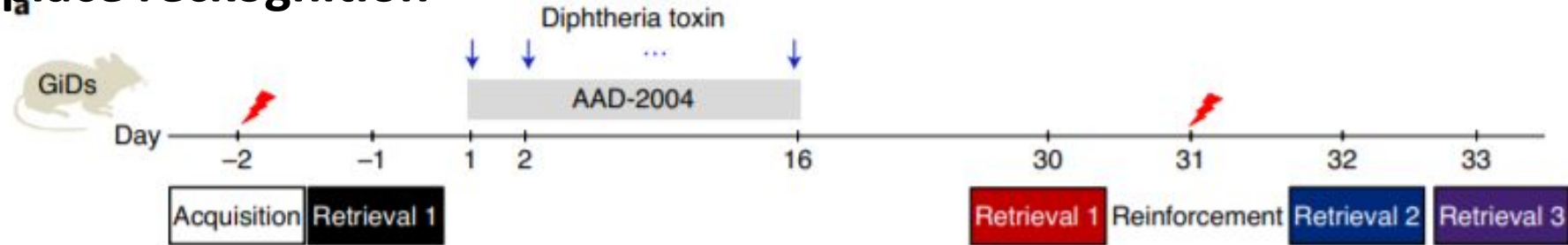


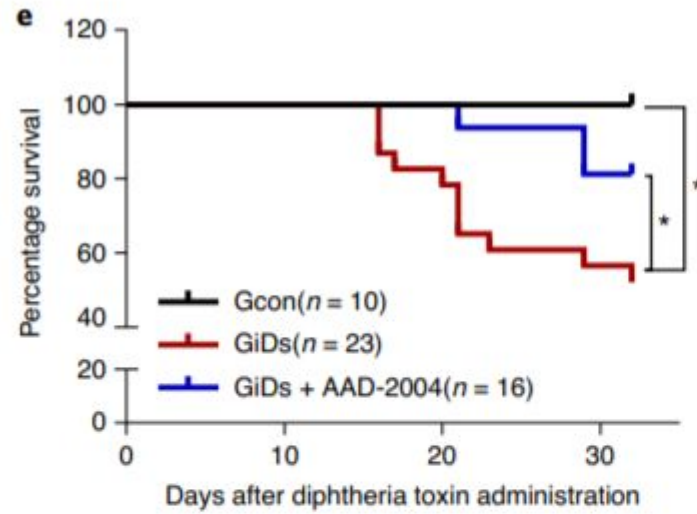
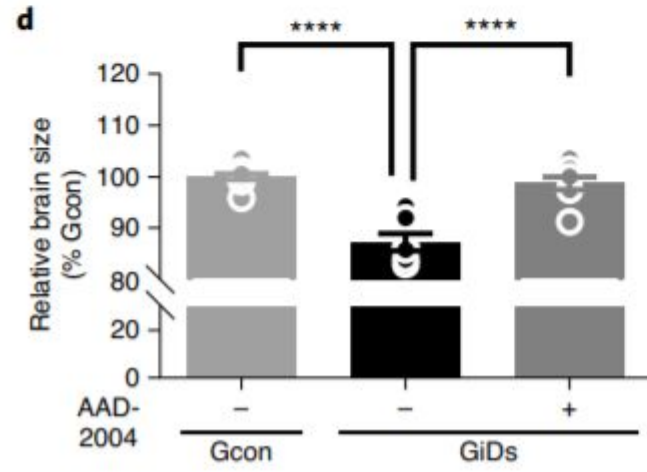
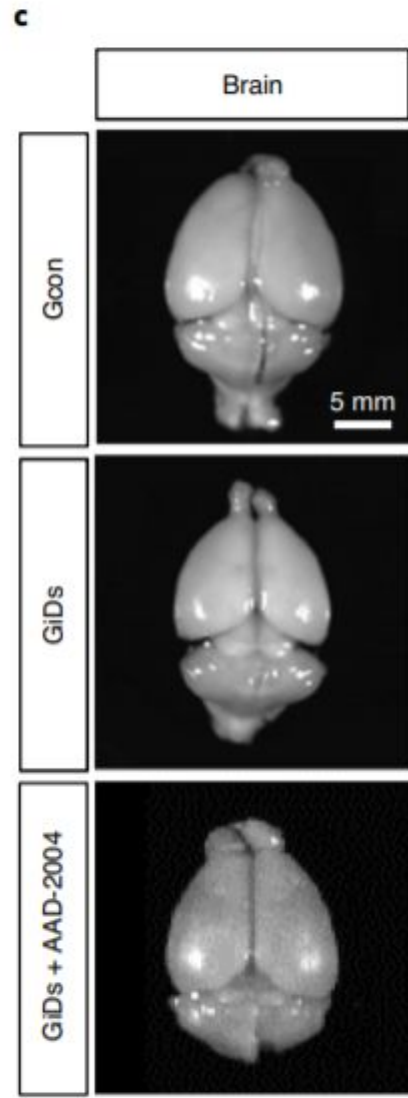




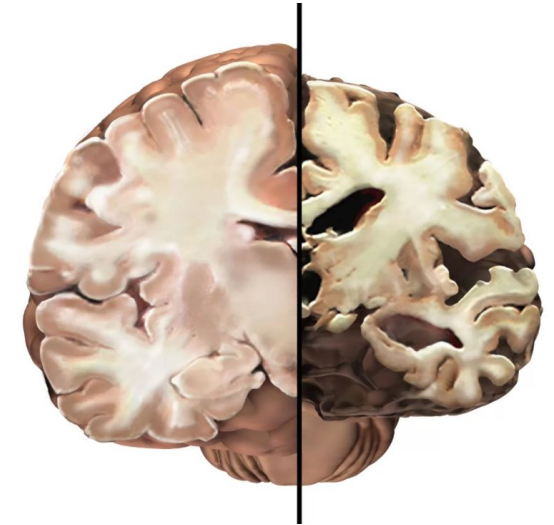
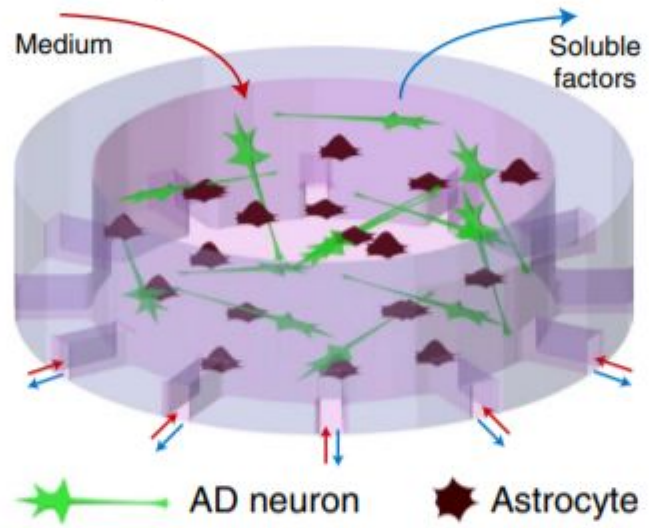


- пассивное избегание
- водный лабиринт Морриса
- novel place recognition



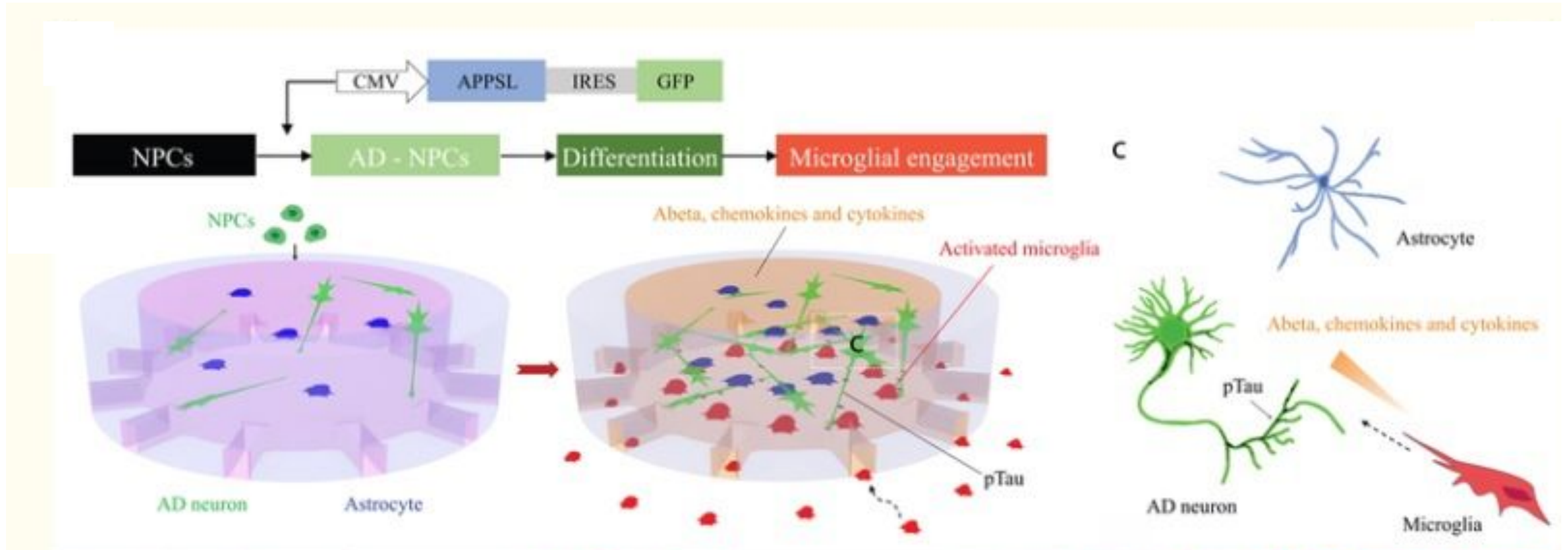


**a** 3D neurocyte AD

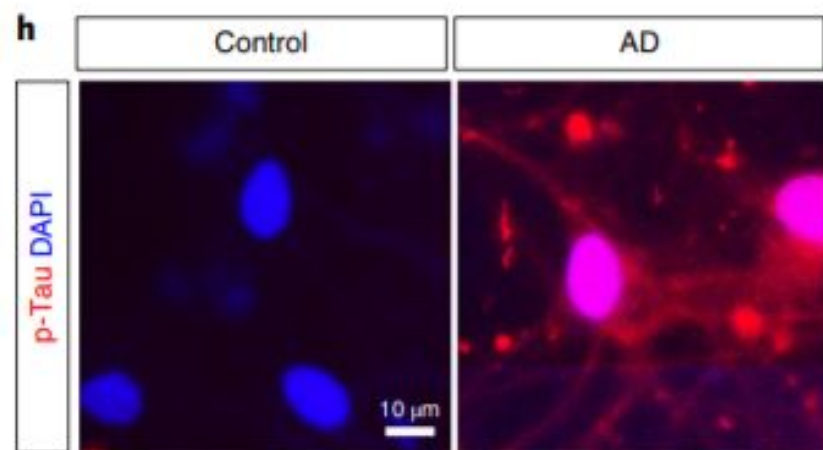
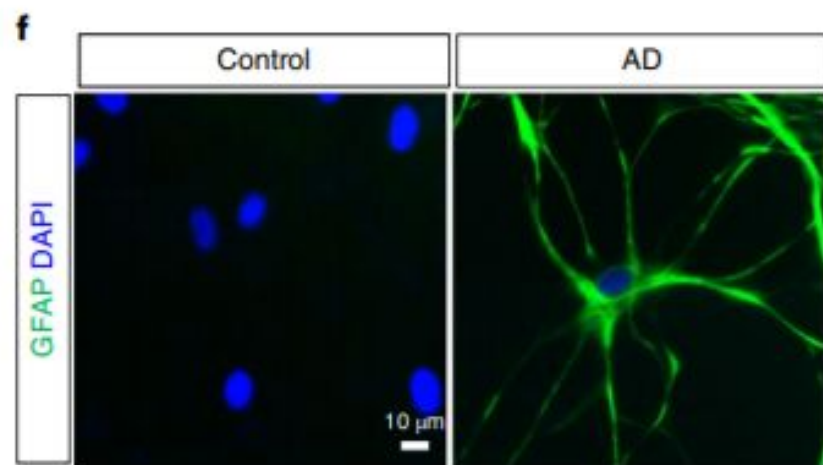
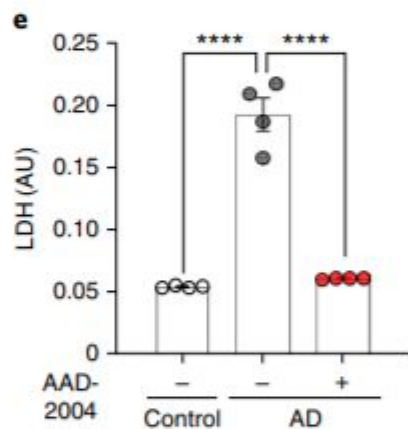
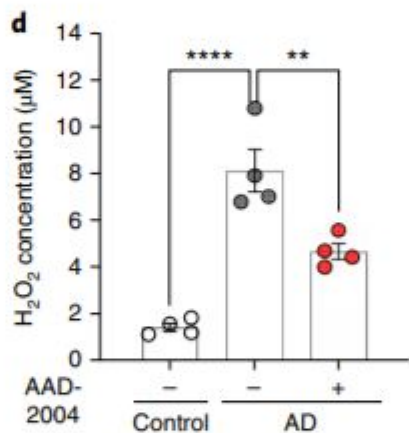
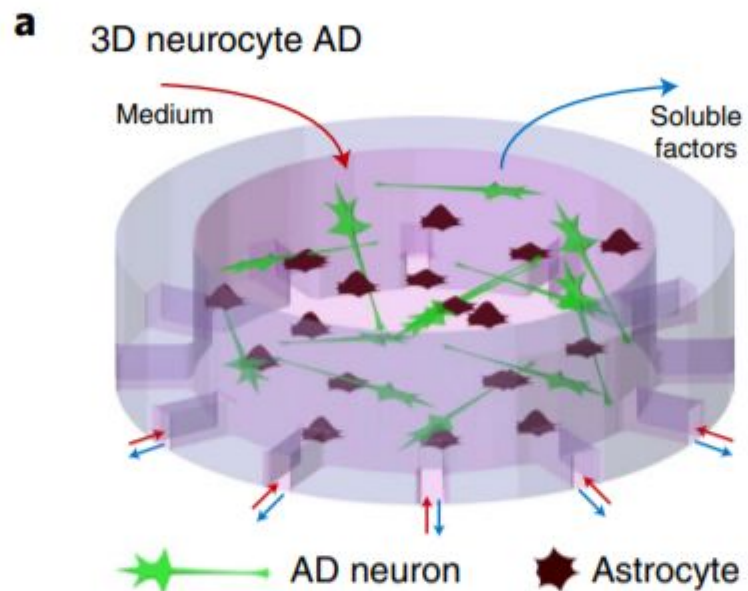


# 3D hNeuroGliAD

NPCs: APP (K670N/M671L, V717I)







**ADD-2004**



- H<sub>2</sub>O<sub>2</sub>
- GFAP
- 

**жизнеспособност**

**и**

- **p-тау**



WT or APP/PS1

**APP:**

K670N/M671L («Swedish»)

1716V («Florida»)

V717I («London»)

**PSEN1:**

M146L

L286

**ADD-2004**

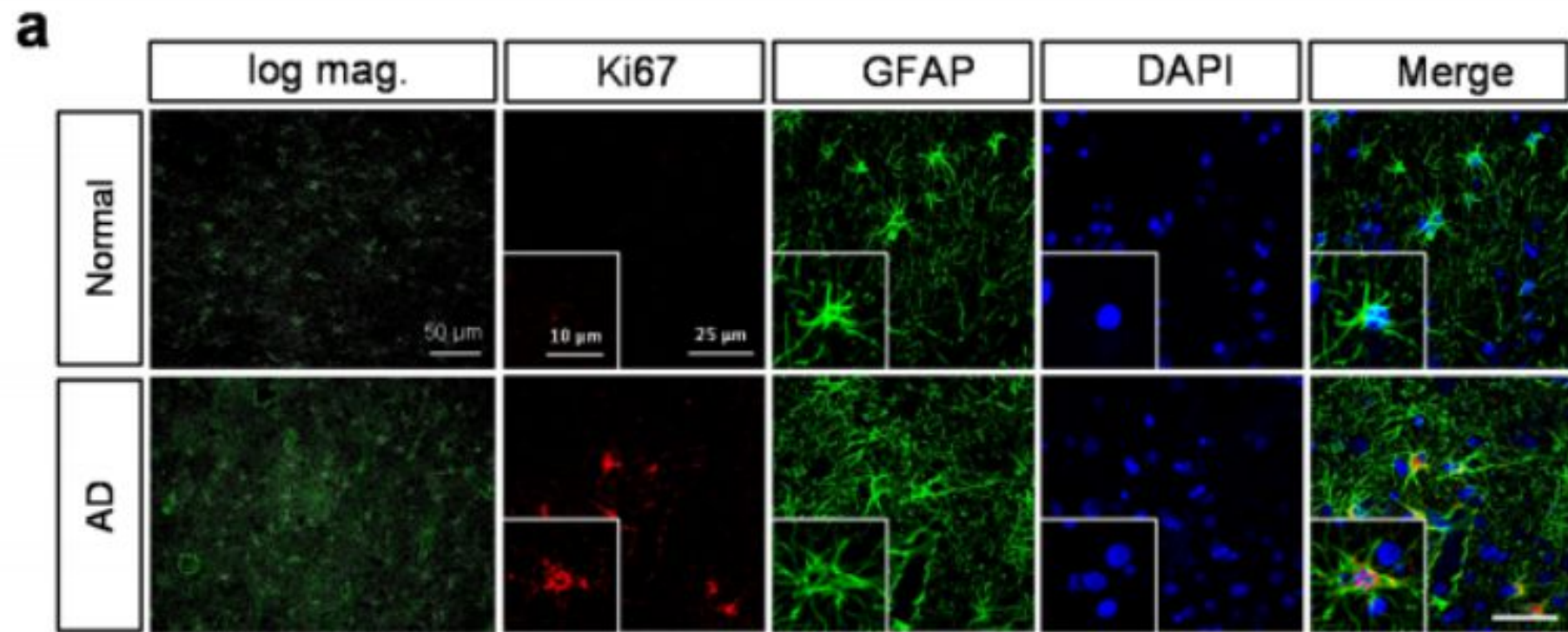
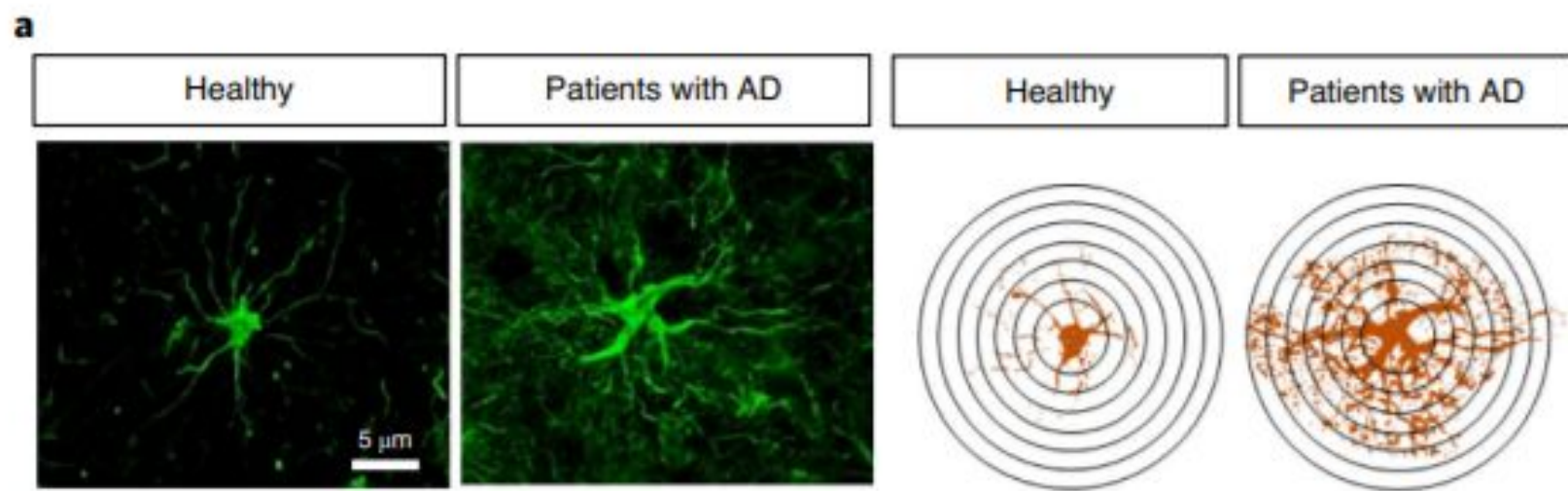
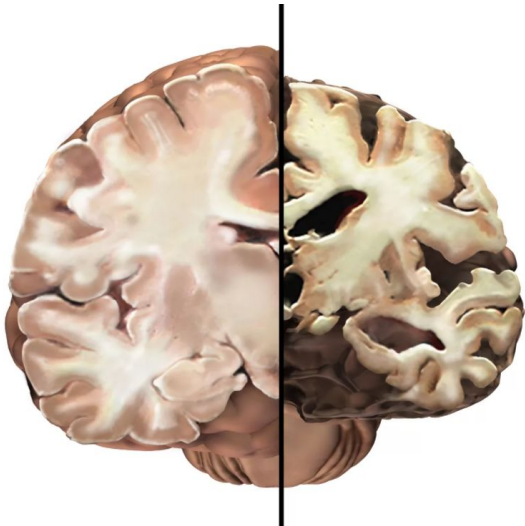


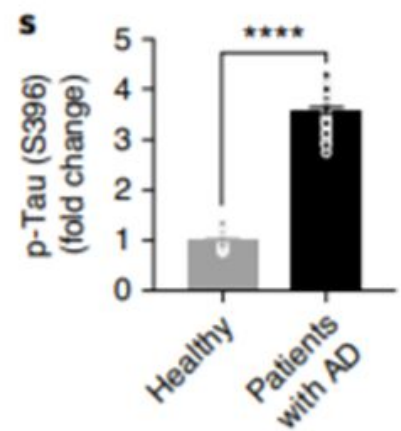
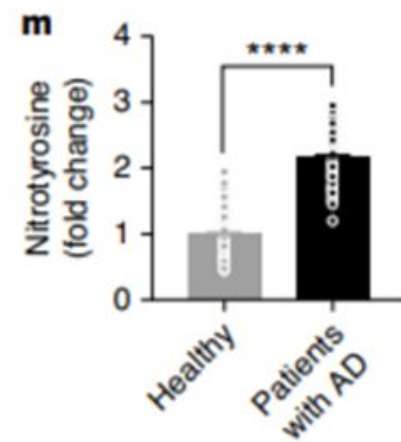
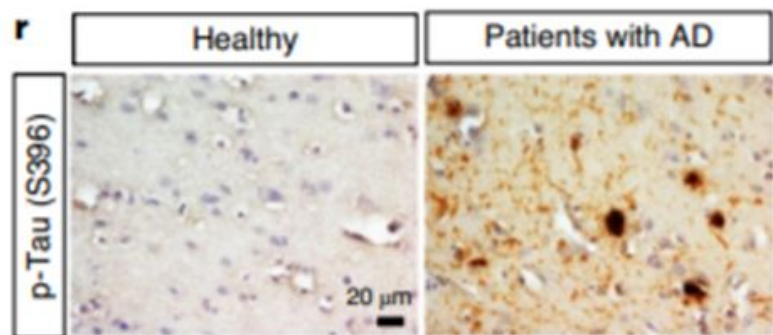
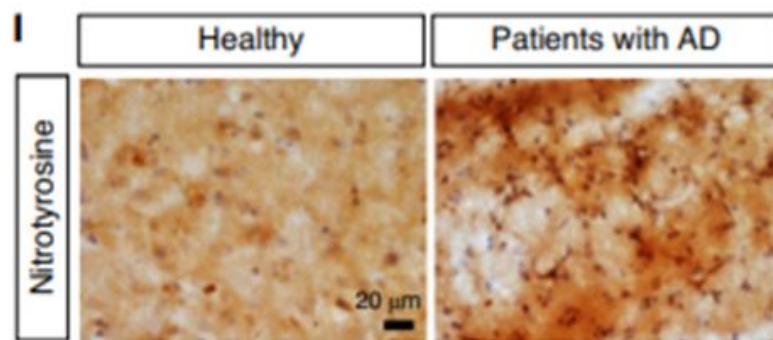
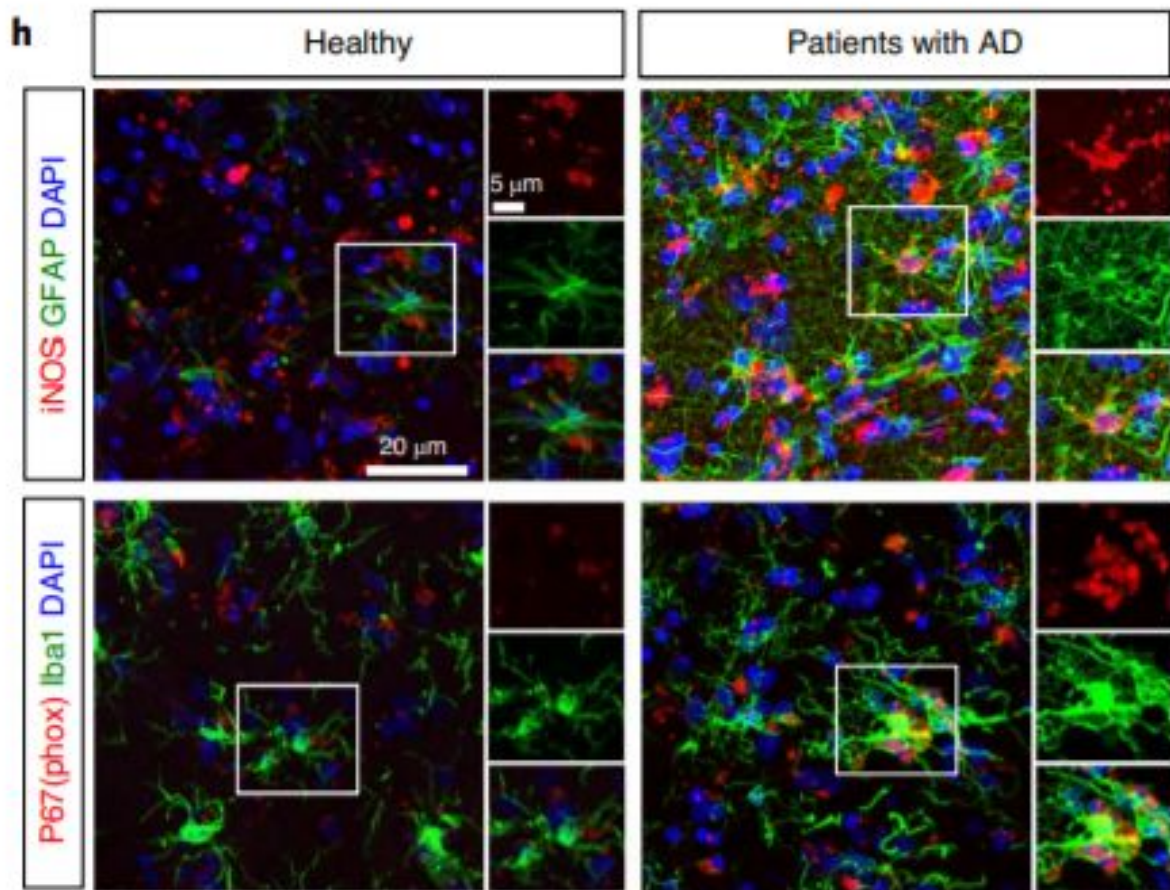
•  **H2O2**

• 

**пространственно  
й**

**памяти**





Virus injection

AAV-GFAP104-GFP

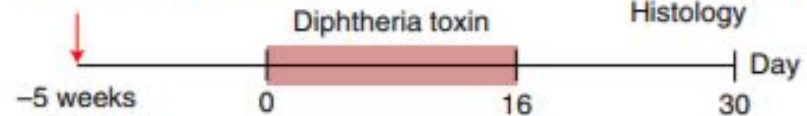
or

AAV-GFAP104-DTR-GFP

Behavior

Electrophysiology

Histology



APP/PS1 + GFP

APP/PS1 + DTR

