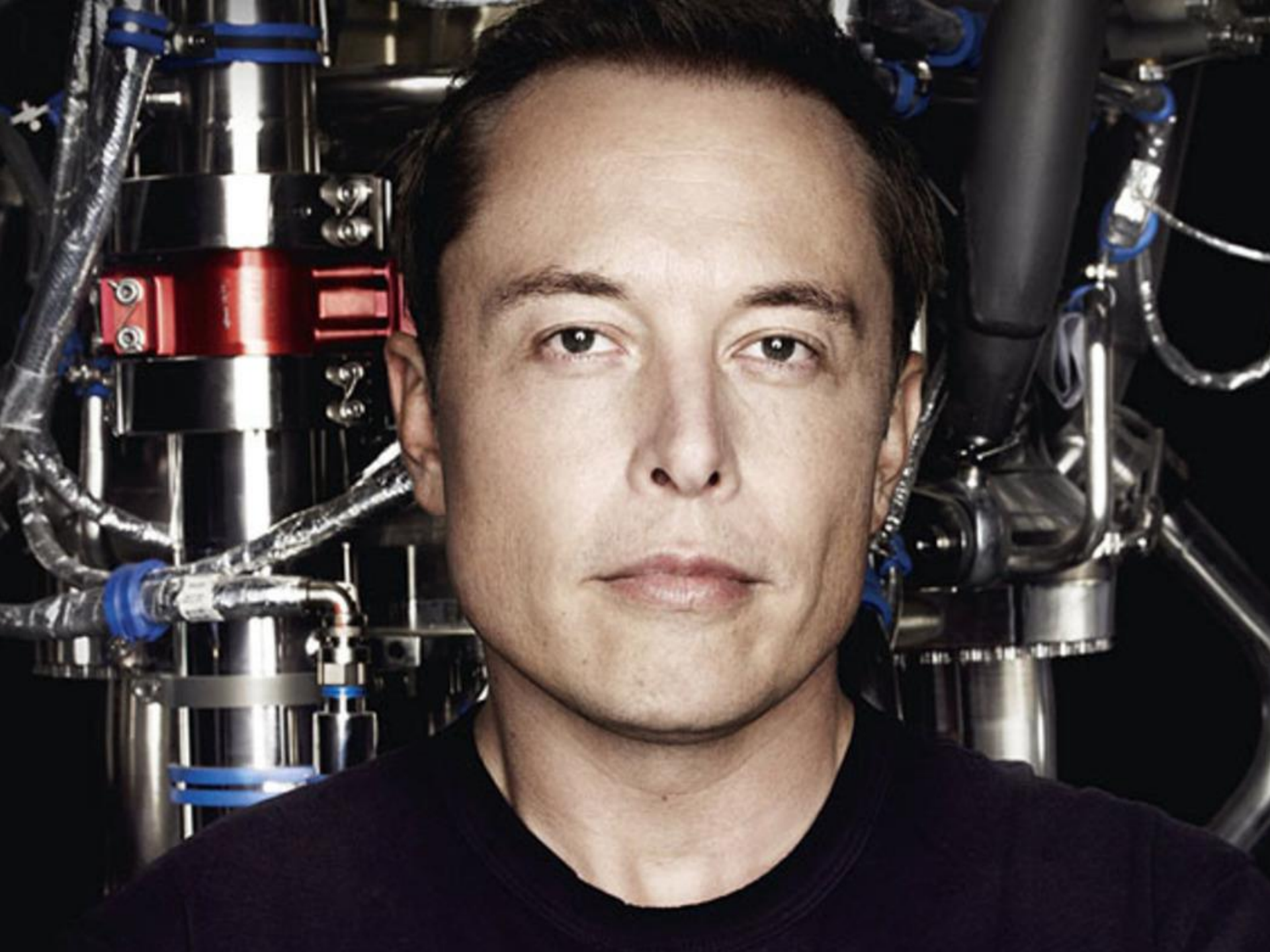
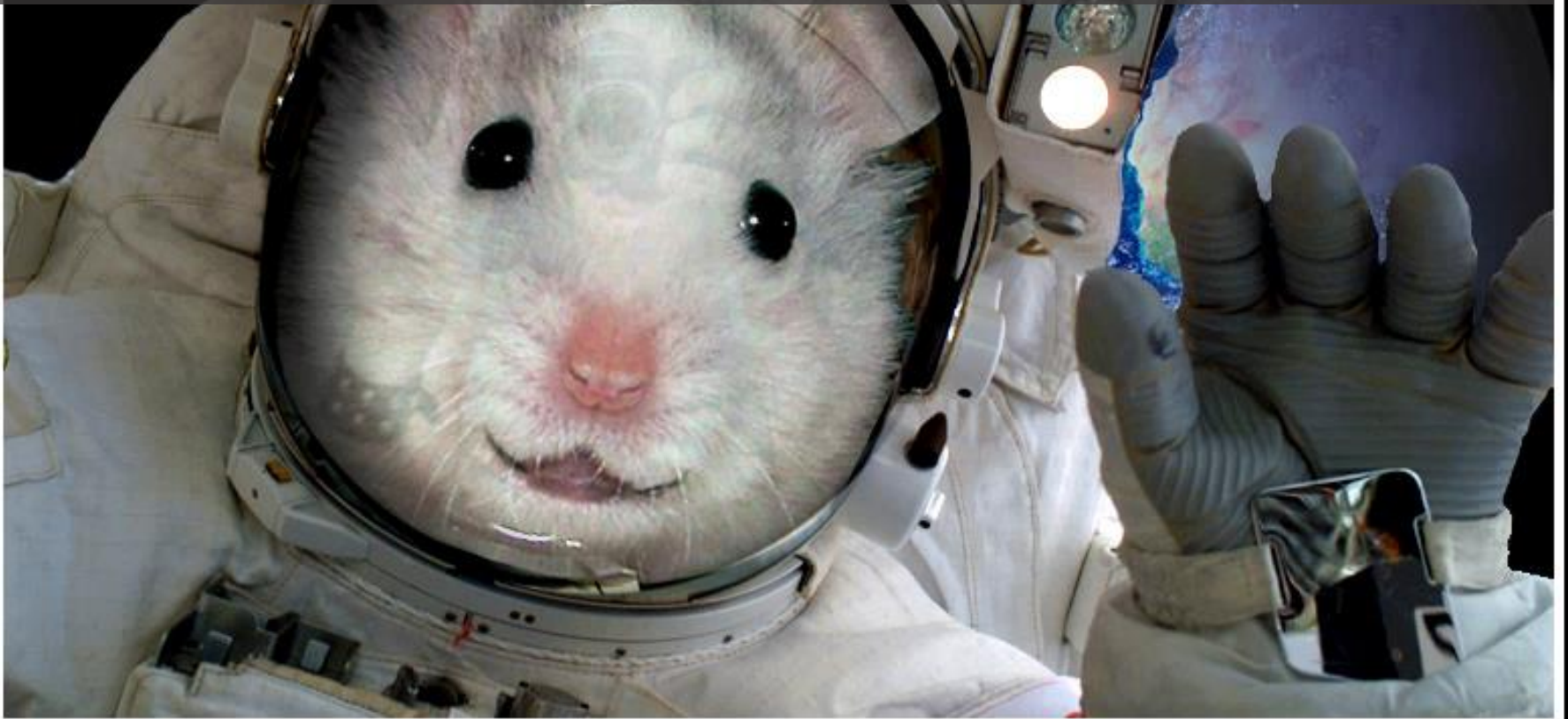


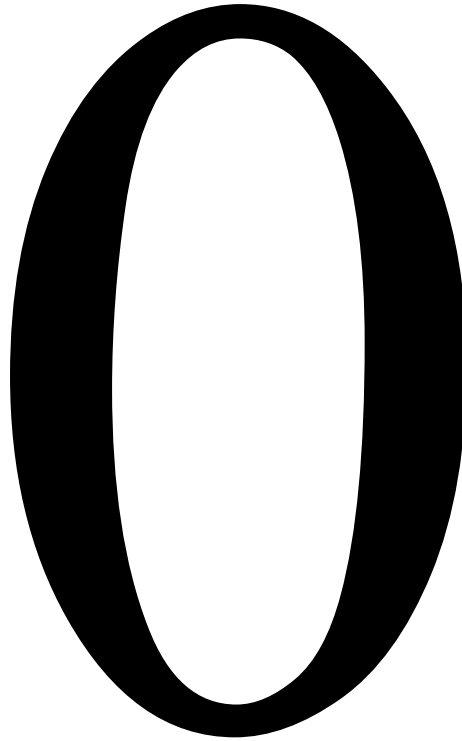
БОЛЕЗНЬ АЛЬЦГЕЙМЕРА: порочный круг



Galactic Cosmic Radiation Leads to Cognitive Impairment and Increased A β Plaque Accumulation in a Mouse Model of Alzheimer's Disease

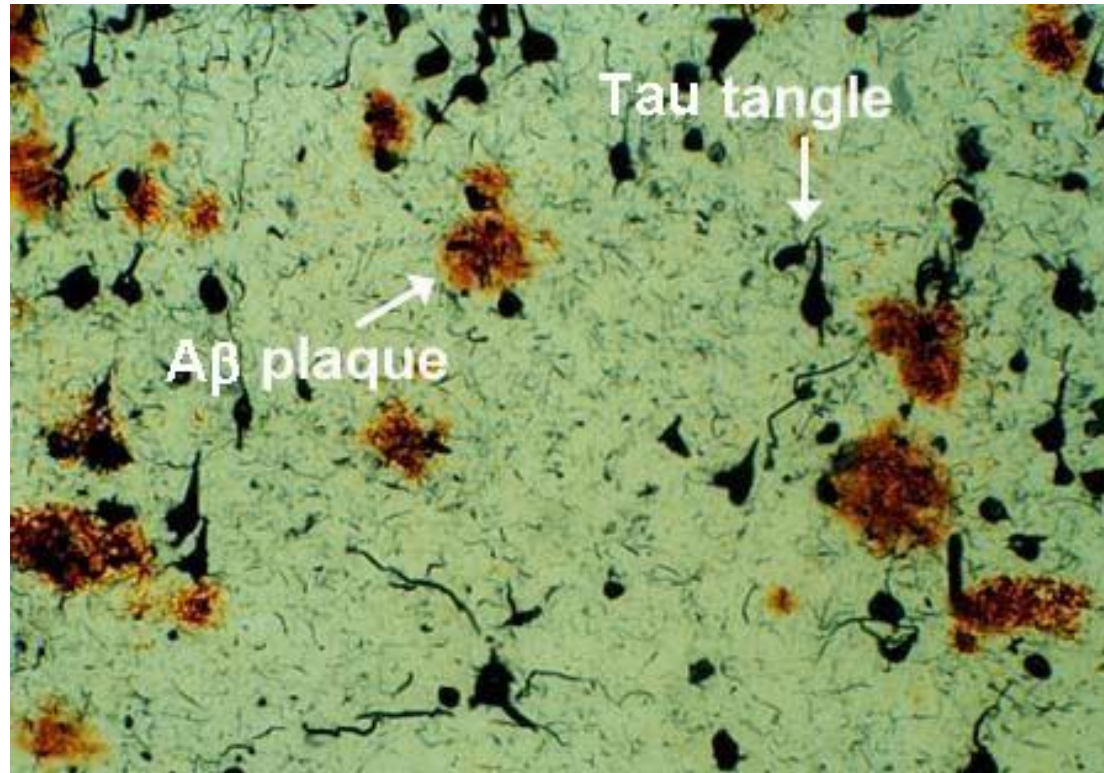
Jonathan D. Cherry, Bin Liu, Jeffrey L. Frost, Cynthia A. Lemere,
Jacqueline P. Williams, John A. Olschowka, M. Kerry O'Banion
Plos One 2013





Такое количество лекарств, дающих несимптоматический эффект при болезни Альцгеймера одобрено для применения в клинике USFDA

Препарат ткани мозга больного Альцгеймером

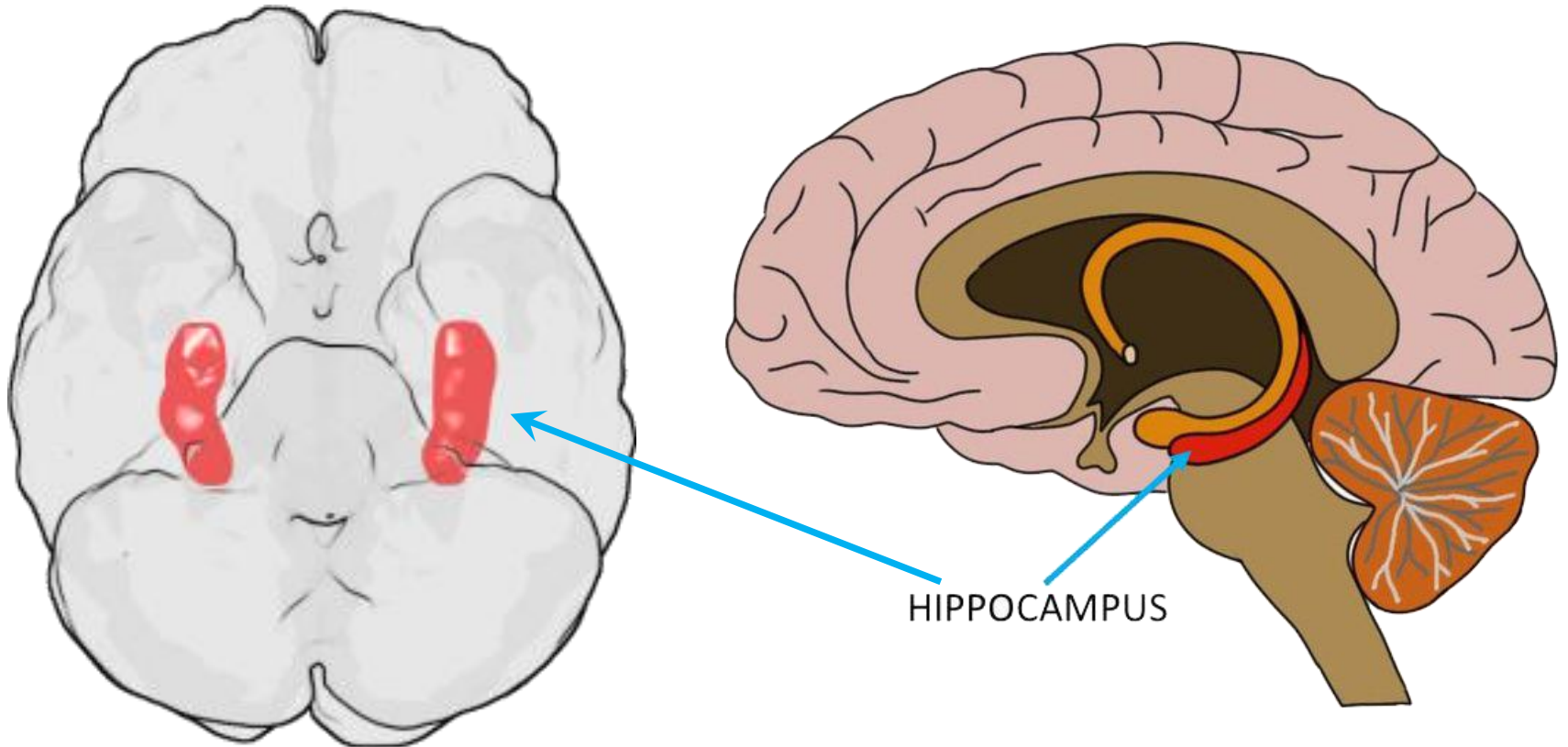


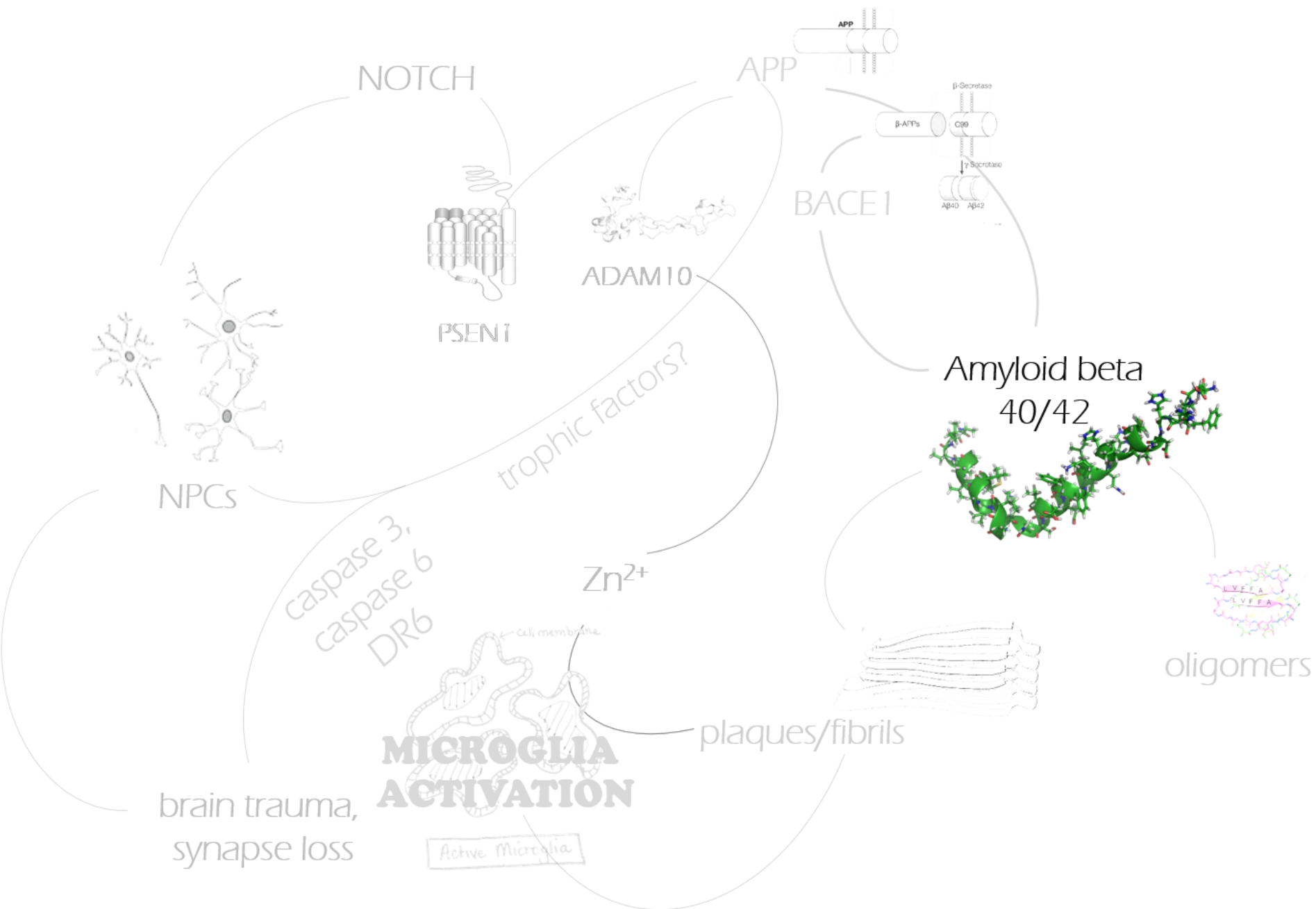
<http://upr.org/post/alzheimers-disease-worldwide-collaboration-research?&cuid=600bb40390b70ca52f8d2fa69ab7495d>

A β = бета-амилоид Альцгеймера

Tau = белок тау

Глутаматергические нейроны гиппокампа

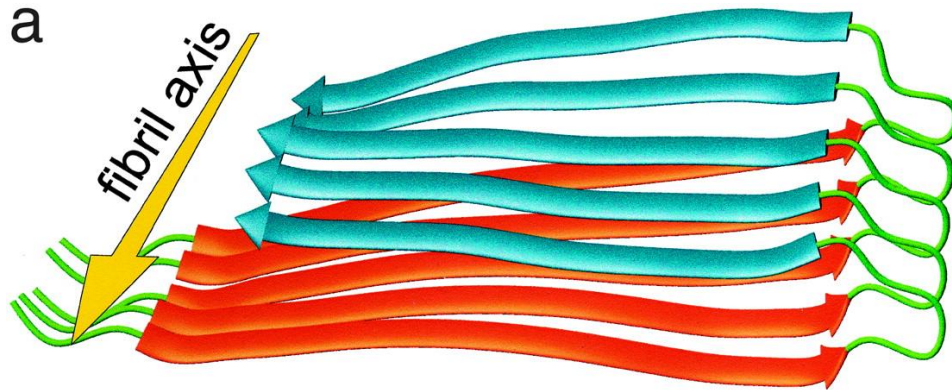




DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA

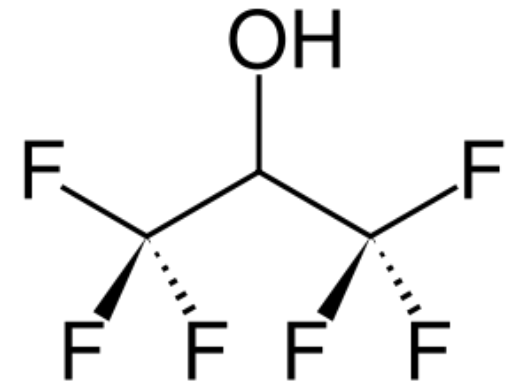
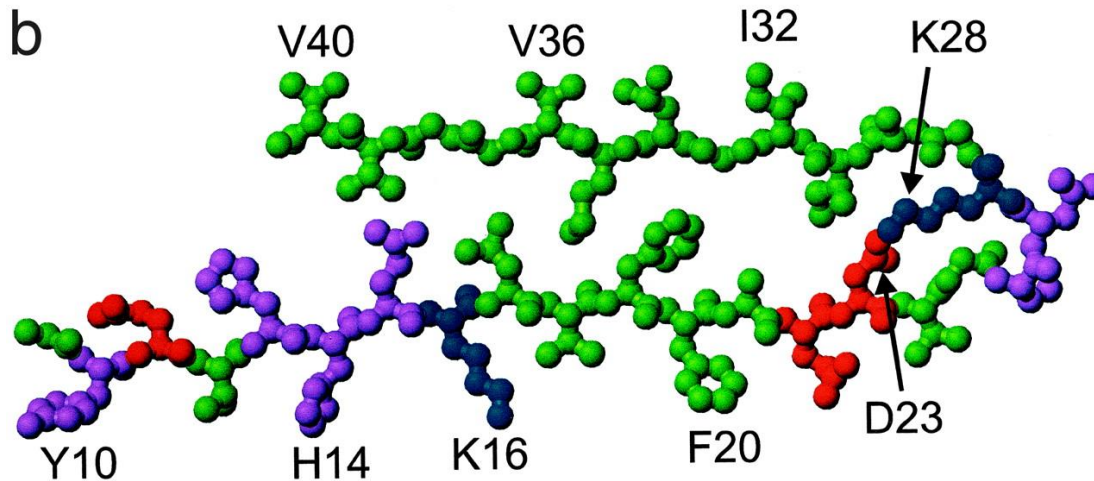
$A\beta_{40}$

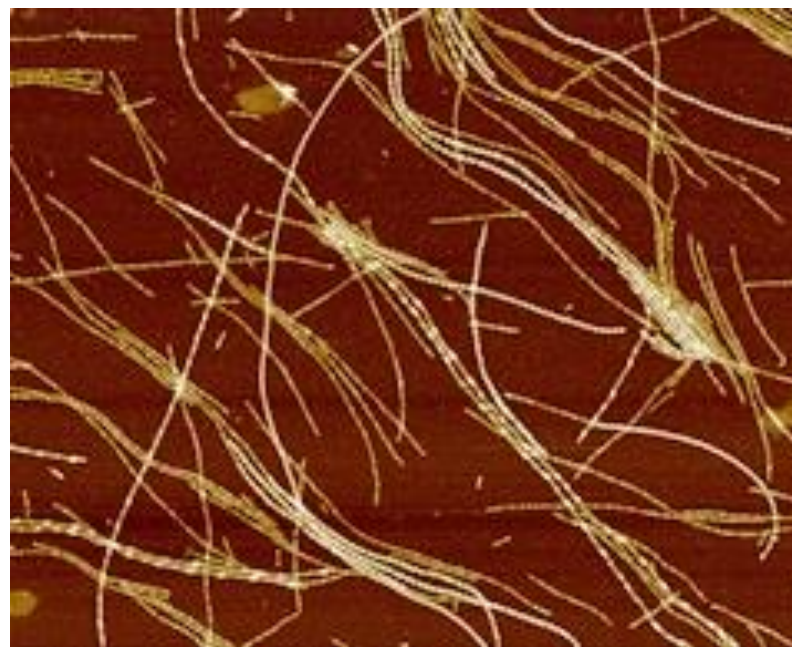
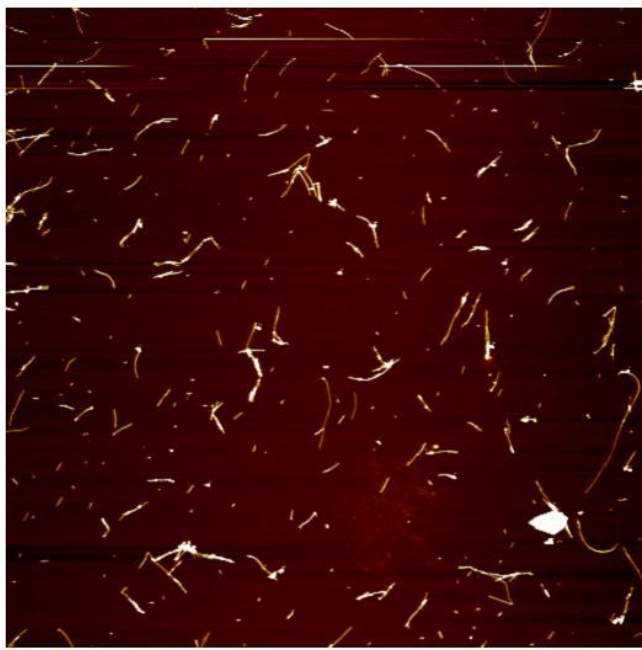
$A\beta_{42}$



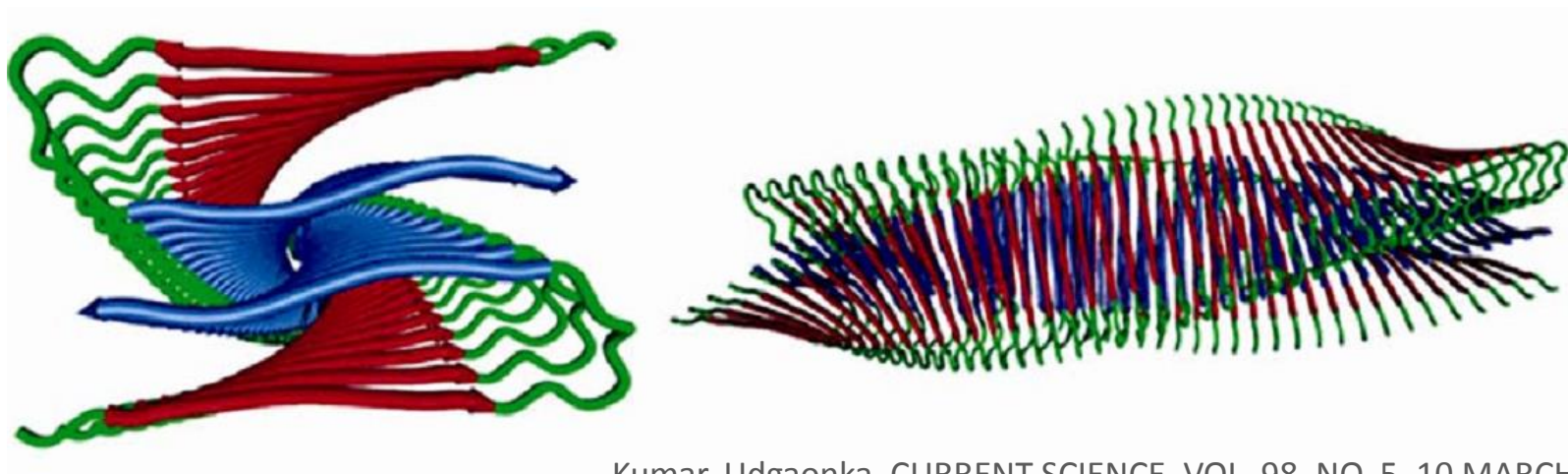
DMSO, SDS, membrane-like detergents: α -helix

H_2O , pH = 7: β -sheet

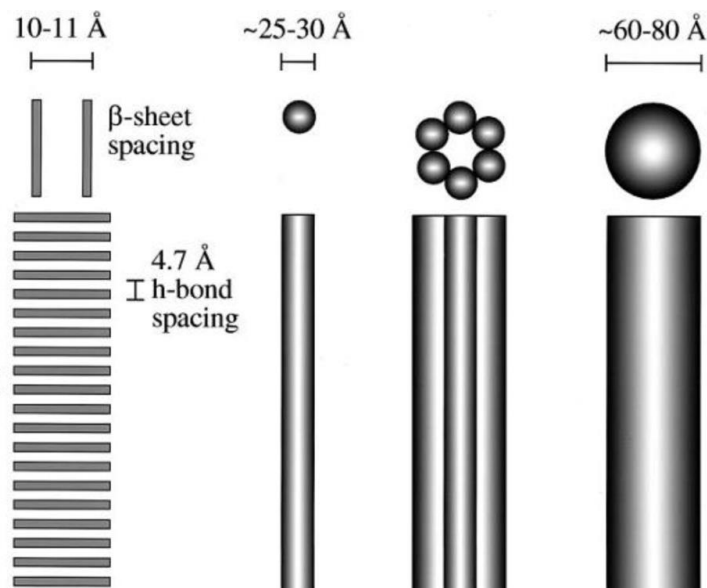
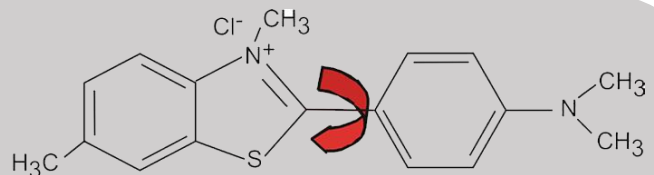
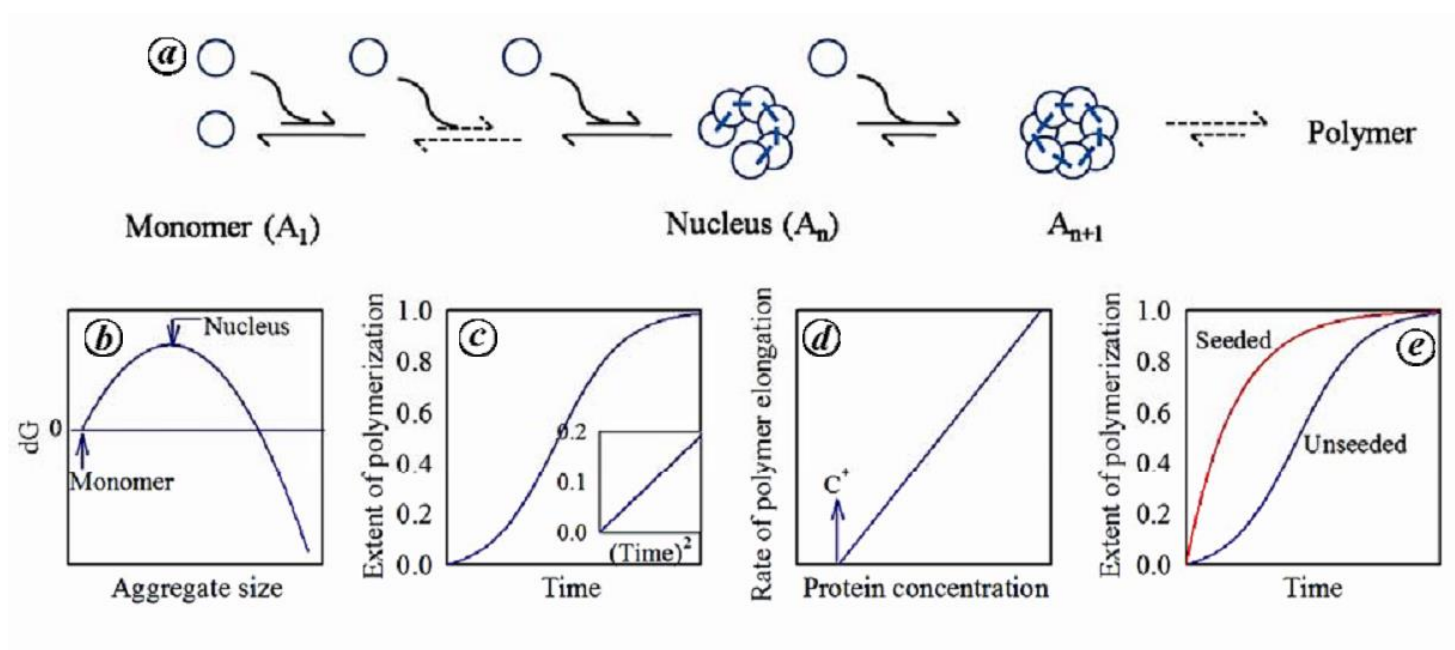


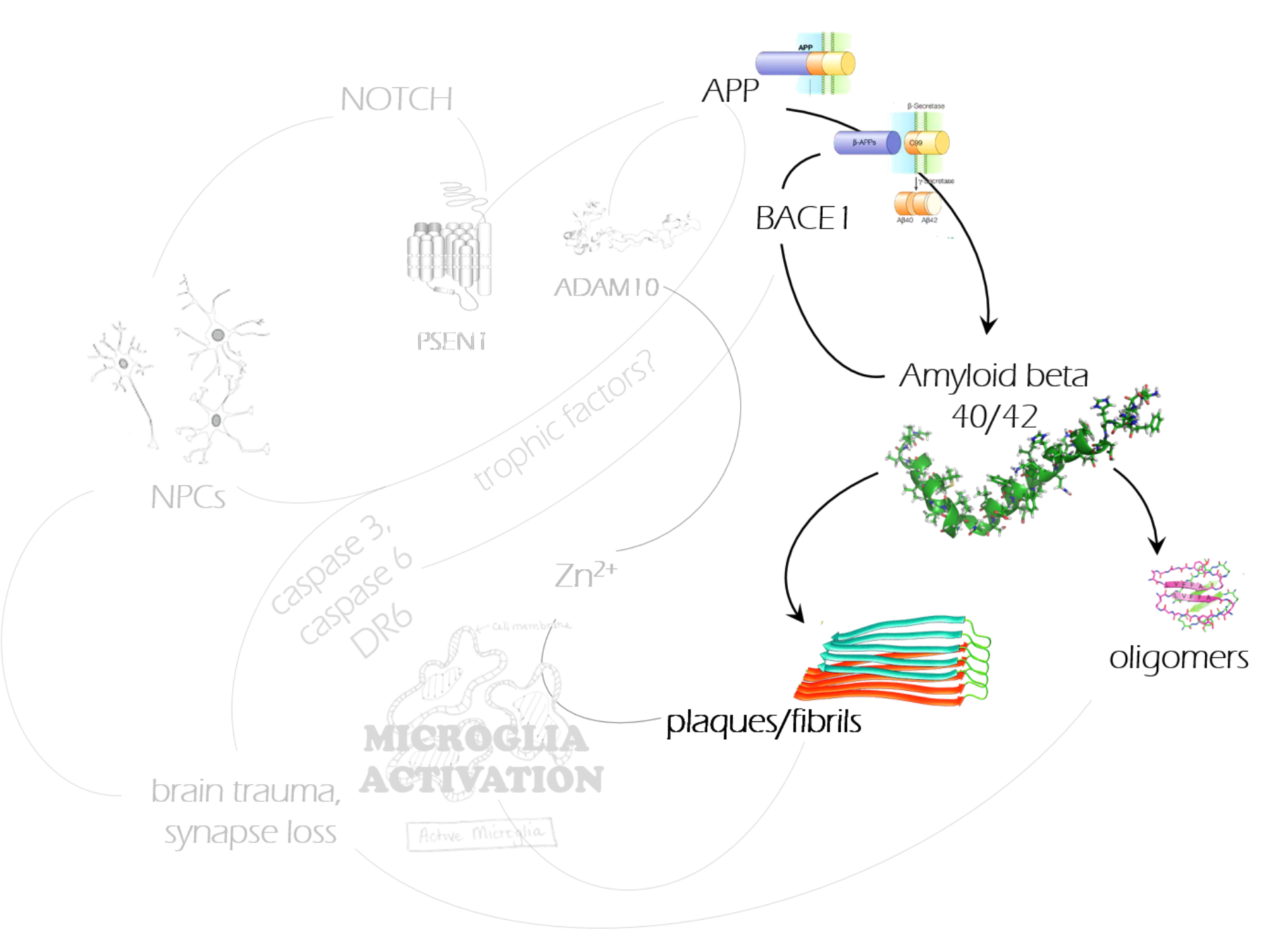


AFM pictures of fibrillizes Abeta 1-40 (left) and 1-42 (right)

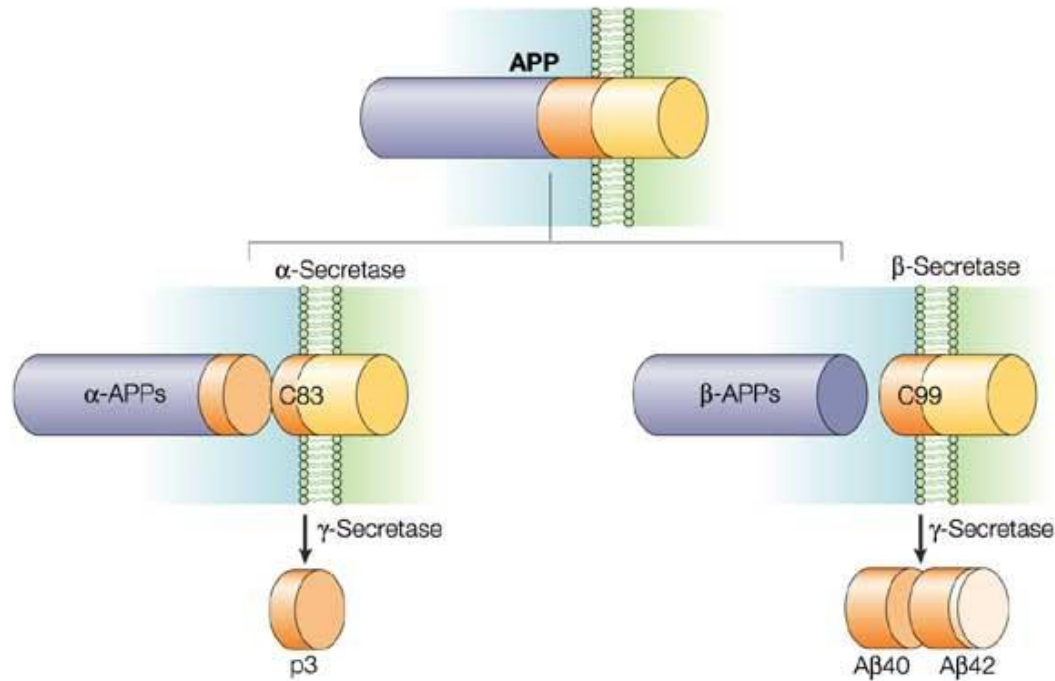


Механизм образования амилоидных фибрилл

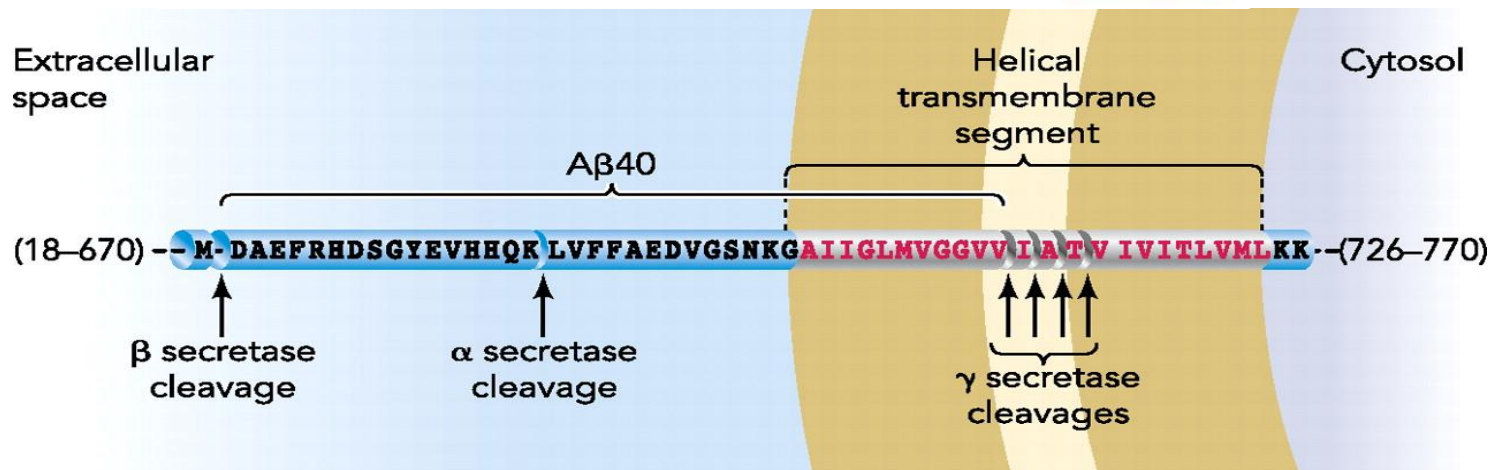




Amyloid precursor protein



Nature Reviews | Neuroscience



Болезнь Альцгеймера

```
graph TD; A[Болезнь Альцгеймера] --> B[Раннее начало]; A --> C[Позднее начало];
```

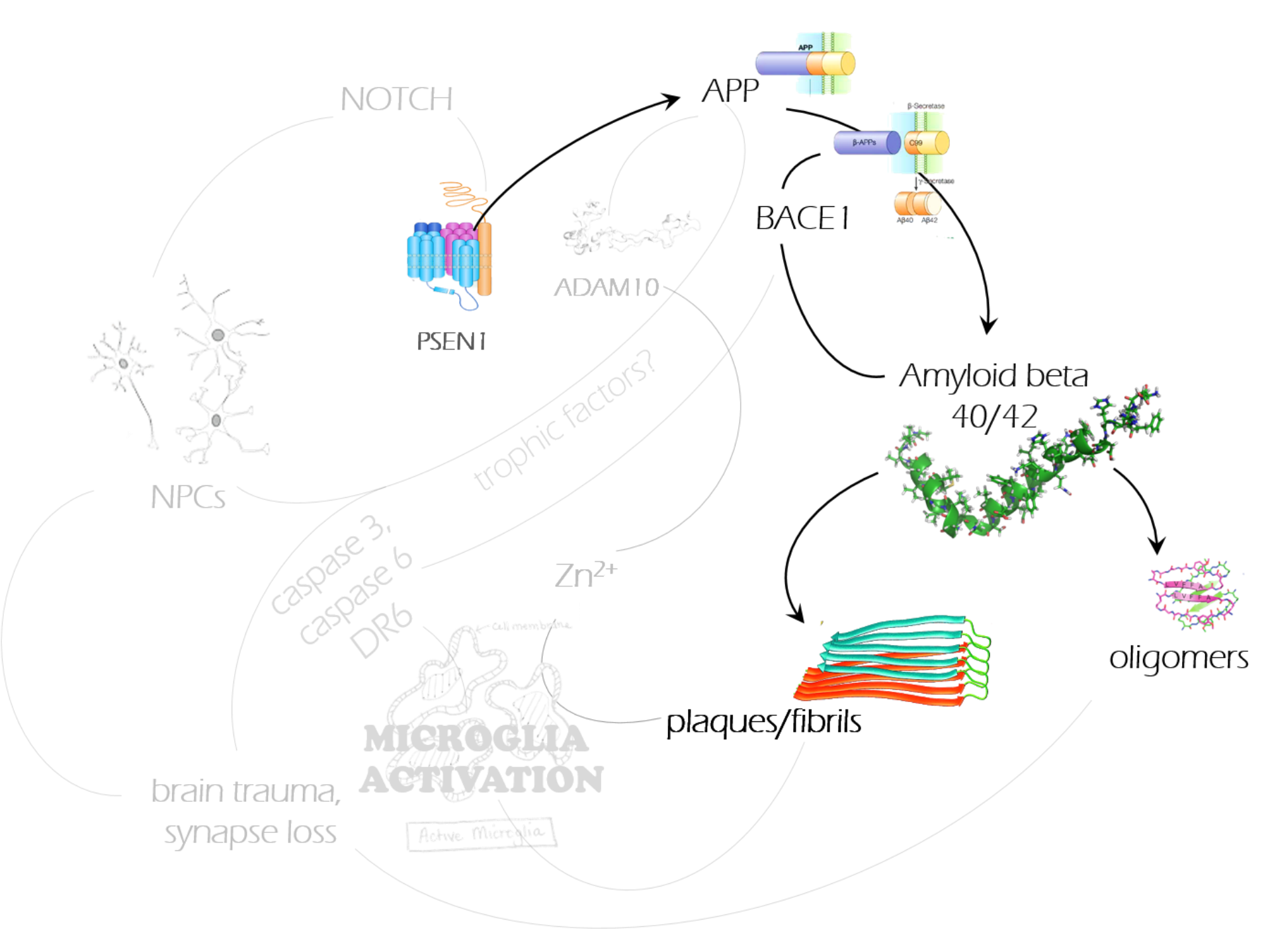
Раннее начало

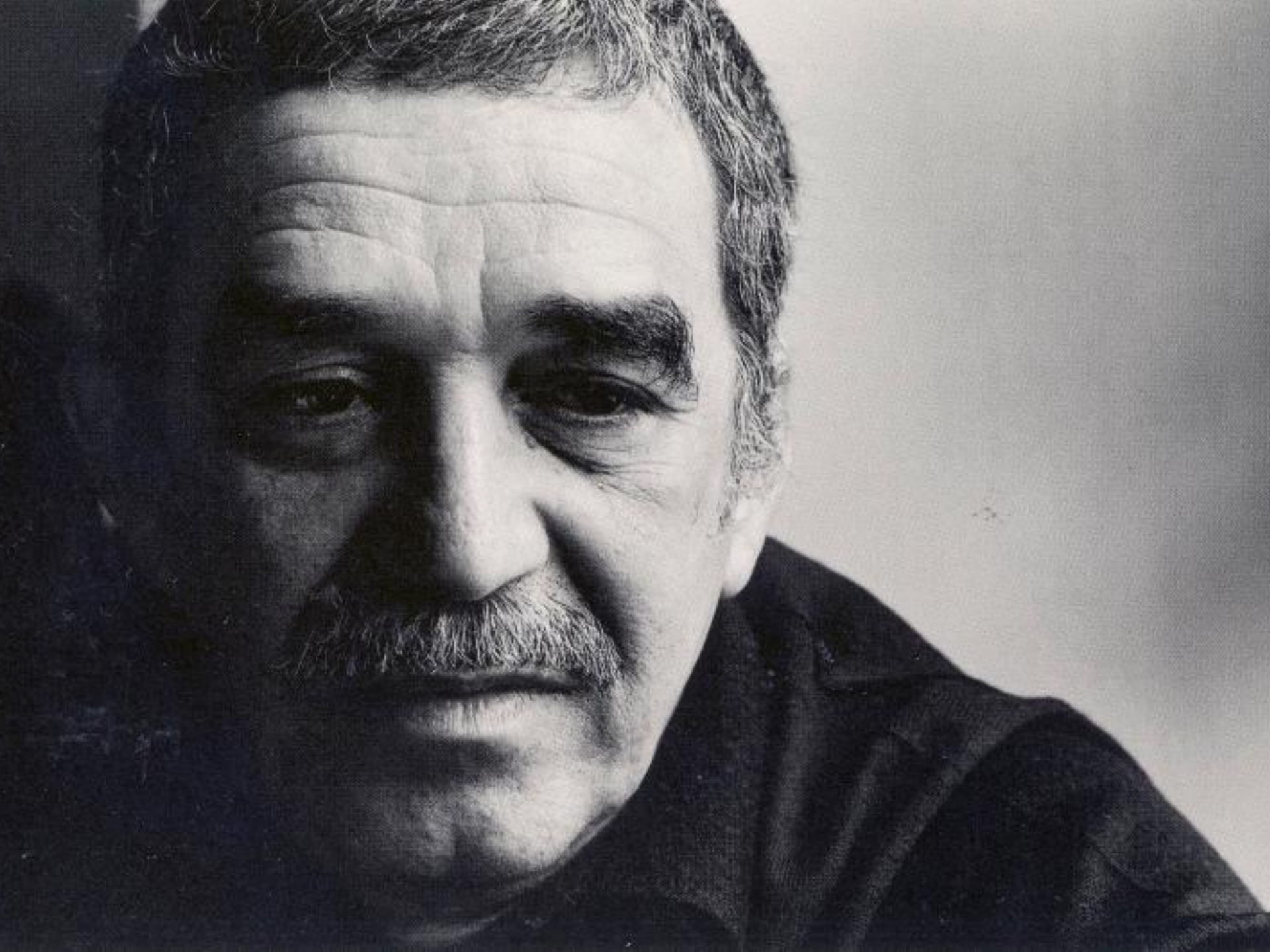
~ 2% случаев
возраст 40-50 лет
семейная форма
Мутации:

APP
PSEN
BACE
APOE

Позднее начало

~ 98% случаев
возраст 70-80 лет
все остальные случаи





Сто лет одиночества

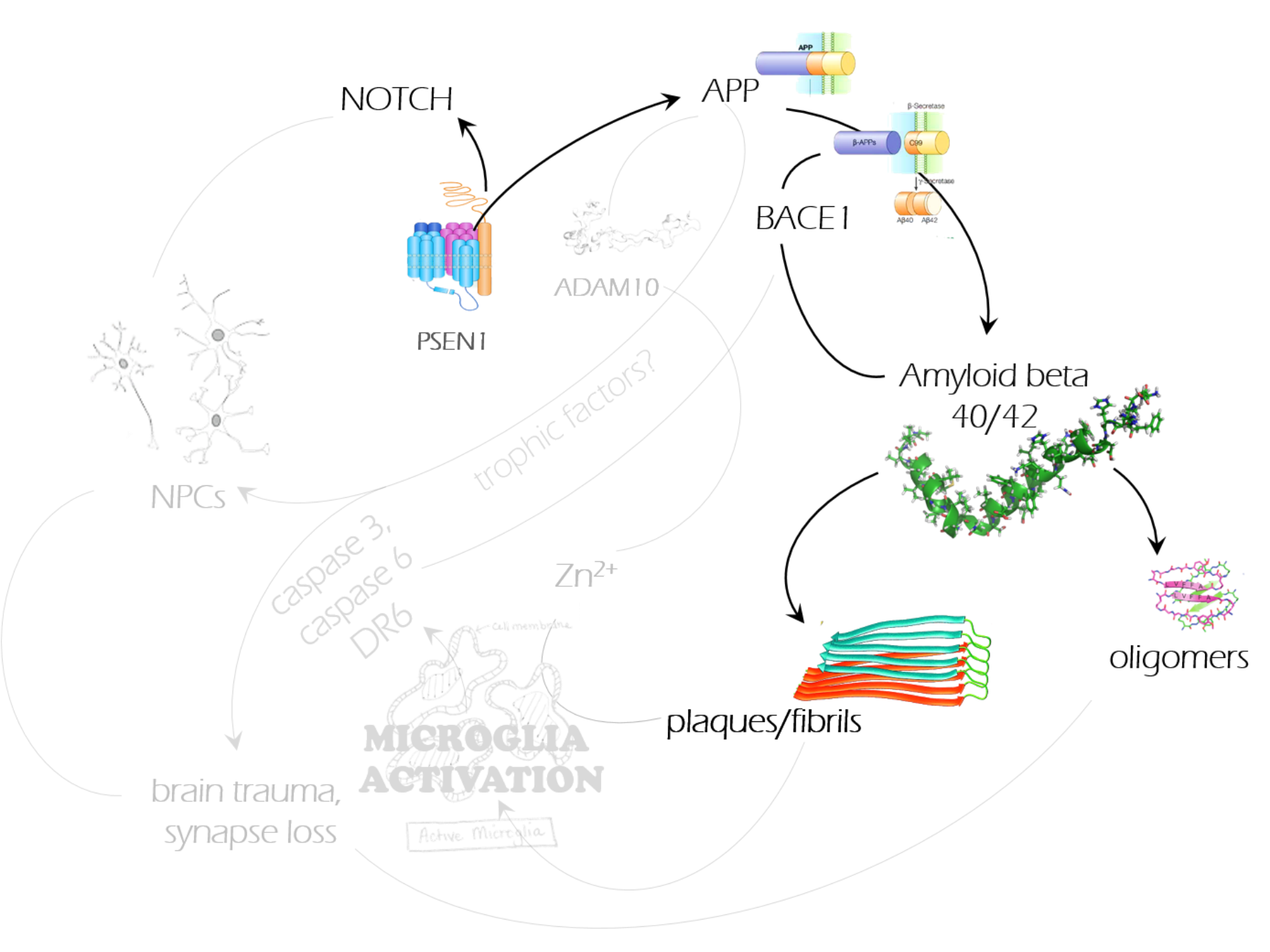


Сто лет одиночества

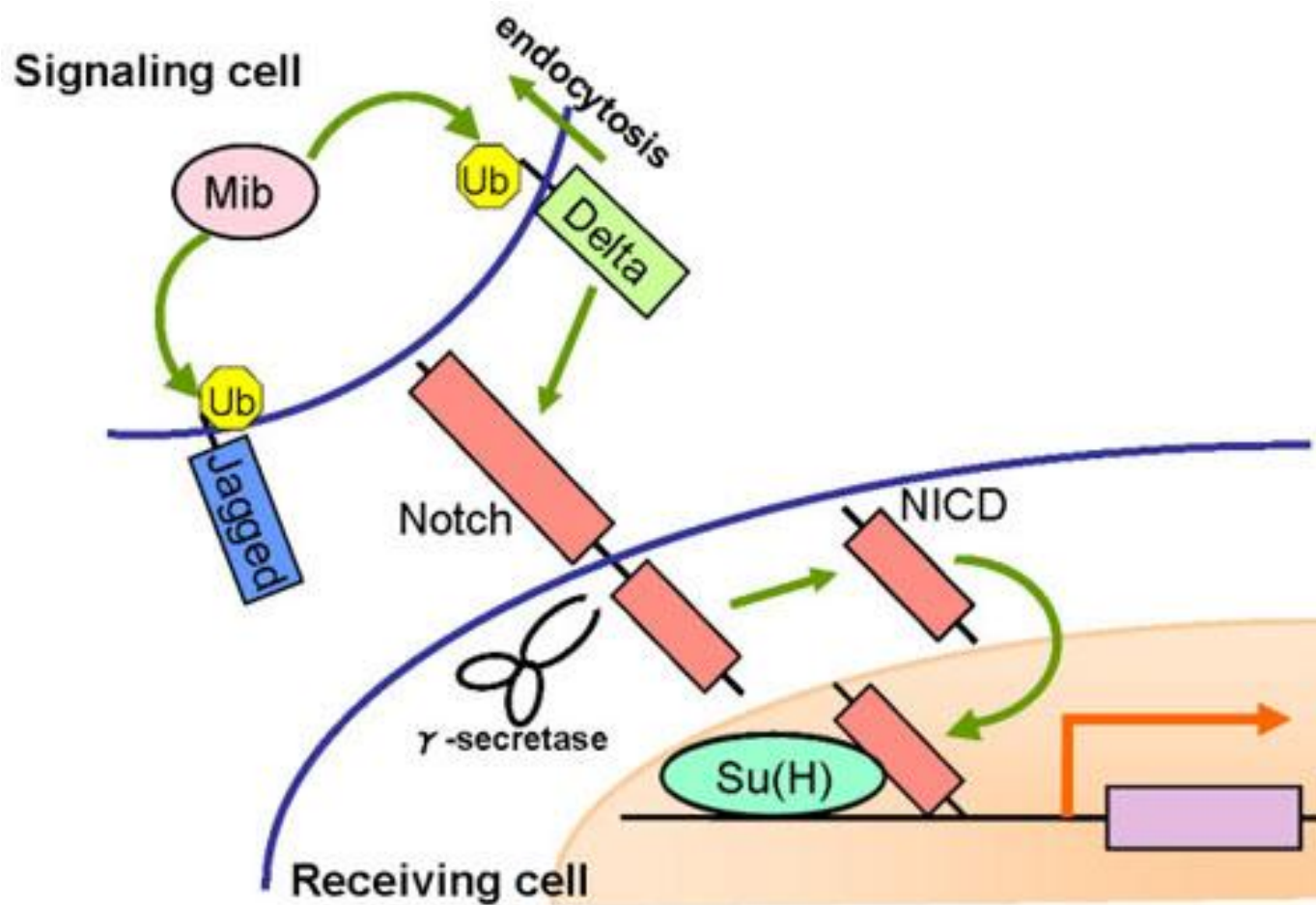
nobody expects Spanish conquistador

PSEN1
E280A

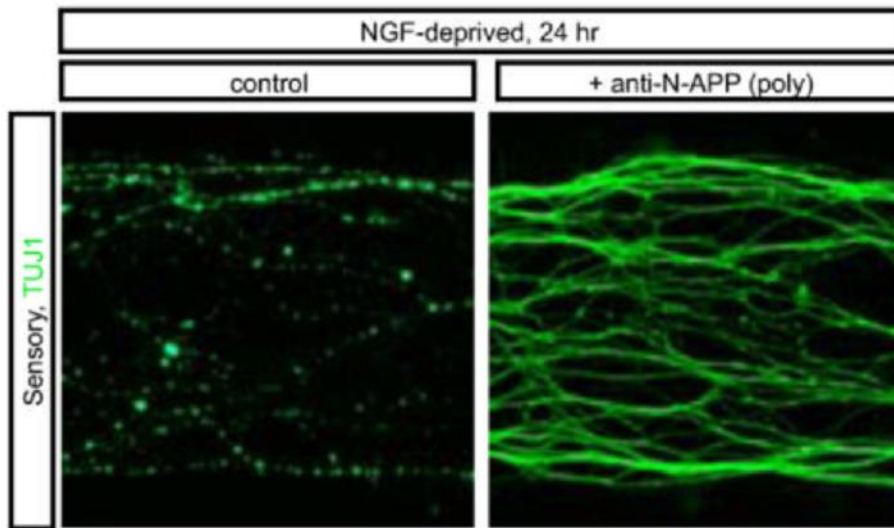




NOTCH cascade



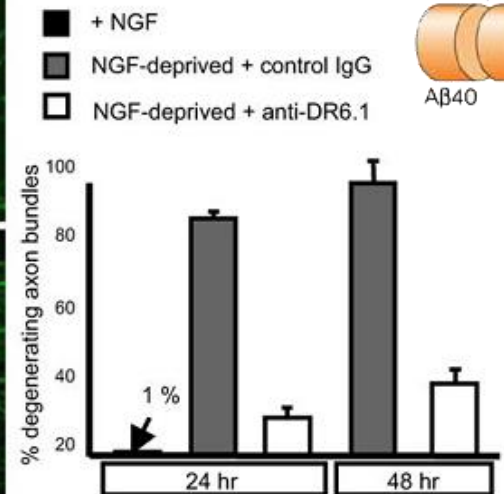
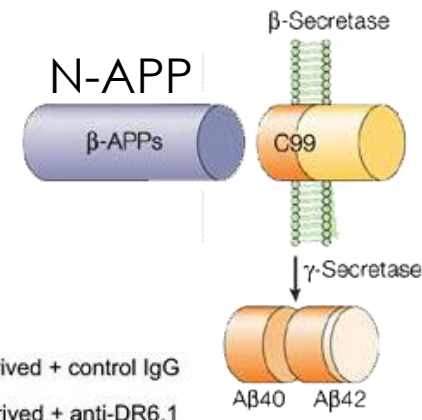
a



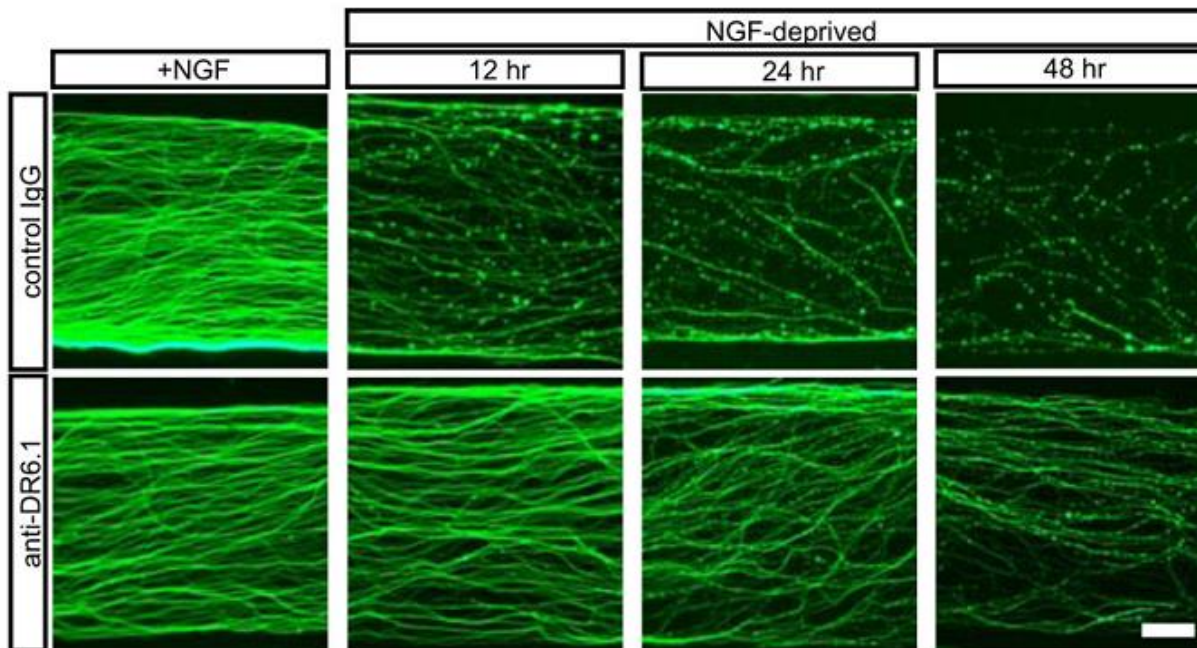
N-APP binds DR6 to cause axon pruning and neuron death via distinct caspases

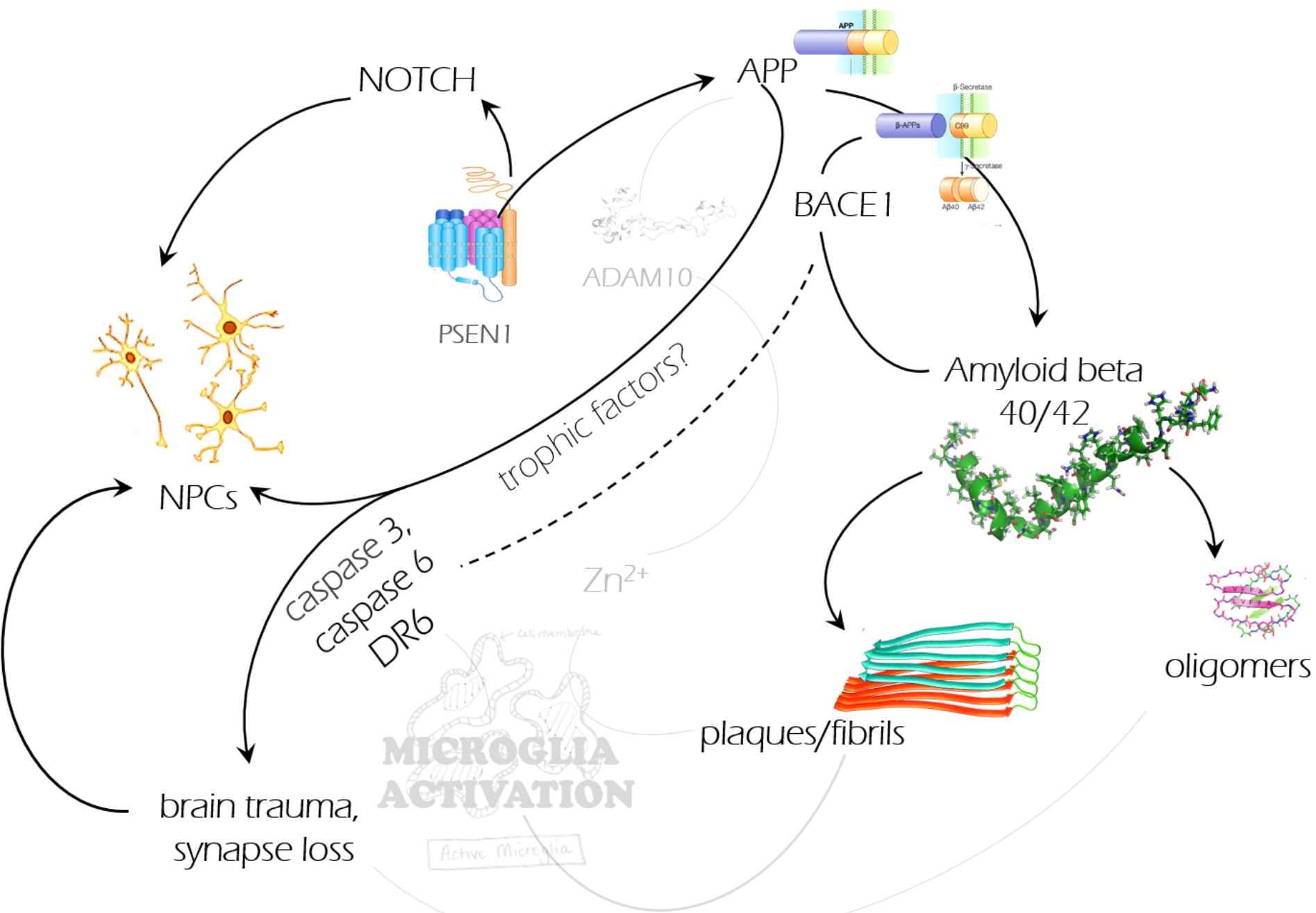
Anatoly Nikolaev, Todd McLaughlin, Dennis O'Leary, and Marc Tessier-Lavigne

NATURE, 2009

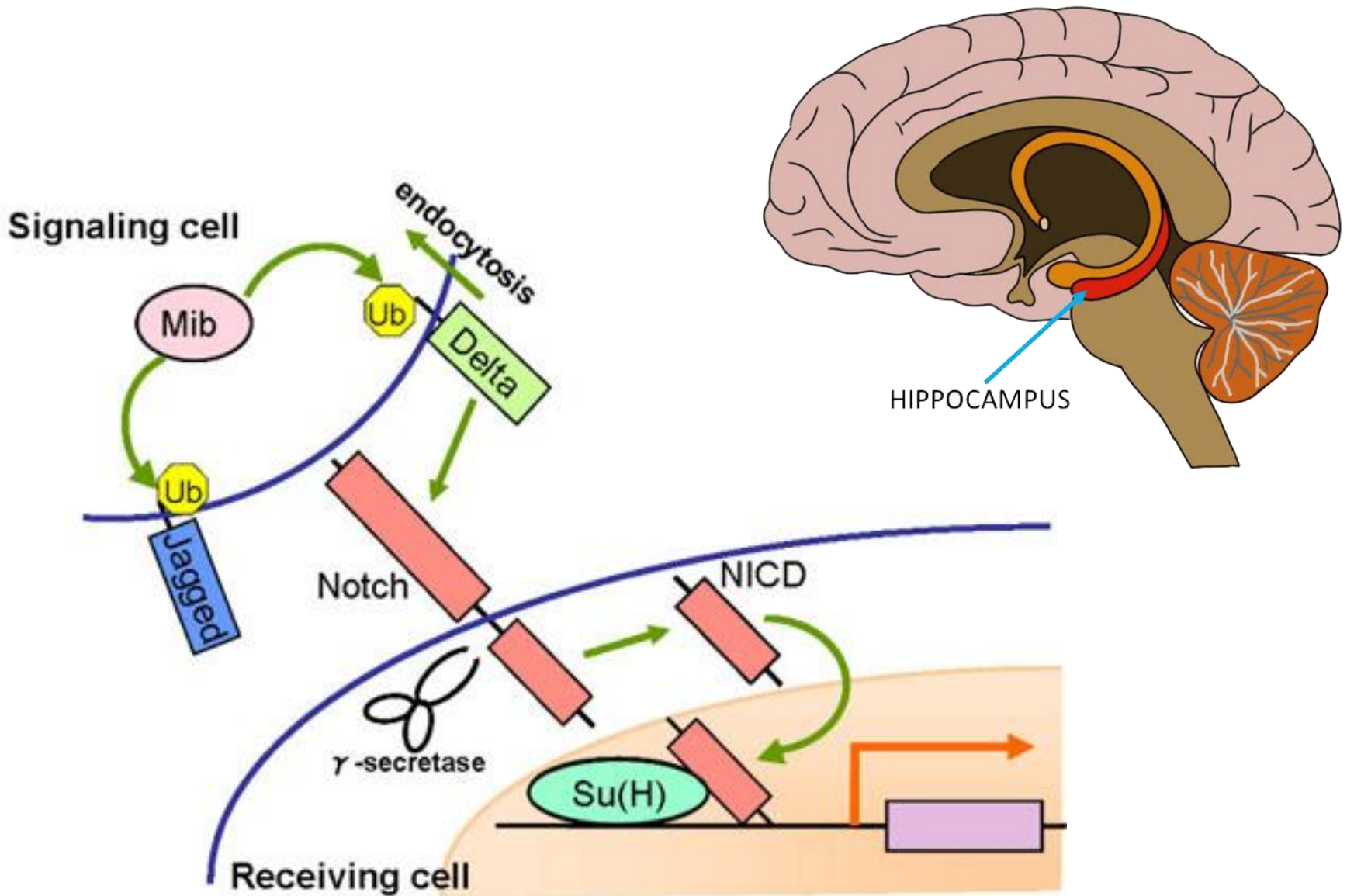


b





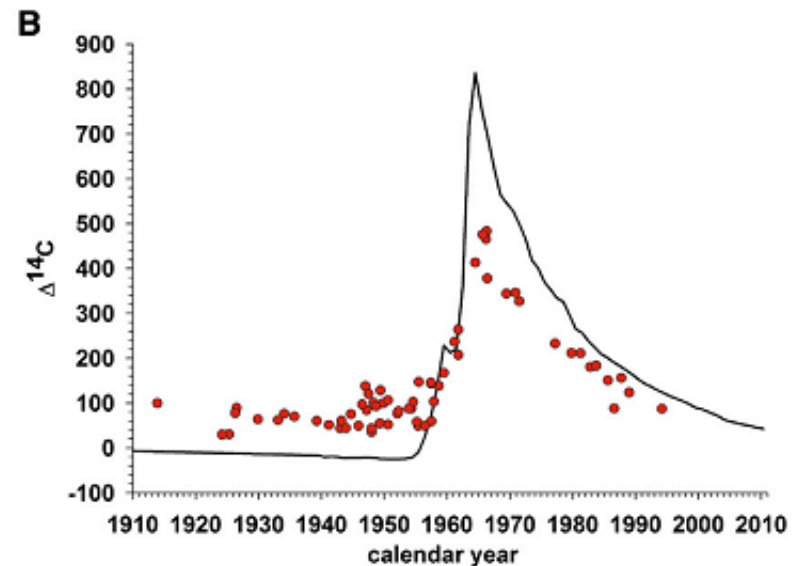
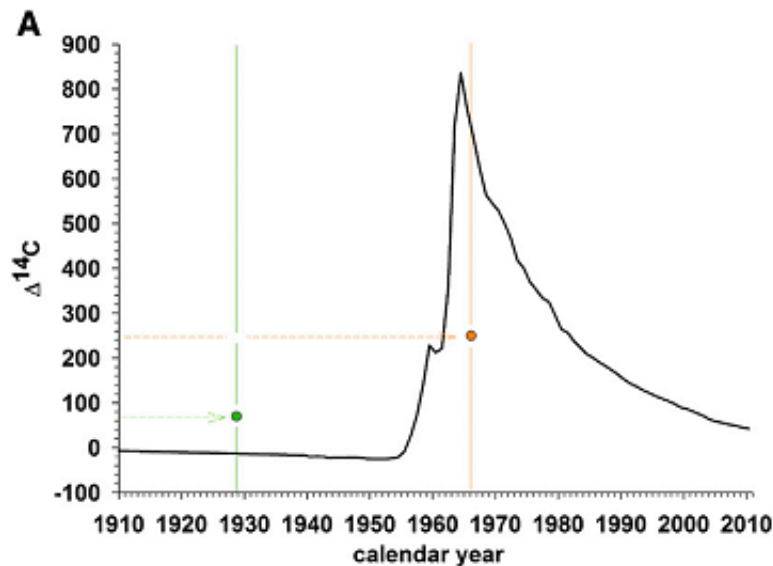
NOTCH cascade



Neuron progenitor cells

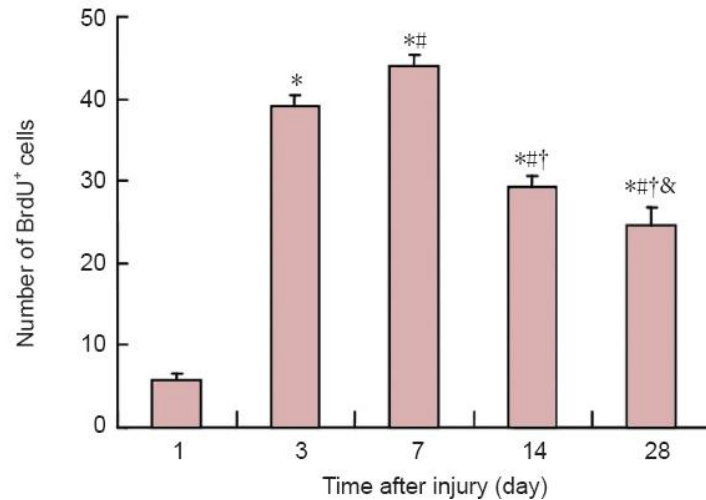
Dynamics of Hippocampal Neurogenesis in Adult Humans

Kirsty L. Spalding,^{1,8} Olaf Bergmann,^{1,8} Kanar Alkass,^{1,2} Samuel Bernard,³ Mehran Salehpour,⁴ Hagen B. Huttner,^{1,5} Emil Boström,¹ Isabelle Westerlund,¹ Céline Vial,³ Bruce A. Buchholz,⁶ Göran Possnert,⁴ Deborah C. Mash,⁷ Henrik Druid,² and Jonas Frisén^{1,*}

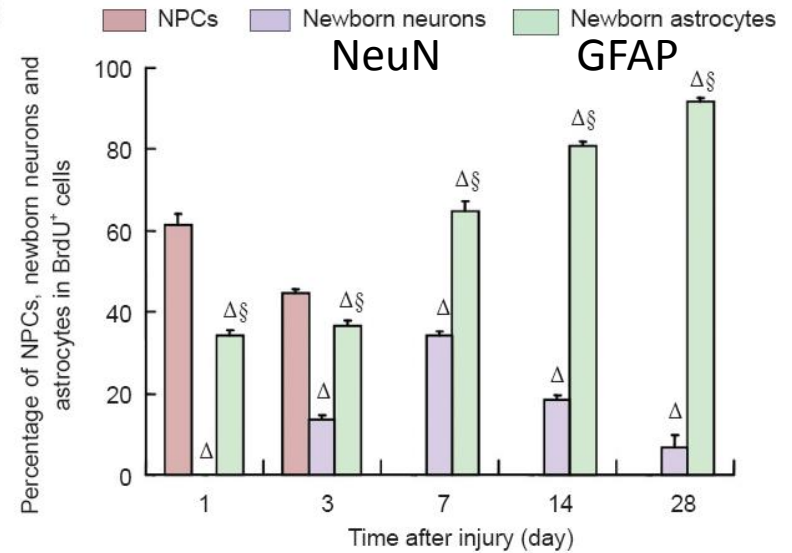


Neuron progenitor cells

A



B



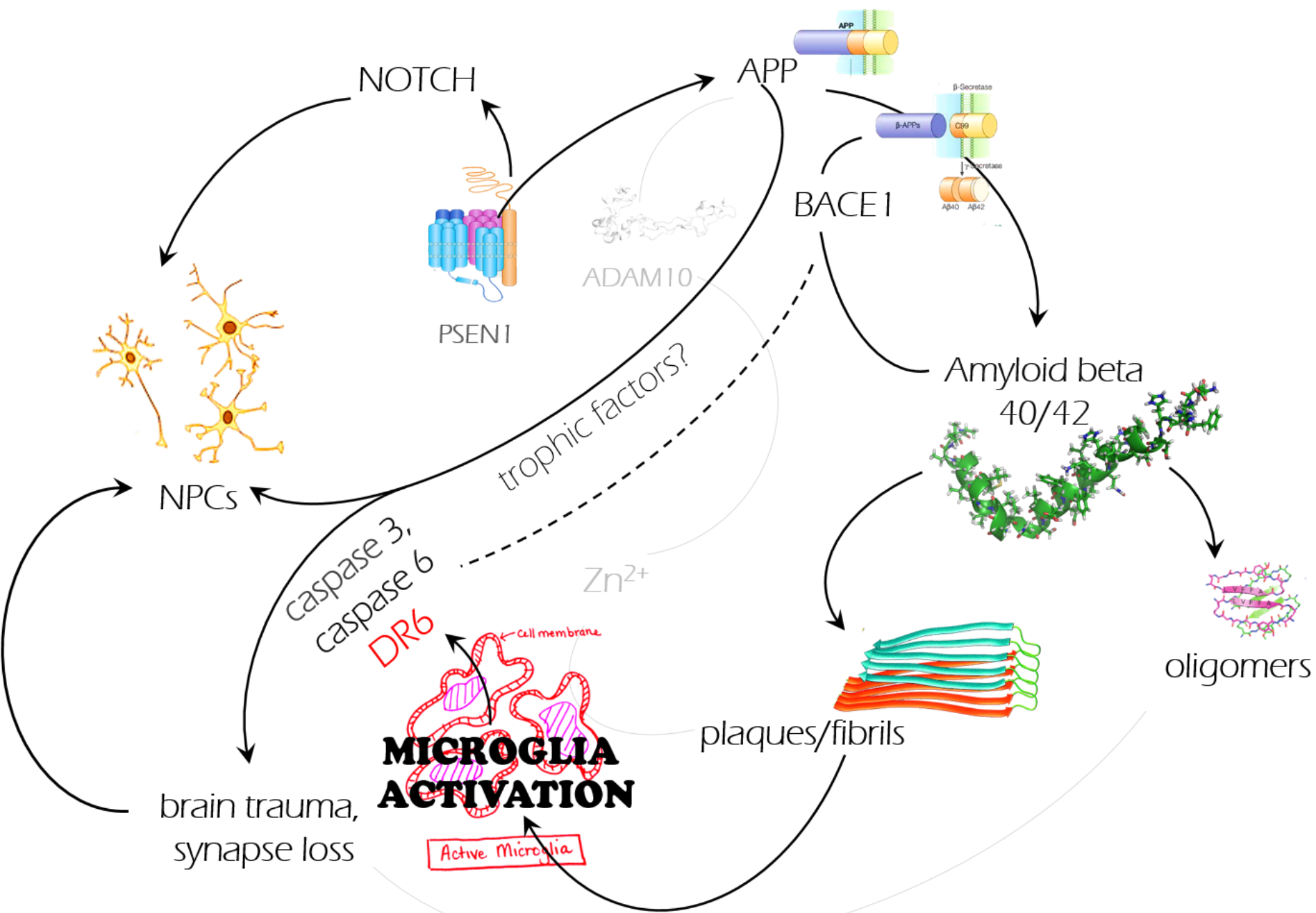
Cortical neurogenesis in adult rats after ischemic brain injury: most new neurons fail to mature

Qing-quan Li¹, Guan-qun Qiao¹, Jun Ma¹, Hong-wei Fan², Ying-bin Li¹,
Neural Regeneration Research, 2015

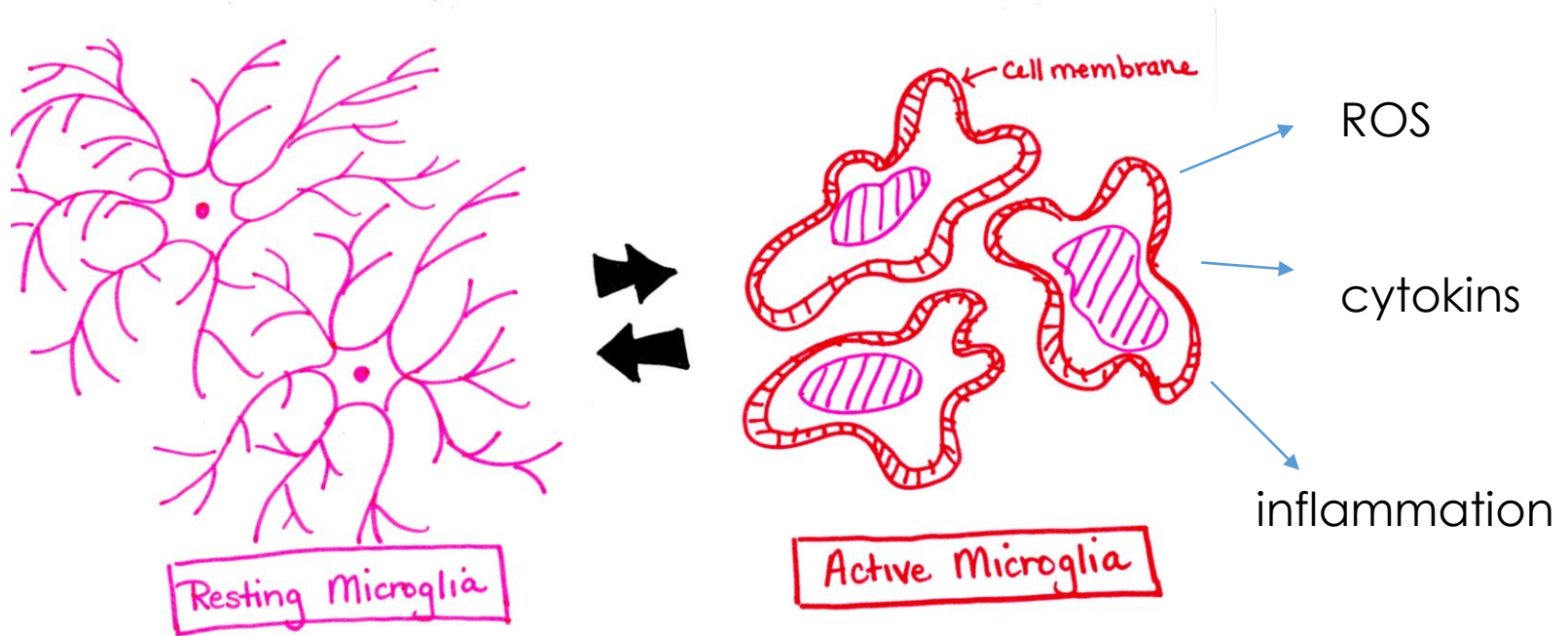
Peptide p3 may play a neuro- protective role in the brain

Medical Hypothesis, 2015

N-APP- α способствует дифференцировке NPCs в астроциты !!!

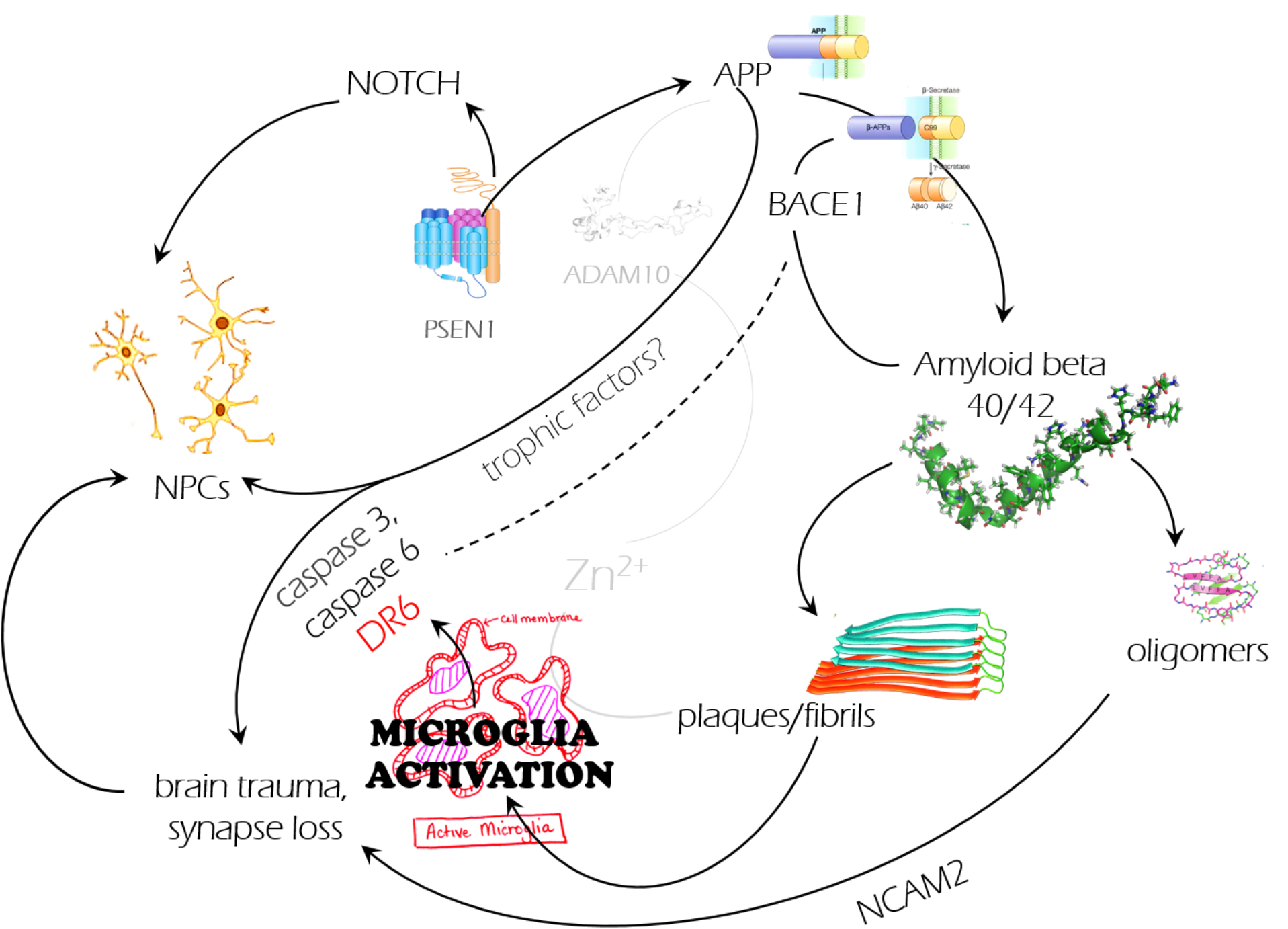


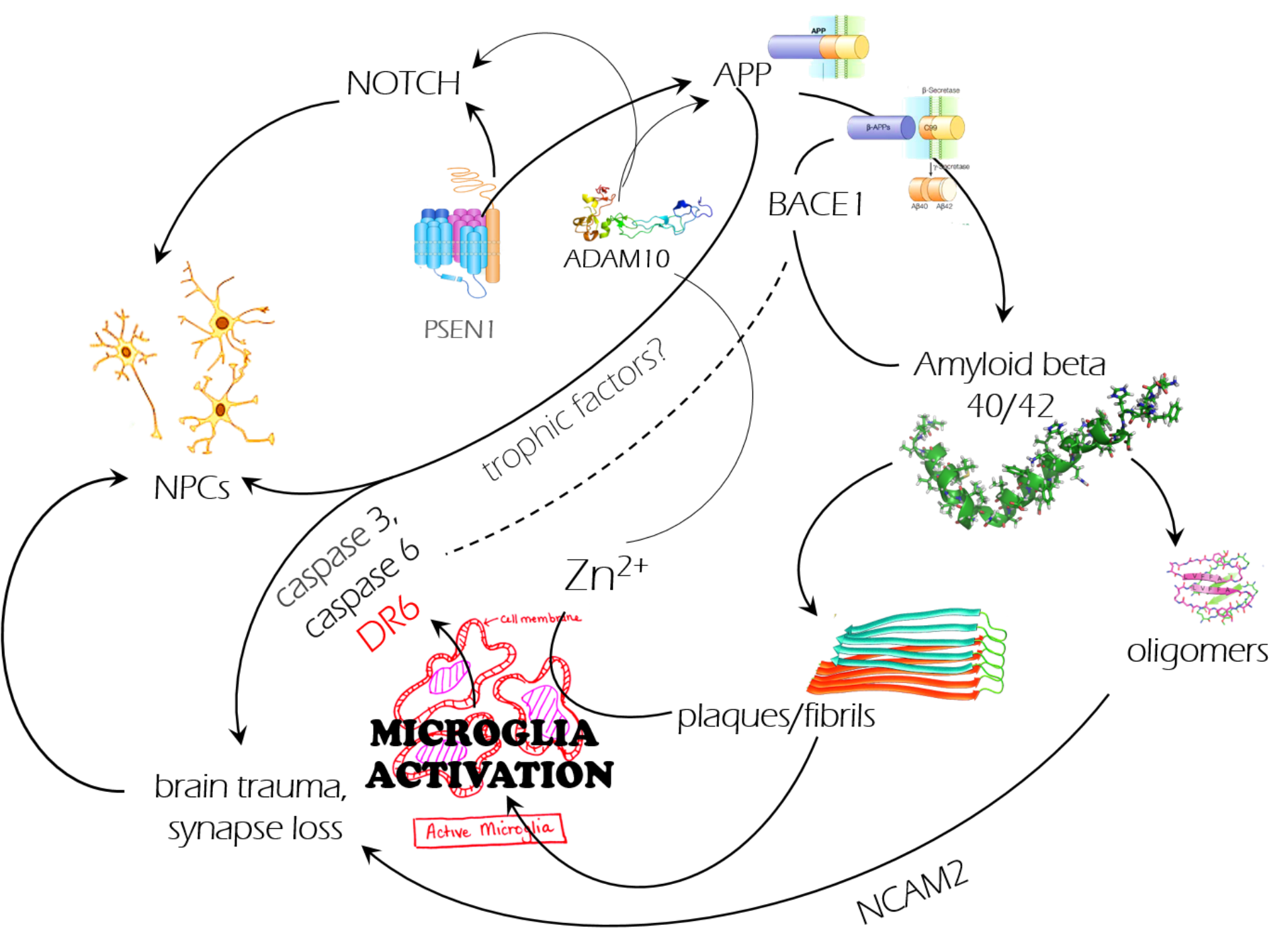
Microglia activation



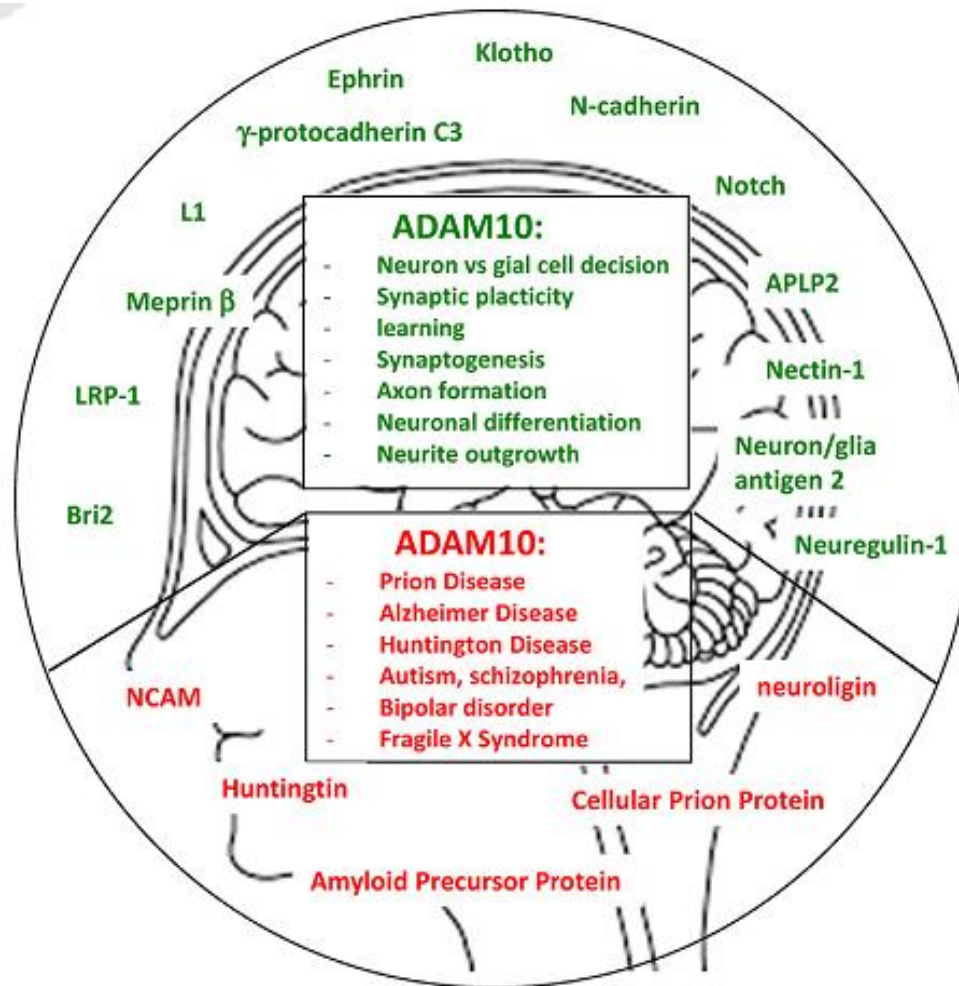
DR6 – TNFRSF (Tumor Necrosis Factor Receptors Superfamily) member

- активирует NF-κB-путь
- miRNA против DR6 снижает воспаление при остеоартрите



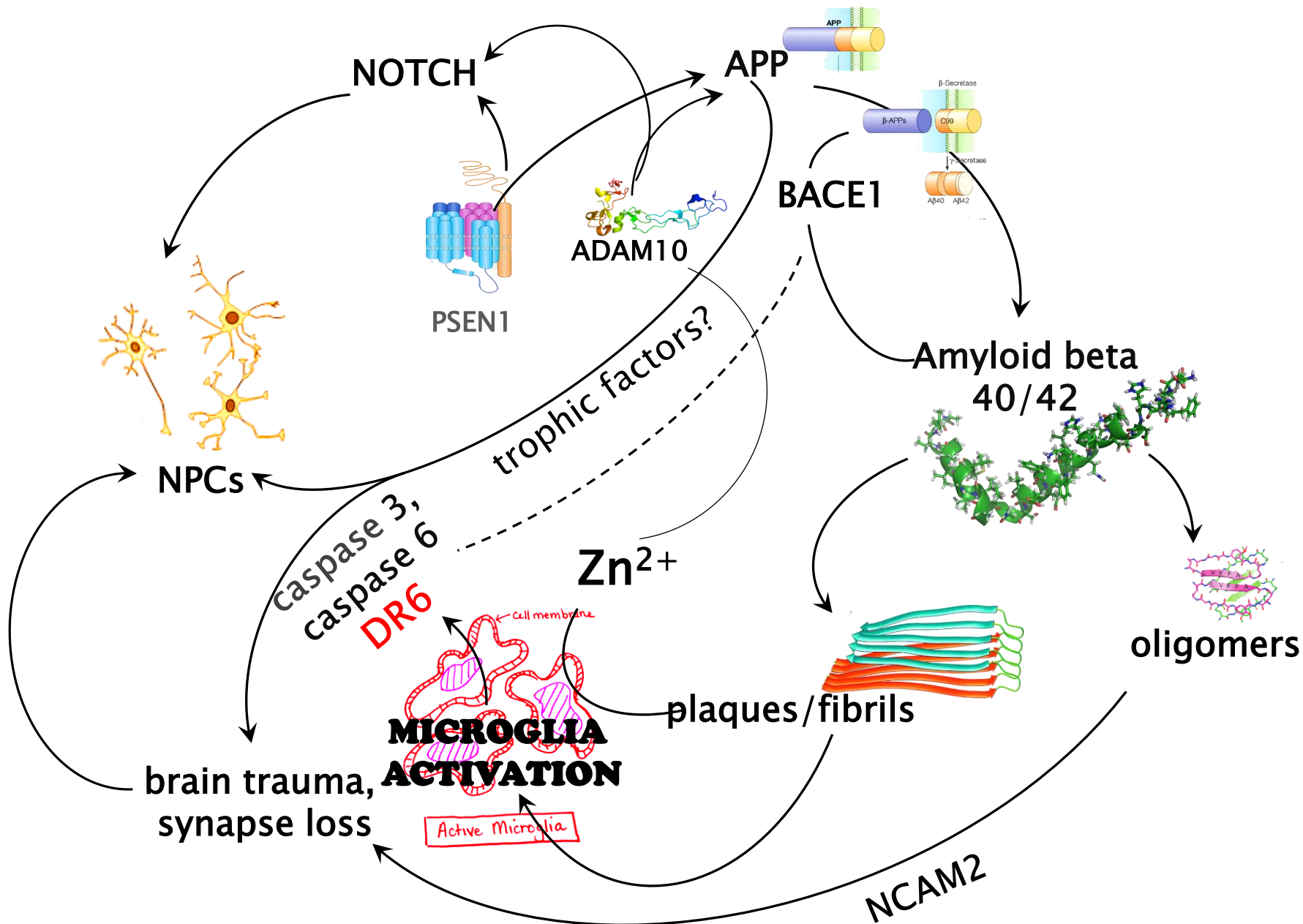


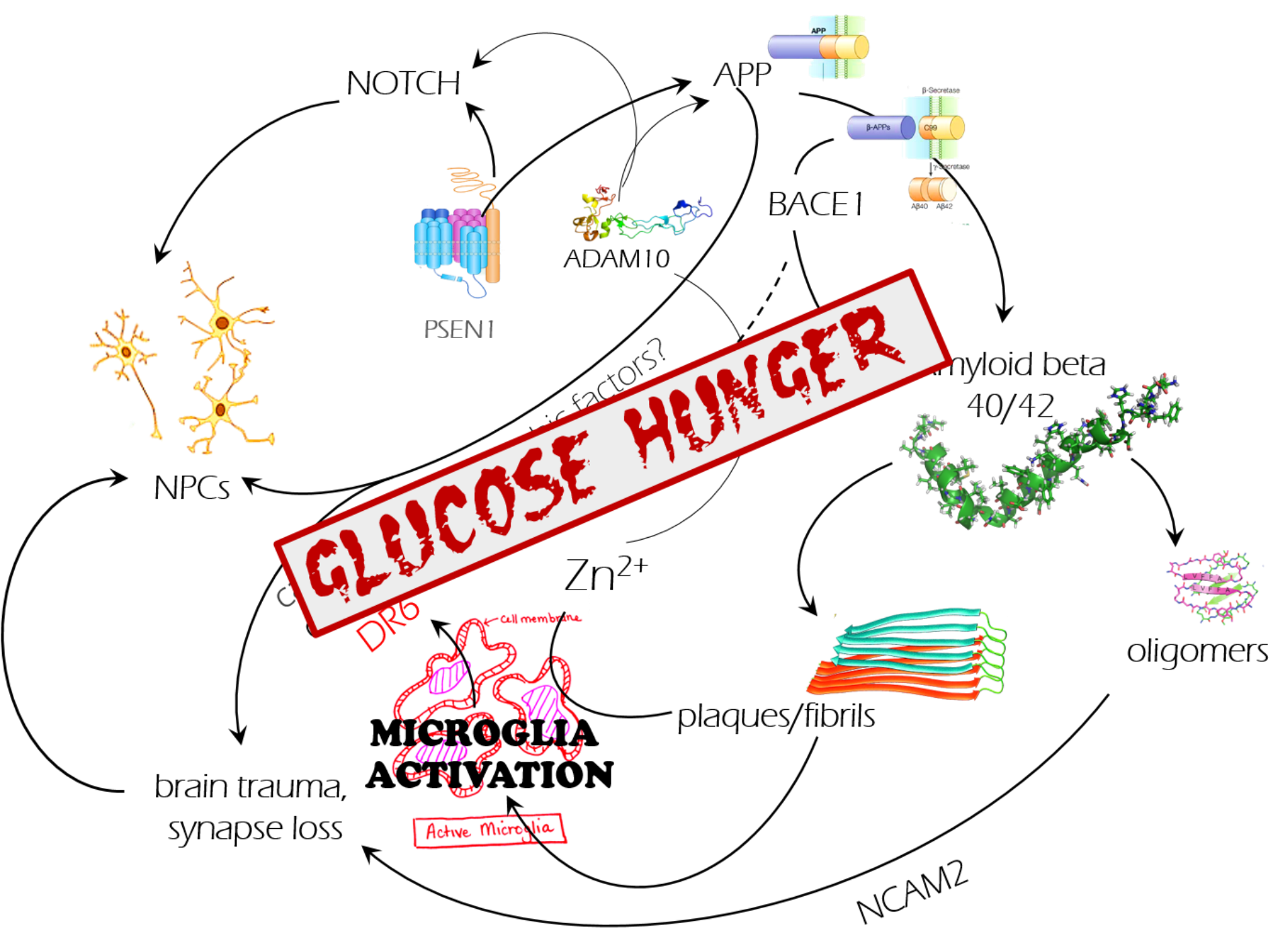
Alpha secretase and Zn^{2+}



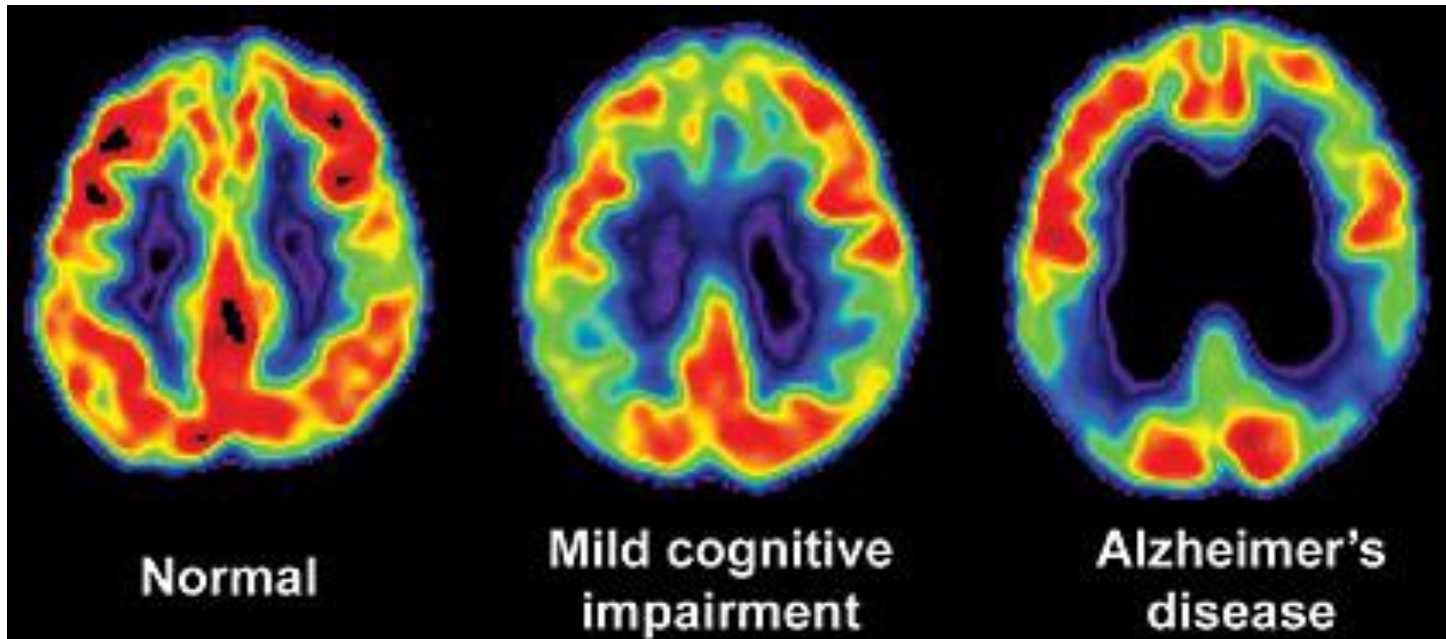
The alpha secretase ADAM10: A metalloprotease
with multiple functions in the brain

Paul Saftig, Stefan F. Lichtenthaler Progress in neurobiology, 2015

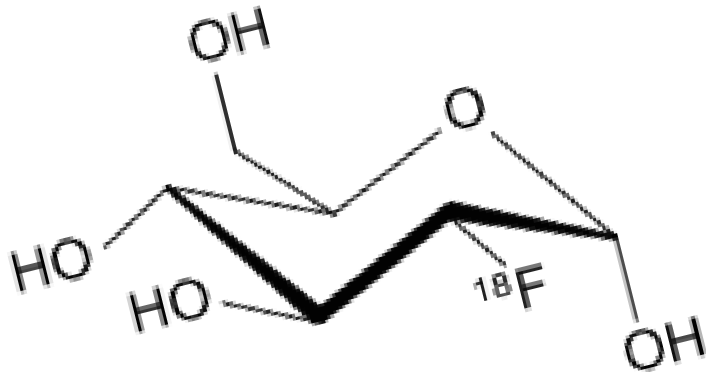




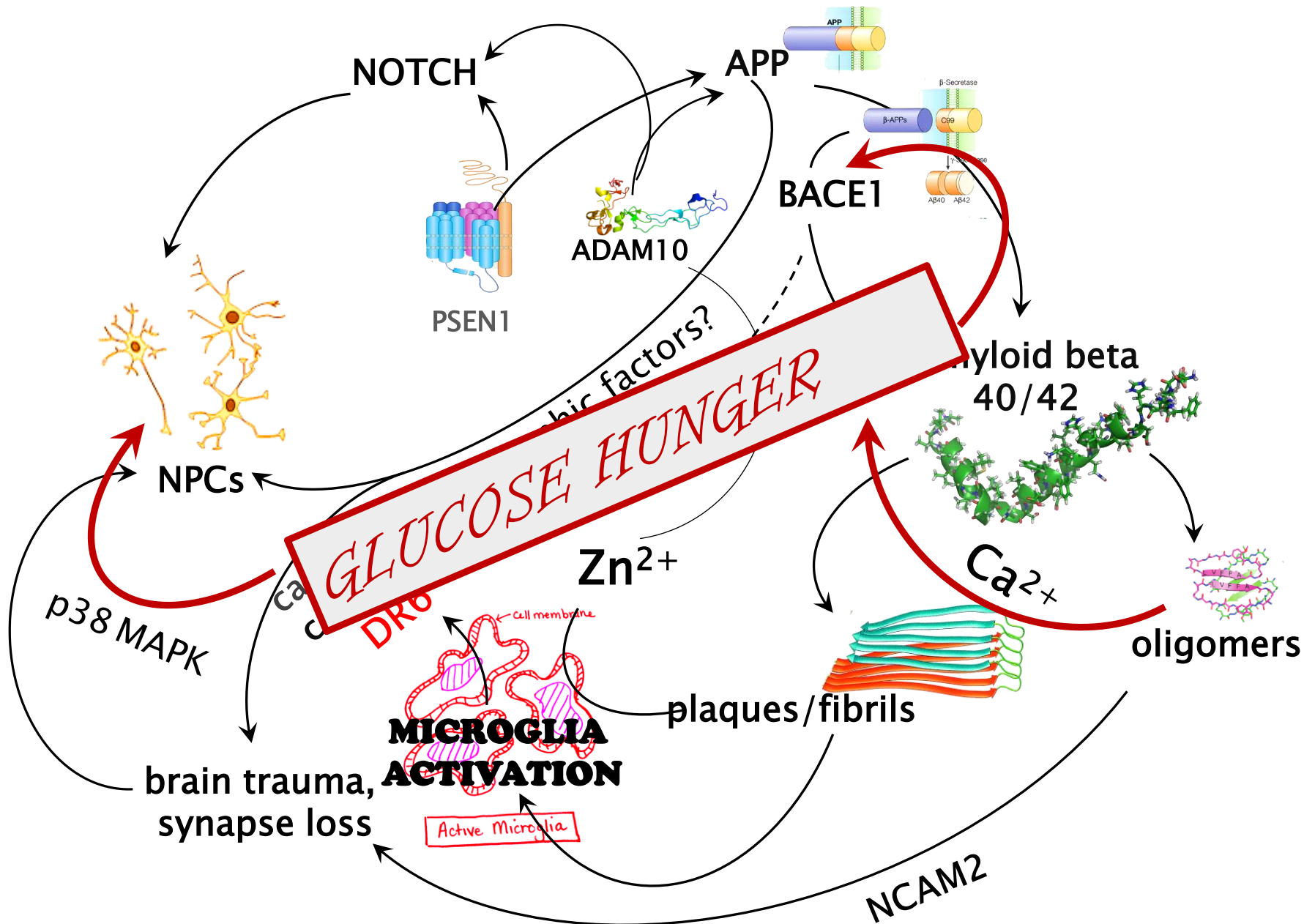
GLUCOSE HUNGER



Cindee Madison and Susan Landau, UC Berkeley



Fludeoxyglucose (^{18}F)

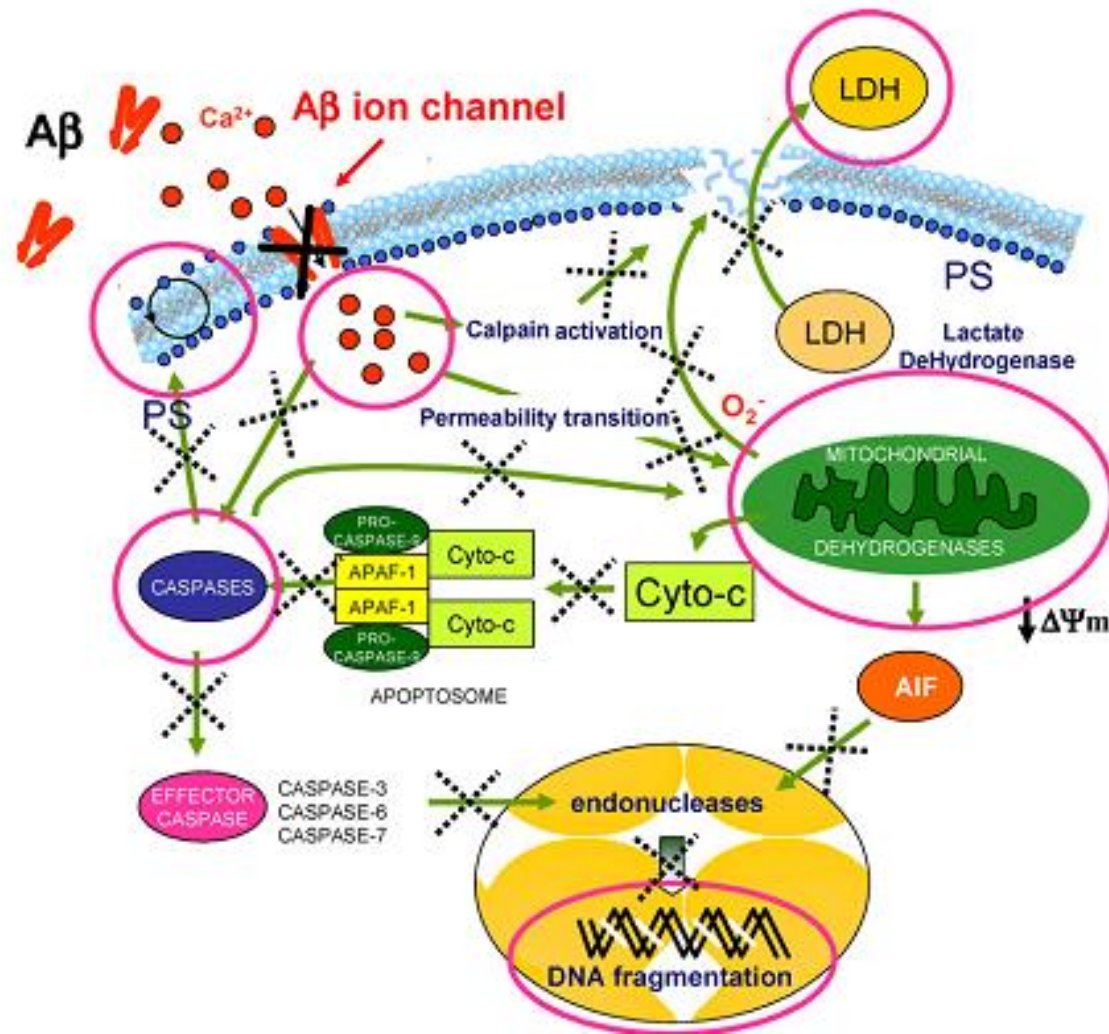


Glucose deprivation increases tau phosphorylation via P38 mitogen-activated protein kinase
Aging Cell, 2015

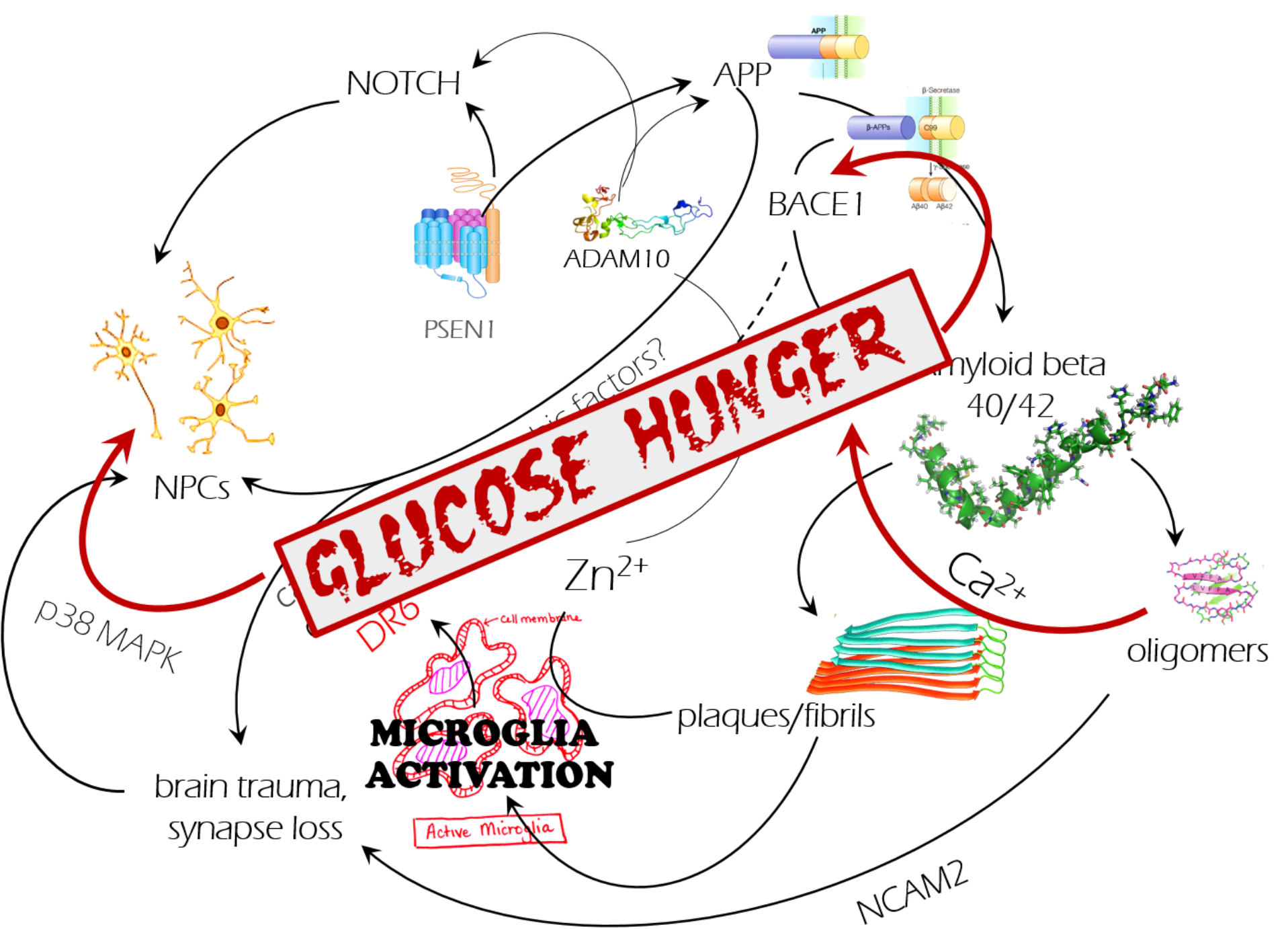
Cell-permeable p38 MAP kinase promotes migration of adult neural stem/progenitor cells
Scientific Reports, 2015

Phosphorylation of the Translation Initiation Factor eIF2 α Increases BACE1 Levels and Promotes Amyloidogenesis
Neuron, 2009

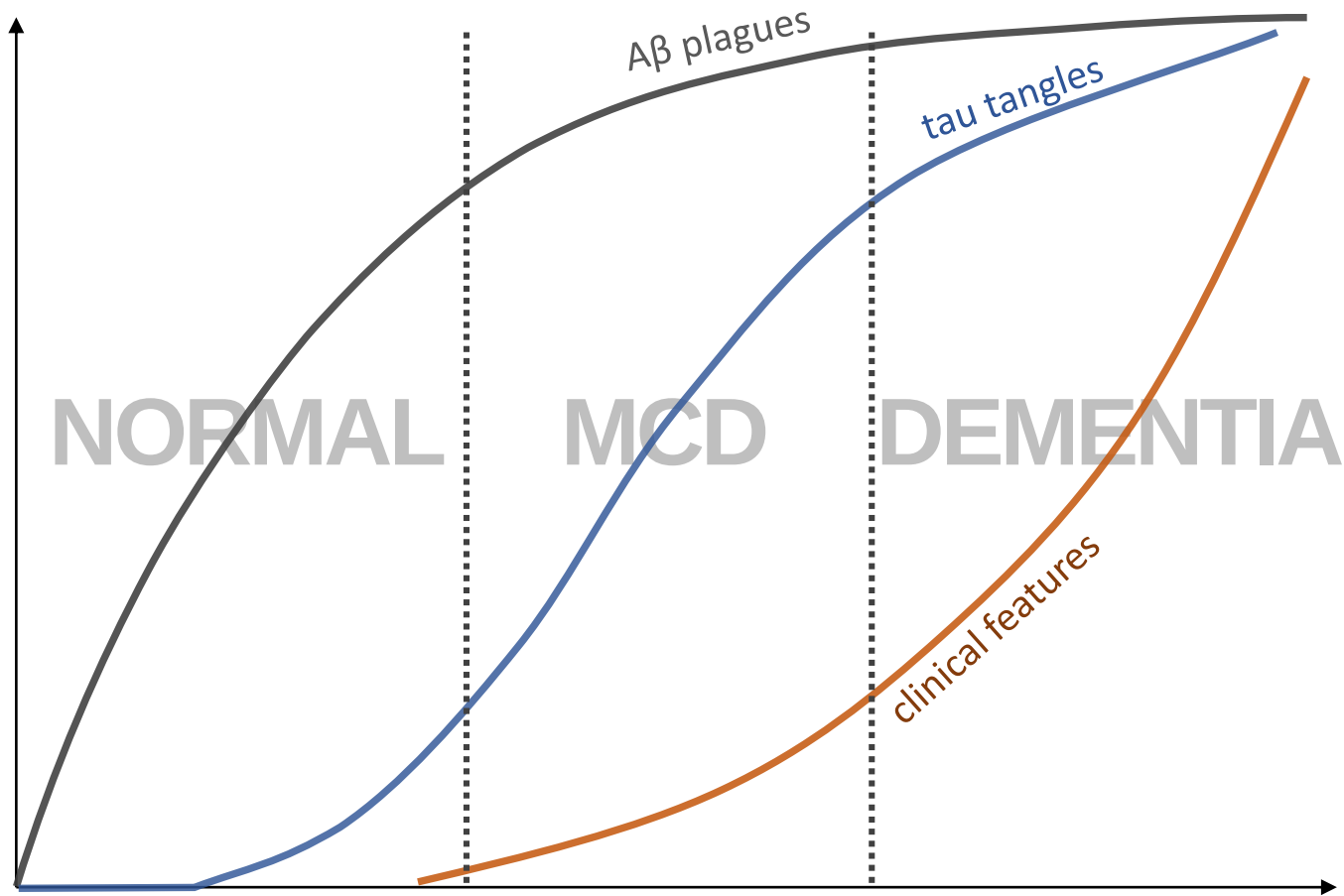
Amyloid ion channels: Ca^{2+}

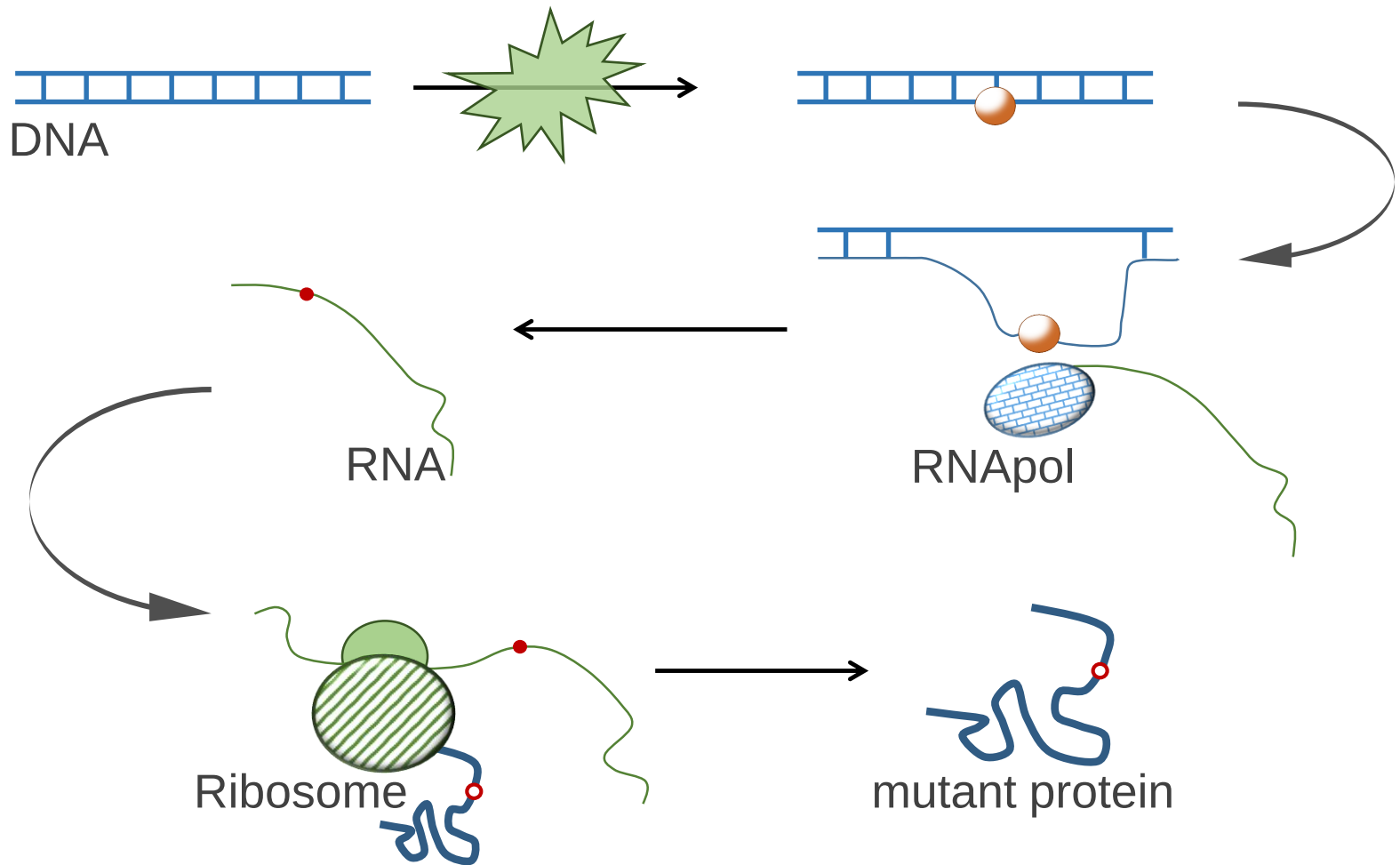


Aβ ion channels. Prospects for treating Alzheimer's disease with Aβ channel block
Nelson Arisp, Juan C. Diaz, Olga Simakova BBA 2007



Клинические данные





СПАСИБО ЗА ВНИМАНИЕ!

