Perineuronal net treatments for neurodegenerative disease

https://neurodegenerationresearch.eu/survey/perineuronal-net-treatments-for-neurodegenerative-disease/

Principal Investigators
Institution
Contact information of lead PI
Country

European Commission

Title of project or programme

Perineuronal net treatments for neurodegenerative disease

Source of funding information

European Commission FP7-Seventh Framework Programme

Total sum awarded (Euro)

€ 2,450,543

Start date of award

01/03/2012

Total duration of award in years

5.0

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords
Research Abstract
Inhibitory chondroitin sulphate proteoglycans (CSPGs) have several roles in CNS damage and repair, revealed by their digestion with chondroitinase. Most recently, digestion of CSPGs in the limbic system and cortex has led to a very substantial enhancement of memory.
The effects of CSPGs on plasticity and memory are largely through their concentration into PNNs, because transgenics lacking the PNN component link protein in the CNS have very attenuated PNNs, and show continuing plasticity into adulthood, and enhanced memory in just the same way as chondroitinase-treated animals. The PNN is therefore a novel therapeutic target that has not been explored.
This application focuses particularly on enhancement of memory through manipulation of PNNs. In Alzheimer’s disease (AD) and ageing the main cognitive disability is loss of memory. The enhancement of memory following chondroitinase treatment or PNN knockout in object memory

is many times greater than obtained using cholinesterase inhibitors (the only currently available treatment for memory enhancement). PNN manipulation is therefore a particularly promising avenue for developing treatments to overcome the main cognitive disability of AD and ageing.
The aims of the application are:
1. Test the extent of memory enhancement due to PNN manipulation in models of AD due to Abeta, tau mutations and in aged CNS.
2. Establish the molecular mechanism for PNN effects on memory, focusing on Semaphorin3 presentation by PNNs, and direct effects via the PTPsigma receptor.
3. Discover the sulphation modifications of the CSPG glycan chains that enable binding of Semaphorin3s, activation of the PTPsigma receptor.
4. Analyse molecules that bind to PNN glycans, to identify new potential effectors of PNN effects on memory and plasticity
5. Testing in memory and plasticity models of novel PNN-targeted approaches.

Lay Summary
Further information available at:

Types:
Investments > €500k

Member States:
European Commission

Diseases:
Alzheimer's disease & other dementias

Years:
2016

Database Categories:
N/A

Database Tags:
N/A