GSK-3 in neuronal plasticity and neurodegeneration: basic mechanisms and pre-clinical assessment (NEURO.GSK3)

https://neurodegenerationresearch.eu/survey/gsk-3-in-neuronal-plasticity-and-neurodegeneration-basic-mechanisms-and-pre-clinical-assessment-neuro-gsk3/

Title of project or programme

GSK-3 in neuronal plasticity and neurodegeneration: basic mechanisms and pre-clinical assessment (NEURO.GSK3)

Principal Investigators of project/programme grant

Title	Forname	Surname	Institution	Country
Professor	Fred	van Leuven	KATHOLIEKE UNIVERSITEIT LEUVEN	Belgium

Address of institution of lead PI

Institution	KATHOLIEKE UNIVERSITEIT LEUVEN
Street Address	
City	
Postcode	

Country

Belgium

Source of funding information

European Commission

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3573842

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01-10-2008

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39

The project/programme is most relevant to

- Alzheimer’s disease and other dementias

Keywords

Alzheimer,plasticity,spines,GSK3,tauopathy,kinase-inhibitors

Research abstract in English

Neuronal circuits in mammalian brain act predominantly via excitatory synapses on dendritic spines. Formation of new spines in adult brain constitutes the structural basis of neuronal plasticity. The underlying molecular mechanisms remain largely unknown but depend essentially on kinase-dependent signalling pathways. Final formation of synapses on spines depends on dynamic interactions of microtubuli and actin-filaments that are also controlled by kinases. Deterioration of these processes to different extents are thought to cause the cognitive decline in normal ageing as well in Alzheimer’s disease (AD) and familial fronto-temporal dementia (FTD).

Protein tau is a microtubule associated protein and GSK-3 kinases are proposed as the major tau-kinases in vivo. Their exact contributions remain to be functionally defined in vivo both in normal neuronal plasticity and in degeneration. We develop pre-clinical models for AD and FTD that have tauopathy in common as essential pathogenic component and will explore the GSK-3 kinases in vivo by manipulating their activity genetically, pharmacologically and biochemically. Inhibitors are wanted that are effective and specific and enter brain in vivo.

Lay summary