

The role of Dkk1 in Amyloid-beta mediated effects on dendritic spines and long-term depression

<https://www.neurodegenerationresearch.eu/survey/the-role-of-dkk1-in-amyloid-beta-mediated-effects-on-dendritic-spines-and-long-term-depression/>

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The role of Dkk1 in Amyloid-beta mediated effects on dendritic spines and long-term depression

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Alzheimer's Research UK

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€ 539,478

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02/07/2012

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4.0

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Research Abstract

Brain function depends on the formation of functional neuronal circuits created by connecting nerve cells together through specific junctions, called synapses. Loss or dysfunction of synapses contributes to diverse neurological disorders. Recent studies have revealed that

synapse loss occurs at early stages of Alzheimer's disease (AD) and that this process might contribute to cognitive and memory deficits in AD. Our research group studies the function of Wnts, proteins that promote the formation, growth and maintenance of synapses. We discovered that a secreted Wnt antagonist, Dkk1, induces synaptic loss and deficits in long-term memory in mice expressing high levels of Dkk1. Dkk1 is elevated in AD brain and in mouse models of AD. Importantly, we found that Amyloid β ($A\beta$) rapidly increases Dkk1 levels and that Dkk1 blockade suppresses the synaptic effects of $A\beta$. Thus, Dkk1 is necessary for $A\beta$ -induced synapse loss and therefore Dkk1 may contribute to cognitive decline in AD. In this proposal, we will investigate the contribution of Dkk1 to $A\beta$ -mediated synaptic changes in the hippocampus, a brain area important for learning and memory. We will also screen for small molecules that modulate Wnt signalling with the aim to identify new therapeutic avenues for the treatment of AD.

Lay Summary

Further information available at:

Types:

Investments > €500k

Member States:

United Kingdom

Diseases:

Alzheimer's disease & other dementias

Years:

2016

Database Categories:

N/A

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