

De rol van SPPL2b bij pathogenese van de ziekte van Alzheimer. The role of SPPL2b in Alzheimer's disease pathogenesis

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Netherlands

Title of project or programme

De rol van SPPL2b bij pathogenese van de ziekte van Alzheimer. The role of SPPL2b in Alzheimer's disease pathogenesis

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€ 100,000

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2

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Research Abstract

This project is focussed on SPPL2b, which is a novel protease that can modulate important mechanisms involved in the formation of plaques and tangles in AD. We recently observed that SPPL2b was increased as much as 10-fold in AD brains and was associated with NFT and neuritic plaques, which occurred in very early stages of AD (Braak II-III). Moreover, SPPL2b expression was less pronounced but also observed in other protein-misfolding dementias where

it was strongly associated with its classical protein-aggregated structures, indicating a key role of SPPL2b in protein aggregation mechanisms. Taken together, we hypothesize that SPPL2b can play a crucial and yet unanticipated role in the aetiology and development of AD. We aim to define the exact involvement of SPPL2b in the aetiology and development of AD pathogenesis using specific cell culture and mice models. We will determine whether SPPL2b overexpression or downregulation induce or caused by changes in the classical proteins and molecular pathways of AD. Additionally, we aim to develop an assay to measure the enzymatic activity of SPPL2b, which will be used as functional read-out in the experiments, and can also have important future pharmacological and clinical applications.

Further information available at:

<https://www.alzheimer.nl/onderzoek/onderzoeksprojecten/project/de-ziekte-van-alzheimer-en-de-epigenetische-programmering-van-neurale-stamcellen-door-stress>

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