# Roles of protein SUMOylation in AMPA receptor trafficking, synaptic dysfunction and cognitive impairment in dementia

https://neurodegenerationresearch.eu/survey/roles-of-protein-sumoylation-in-ampa-receptor-trafficking-synaptic-dysfunction-and-cognitive-impairment-in-dementia/

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**Country**

United Kingdom

**Title of project or programme**

Roles of protein SUMOylation in AMPA receptor trafficking, synaptic dysfunction and cognitive impairment in dementia

**Source of funding information**

MRC

**Total sum awarded (Euro)**

€ 1,562,997

**Start date of award**

01/03/2014

**Total duration of award in years**

4.0

**The project/programme is most relevant to:**

Alzheimer's disease & other dementias

**Keywords**
**Research Abstract**

Understanding the fundamental causes of dementia is one of the most important challenges in neuroscience. Synaptic dysfunction, with a persistent and pathological enhancement of LTD, is

the earliest and most reliable indicator of dementia pathogenesis. LTD is mediated by dynamic changes in synaptic AMPARs and we have shown that activity-dependent AMPAR trafficking requires protein SUMOylation. More recently we have obtained preliminary data revealing that SUMOylation is a key regulator of both NMDAR-LTD and mGluR-LTD. The purpose of this application is to test the hypothesis that dysregulation of synaptic protein SUMOylation is a causative factor in the defective AMPAR trafficking and synaptic plasticity that leads to dendritic spine regression, synaptic collapse, neuronal death and network failure in dementia. We shall determine 1) how levels of protein SUMOylation are altered in human AD brain and animal models of dementia; 2) how SUMOylation regulates AMPAR trafficking in NMDAR-LTD and mGluR-LTD, and how this is affected in disease models of dementia 3) if manipulation of protein SUMOylation can be protective against synaptic dysfunction, synaptic loss and cognitive deficits in dementia. We will use biochemical and histological analyses of post mortem human tissue in combination with functional and intervention studies in transgenic mouse models of dementia. The study will exploit a multidisciplinary array of techniques ranging from molecular biology, biochemistry and immunocytochemistry through electrophysiology and live cell imaging to animal behaviour. The applicants have complementary expertise and proven track records in all of these approaches. Our ultimate aim is to identify one or more SUMO-substrate proteins that could provide tractable therapeutic targets to reduce or prevent synaptic dysfunction associated with dementia.

**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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