Pathway-driven identification of therapeutic targets for combatting Alzheimer’s disease.

https://neurodegenerationresearch.eu/survey/pathway-driven-identification-of-therapeutic-targets-for-combatting-alzheimers-disease/

Principal Investigators

Dr R Killick

Institution

King's College London

Contact information of lead PI
Country

United Kingdom

Title of project or programme

Pathway-driven identification of therapeutic targets for combatting Alzheimer's disease.

Source of funding information

MRC

Total sum awarded (Euro)

€ 1,357,029

Start date of award

01/06/2015

Total duration of award in years

2.5

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords
Research Abstract

Our aim is to gain a better understanding of the signaling mechanisms driving beta-amyloid neurotoxicity, to identify effective and tractable novel therapeutic targets in the pathway and to develop assays suitable for future high throughput screening ready to identify small molecules acting on them. We are in a unique position to do this following our discoveries concerning the pathway activated by beta-amyloid, which mediates its neurotoxic properties including; tau

phosphorylation, neuronal death, synaptotoxicity and, in vivo, cognitive impairment. This pathway, the wnt-Planar Cell Polarity (wnt-PCP) pathway, is also detectable in the Alzheimer's disease (AD) brain. Of major significance for our understanding of AD pathology, the beta-amyloid precursor protein (APP), from which beta-amyloid is derived, has been identified as a necessary component of the wnt-PCP pathway where it is needed to drive it through recruitment of Abl: Thus, the beta-amyloid induction of wnt-PCP signaling is APP-dependent! Our understanding of the pathway will now enable us to decipher it further and more fully define the roles of APP and beta-amyloid within it. We will employ a range of techniques in cell lines and neurons, and validate findings in tissues from animal models and man. In the process we will identify novel, apt therapeutic targets through which to target the disease. Our adoption of peptide array technology to rapidly and accurately map specific protein-protein interactions, will not only help pathway elucidation but will also generate binding peptides, with which, and their binding partner proteins, we will generate assay suitable for future high throughput screening. Thus at the end of this project we will be in good position to commence small molecule identification with a battery of neuron based assays in place ready to evaluate active compounds. Such undertakings will, of course, be dependent on our obtaining further funding.

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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