The dynamic role of astrocyte secreted APO?4 in Alzheimer’s disease: investigations using human induced pluripotent stem cells

https://neurodegenerationresearch.eu/survey/the-dynamic-role-of-astrocyte-secreted-apo4-in-alzheimer%c2%92s-disease-investigations-using-human-induced-pluripotent-stem-cells/

Principal Investigators

Professor Seth Love

Institution

University of Bristol

Contact information of lead PI
Country

United Kingdom

Title of project or programme

The dynamic role of astrocyte secreted APO?4 in Alzheimer’s disease: investigations using human induced pluripotent stem cells

Source of funding information

Alzheimer's Society

Total sum awarded (Euro)

€ 303,400

Start date of award

01/01/2016

Total duration of award in years

3

Keywords
Research Abstract
The e4 allele of the APOE gene is a strong genetic risk factor for Alzheimer’s disease (AD). APOE has roles in neuronal homeostasis, regeneration and synaptogenesis, and in clearance of A? from the brain. APOE-dependent clearance of A? is partly mediated by astrocytes. APOE is required for their localization to A? plaques, and internalization and degradation of A?. APOE4 is less effective than other APOE isoforms in these and other roles that affect neuronal

function. Assessment of the mechanisms of influence of APOE genotype on astrocyte function and neuronal interaction in AD has been limited by a lack of representative experimental models. We have generated a collection of human induced pluripotent stem cell (hiPSC) lines from human adult skin fibroblasts with different combinations of APOE alleles, from AD patients and controls. We are able to differentiate the hiPSCs into cholinergic or glutamatergic neurons or mature astrocytes, together providing a suitable human model to study the differential effects of APOE isoforms on astrocyte function and neuronal interaction in AD and control astrocytes and neurons. We will examine how APOE4 vs APOE3 isoforms influence the health, survival and function of neurons in normal conditions and also in the presence of A?. We will also examine the role of APOE in the cell-autonomous response of neurons to A?, the APOE-mediated support provided by astrocytes and in astrocytic clearance of A?, and explore some preliminary approaches to therapeutic targeting of these processes.

Further information available at:

Types:
Investments < €500k

Member States:
United Kingdom

Diseases:
N/A

Years:
2016

Database Categories:
N/A

Database Tags:
N/A