Regulation of microglial proliferation and its contribution to chronic neurodegeneration

https://neurodegenerationresearch.eu/survey/regulation-of-microglial-proliferation-and-its-contribution-to-chronic-neurodegeneration/

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Country

United Kingdom

Title of project or programme

Regulation of microglial proliferation and its contribution to chronic neurodegeneration

Source of funding information

MRC

Total sum awarded (Euro)

€ 538,978

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01/09/2013

Total duration of award in years

3.0

The project/programme is most relevant to:

Alzheimer's disease & other dementias|Prion Disease

Keywords
Research Abstract

A growing body of evidence suggests that systemic inflammation may contribute to the progression of chronic neurodegeneration and the exacerbation of symptoms. We have proposed that signals generated during neurodegeneration prime microglia and exaggerate their response to systemic inflammation. Here we will characterise and target one of the most prominent innate immune activities: the control of microglial proliferation and priming. We

hypothesise that priming and proliferation of macrophages and microglia in the brain are intimately related. We will use the delivery of novel RGB viral vectors (collaborators in Hamburg) to the bone marrow using X-ray guidance (collaborators in Southampton), to identify the recruitment of BM cells to the perivascular, meningeal or microglia populations. We will do this in naïve animals, in animals with neurodegeneration, those with systemic inflammation and when these are combined. We will investigate how neurodegeneration in combination with systemic inflammation drives proliferation of recruited or local macrophage populations focussing on the induction of the mitogenic signalling pathways. We will use animal models of neurodegeneration: the ME7 model of prion disease and the APP PS1 transgenic model of Alzheimer's disease. We will correlate our findings with the study of human tissue from AD patients who have died with or without systemic inflammation. To address the contribution of the CSF1R pathway to proliferation and priming we will use an inhibitor of the CSF1R tyrosine kinase activity and assess the impact using behavioural, cellular, molecular and histopathological assays. The proposed multidisciplinary and collaborative research plan will provide novel insights into the understanding of the innate immune response in chronic neurodegeneration and characterize microglial proliferation, identify molecular targets and design and analyse therapeutic approaches to control the progression of neurodegenerative diseases.

Lay Summary
Further information available at:

Types:
Investments > €500k

Member States:
United Kingdom

Diseases:
Alzheimer's disease & other dementias, Prion disease

Years:
2016

Database Categories:
N/A

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