Role of inflammation in age-related neurodegeneration

https://www.neurodegenerationresearch.eu/survey/title-of-pirole-of-inflammation-in-age-related-neurodegeneration/

Title of project or programme

Title of PI Role of inflammation in age-related neurodegeneration

Principal Investigators of project/programme grant

Title	Forname	Surname	Institution	Country
Prof	Marina	Lynch	TCD	Ireland

Address of institution of lead PI

Institution	Trinity College Dublin
Street Address	College Green
City	Dublin
Postcode	2

Country

- Ireland

Source of funding information

Science Foundation Ireland

Total sum awarded (Euro)

1591142.00

Start date of award

01-03-2008

Total duration of award in months

48

The project/programme is most relevant to

- Alzheimer’s disease and other dementias

Keywords

Age, neuroinflammation, hippocampus, microglial activation, cytokines, IL-1 beta, IL-4, IL-1F5, CD200, synaptic plasticity, neurodegeneration, amyloid

Research abstract in English

Neuroinflammation has been identified as a common denominator in several neurodegenerative conditions, and

recent work has demonstration that inflammatory changes also occur in the brain. Age-related inflammatory
changes are characterized by increased expression of proinflammatory cytokines and increased microglial
activation. In aged animals, in animal models of Alzheimers Disease, and in animals treated with amyloid-b (Ab)
the neuroinflammatory changes are associated with deficits in synaptic function typified by a decrease in
long-term potentiation (LTP) and blocking microglial attenuates at least some of these changes. This study is
designed to investigate the causes and consequences of microglial activation and to identify mechanisms by
which activation can be modulated. Recent studies have established that IL-1F5, a member of the growing family
of IL-1 ligands, exerts anti-inflammatory effects in brain; the evidence suggests that these are mediated by
interaction with the IL-1 receptor, SIGGIR and the subsequent production of IL-4. Here the actions of IL-1F5,
including its ability to modulate microglial activation will be investigated and the precise role of IL-4 will be
assessed. IL-4 attenuates several Ab- and age-related changes and our recent work suggests that this may a
consequence of its ability to increase the interaction between CD200, which is expressed on neurons, and
CD200R, which is expressed on microglia. This programme of work is designed to address these questions and
will exploit the availability of SIGIRR, IL-4 and CD200 knockout mice in an effort to do so.

Lay summary

The demographic changes in the developed world, specifically the increased ageing population, has highlighted to need to increase our understanding of age-related disorders and therefore identify effective means by which individuals can live a healthier, longer life. Several neurodegenerative diseases are age-related but, because of the complexity of the central nervous system (CNS) and the relatively poor understanding of CNS function, few effective treatments have been identified. The primary goal of neuroscience is to deepen our understanding of the processes which lead to deterioration in function with age and neurodegenerative diseases, and therefore contribute to the development of effective preventative or treatment strategies to minimize the deficits in function. It has become clear that inflammatory changes are a common feature of many neurodegenerative disorders and age and this programme of work is designed to study the causes and consequences of age-related inflammation and to identify strategies which attenuate these changes.

In which category does this research fall?

- Basic research