Alzheimer's Disease Modelling Using Induced Pluripotent Stem Cell Derived Astrocytes.

Research Team
Dr Lisa Mohamet: Stem Cell Research Fellow. School of Dentistry, University of Manchester.
Dr Vicky Jones: Lecturer in Molecular Biology. University of Central Lancashire.
Dr Kate Meade: Research Associate. School of Materials, University of Manchester.

Introduction
Diseases of ageing are a priority area for pharma and western governments, reflecting the large number of patients and high costs associated with treatment and care. Alzheimer's disease is the most common form of dementia and contributes to 60–70% of cases. A recent report by the House of Commons All-Party Parliamentary Group on Dementia recommends that early diagnosis should be made a priority as there is strong evidence that this will benefit patients, their families and the taxpayer. However, progress in understanding many diseases has been hindered by a lack of suitable *in vitro* models, particularly for diseases in which affected cell types are difficult to access or obtain. Induced pluripotent stem cells (iPSCs) are an ideal alternative model as they can be derived from patients' skin cells and are able to form any cell type given the correct cues. Importantly, previous work by others and us has shown that neural cells grown from iPSCs harvested from individuals suffering from AD show similar disease characteristics *in vitro* to cells inside the body of the patient[1]. This allows us to essentially create a 'disease in a dish' to help us understand the mechanisms underlying AD progression and identify novel drug targets. Astrocytes are a type of neural cell (involved in the proper functioning of neurons) and neurodegenerative disorders such as AD are known to affect them[2]. In most cases, astrocytes become reactive, manifested by a change in both their function and their structure[3]. These changes may represent a major causal factor in early nerve impulse loss seen in AD, but is not yet fully understood.

Aims
This award will allow us to **(1)** create a novel *in vitro* method to grow iPSC-derived astrocytes from both healthy patients with patients suffering with AD and **(2)** assess for **early changes** in their structure and function comparing healthy and diseased cells.

Outputs
As an interdisciplinary grouping of early career researchers, this project will support a critical stage in our career progression and in the development of technology. We aim to deliver preliminary data showing **(1)** a novel method for the culture of iPSC-derived astrocytes and **(2)** differences in astrocyte structure and/or function between healthy and diseased samples. **(3)** This work will be used to help strengthen applications to fund a larger scale study investigating early changes in neural cell biology of AD.

References
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