Dysregulated monocyte-derived microglia contribute to neuroinflammation in Alzheimer’s disease patients

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Background and Introduction

The role of microglia in Alzheimer’s disease (AD) is supported by large GWAS studies.

Translational outcomes of new microglia drugs is hampered by difficulty of patient selection.

A rapid and cost-effective method of generating patient-derived microglia is required for personalized therapeutic treatment in Alzheimer’s patients.

We have adopted the method to generate microglia-like cells from peripheral blood mononuclear cells of Alzheimer’s patients.

Alzheimer’s monocyte-derived microglia can be used to rapidly screen for patient-specific differences in microglia function and potentially target drugs to individual patients.

Generation of AD monocyte-derived microglia (MDMi)

Objective

To demonstrate that human monocyte-derived microglia can provide a platform for personalised patient treatment in Alzheimer’s disease.

Aims

1. Demonstrate that patient monocyte-derived microglia reveal patient differences in microglial function.
2. Demonstrate that potential therapeutics generate different responses in individual patients as a basis for personalized medicine.

Characterisation of monocyte-derived microglia (MDMi)

Drug effects on cytokine expression

Alzheimer’s

Dasatinib treated

Untreated

AD1

AD2

AD3

IL-6 expression

TNFα expression

Summary and Future directions

- We describe a relatively rapid and simple protocol to generate microglia-like cells from patient peripheral blood cells.
- Monocyte-derived microglia reveal patient-specific differences in microglia function.
- Preliminary evidence suggests that patient microglia will respond differently to different drugs, providing a rational for future personalized medicine approaches.