# Consequences of impaired insulin signalling in astrocytes: A role in Alzheimer’s disease

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**Name of Fellow**

Dr Claire Garwood

**Institution**
**Funder**

Alzheimer's Society

**Contact information of fellow**
**Country**

United Kingdom

**Title of project/programme**

Consequences of impaired insulin signalling in astrocytes: A role in Alzheimer's disease

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3.0

**The project/programme is most relevant to:**

Alzheimer's disease & other dementias

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**Research Abstract**

Aims: The aim of this application is to test the hypothesis that insulin-impaired human astrocytes are compromised in their ability to support neuronal function and have an altered response to amyloid-beta and that this might contribute to disease development and progression.

Methods: Human astrocytes will be treated with a combination of insulin and fructose which I have recently shown results in reductions in the insulin receptor and decreased phosphorylation of the downsteam substrate Akt. These astrocytes will be co-cultured with Lund human mescencephalic cells to determine the impact of impaired astrocytic insulin signalling on neurons. Astrocytes (control and insulin-impaired) will be treated with A? oligomers derived from 7PA2 cells and their inflammatory response, ability to uptake A?, and changes in their spontaneous calcium activity will be measured. I will also develop a 3D co-culture system using polycaprolactone electrospun scaffolds and will assess cell morphology, insulin signalling and cellular stress using confocal microscopy and compare these to cells grown in 2D.

Expected outcomes: It is predicted that impairments in astrocyte function, resulting from impaired insulin sigalling, will impact neuronal function because of the inherent communication between astrocytes and neurons and the role of astrocytes in maintaining brain homeostasis. Furthermore it is expected that insulin-impaired astrocytes are less able to appropriately respond to A?. Development of the 3D co-culture system is important in taking the work forward in the future and ensuring that I investigate these events in a model that is directly translatable to impaired insulin signalling in human AD brain.

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