Project Title: Modifying Keap1-Nrf2 binding to prevent neuronal damage in Alzheimer’s disease.

Project Reference Number: SHLS2018004

Key words: Life Sciences, Long-term Conditions, Alzheimer's Disease

Applications are invited for a full-time PhD research studentship at Glasgow Caledonian University within the School of Health and Life Sciences. The studentship of £19,300 per year is for a period of three years, subject to satisfactory progress. The studentship covers the payment of tuition fees (currently £4,500 for UK/EU students or £15,000 for International students) plus an annual stipend of £14,800 for UK/EU students or an annual scholarship of £4,300 for International students.

Project Summary

Background
Alzheimer’s disease (AD) is the leading cause of dementia in humans, affecting almost 47 million patients world-wide. Current therapies do not slow-down the progression of memory loss in AD and this presents a significant healthcare challenge for future generations. A priority area for medical research is therefore to develop new drugs to halt dementia.

Most scientists believe that, early in the pathological process of AD, deposits of a protein called amyloid (Aβ) build up and cause damage to nerve cell connections (synapses). Since the protein Nrf2 is a master controller of cell protection, it has potential to prevent synapse damage in AD even after the build-up of amyloid has begun. Drugs which increase Nrf2 activity protect against memory loss in mouse models of AD, but display toxic side-effects in humans. Our published studies, using fruit flies and mouse nerve cells, suggest that blocking another protein, Keap1 (which dampens Nrf2), is a novel and safe way to maintain Nrf2 and prevent amyloid damage. Research in this project will investigate whether this strategy is relevant to human AD and when and why Keap1-Nrf2 disruption has beneficial effects as disease progresses.

References

Aims & hypotheses
Using human induced pluripotent stem cell technologies, confocal imaging, electrophysiology and molecular biology techniques, this project will investigate the following questions:

(1) Can drugs which disrupt Keap1-Nrf2 binding protect human neurons from synaptic dysfunction, when administered before or after Aβ oligomer treatment?
(2) Is Nrf2 required for Keap1-Nrf2 disruption to protect neurons against Aβ toxicity?
(3) Do specific target genes, downstream of Nrf2, mediate neuronal protection in response to Keap1-Nrf2 disruption in AD?

As Nrf2 is a general mediator of neuro-protection, this project has the added benefit of uncovering new targets for drugs to protect neurons in AD and other forms of dementia.
Research Supervisors
Candidates are encouraged to contact the following researchers for further details:

- Dr Fiona Kerr (fiona.kerr2@gcu.ac.uk)
- Professor Annette Graham
- Dr Gillian Hunter

Mode(s) of Study
The studentship is available as a 3 years full-time PhD.

Eligibility
Applicants will normally hold a UK honours degree 2:1 (or equivalent); or a Masters degree in a subject relevant to the research project. Equivalent professional qualifications and any appropriate research experience may be considered. A minimum English language level of IELTS score of 6.5 (or equivalent) with no element below 6.0 is required. Some research disciplines may require higher levels.

Specific requirements of the project:
The successful applicant will have a strong interest in exploring therapeutic strategies for the treatment of dementia, and hold a minimum of a first degree (2:1) or above, ideally in Neuroscience, Cell Biology, Biochemistry or Molecular Biology. Experience in tissue culture, electrophysiology, molecular biology or immunocytochemistry techniques, would be an advantage.

How to Apply
Candidates are encouraged to contact the research supervisor(s) for the project before applying. Applicants should download and complete the GCU Research Application Form, available from: http://www.gcu.ac.uk/phdopportunities stating the Project Title and Reference Number (listed above).

The completed GCU Research Application form should be sent with copies of academic qualifications (including IELTS if required), 2 references and any other relevant documentation to: researchapplications@gcu.ac.uk. Applicants shortlisted for a PhD studentship will be contacted for an interview.

The closing date for applications is Wednesday 21 March 2018