Autophagy control of human neuroinflammatory signalling pathways

Supervisory team:
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Host institution: University of Bristol, University of the West of England; UWE
Submit applications for this project to the University of Bristol

Project description:

Neuroinflammation is a prominent feature of the ageing and/or diseased brain. It can be detected early in human neurodegenerative disease, and can be blocked to halt neuronal decline in animal models of disease. Neuroinflammation is triggered and controlled by astrocytes and microglia. These glial cells are initially protective to neurons, but become progressively 'reactive' and toxic during chronic neuroinflammation. We want to understand the molecular control of neuroinflammation in specific regions of the brain, so that it might be controlled to protect the brain during ageing and disease. Using human induced pluripotent stem cells (hiPSCs) that are differentiated to become brain region-specific astrocytes and neurons, we can replicate aspects of neuroinflammation in vitro.

In this project, we will advance this work by combining hiPSC astrocytes and neurons with microglia in monolayer and organoid co-cultures. We will focus on the roles of glial stress and autophagy (a crucial cytoplasmic quality control process) during the neuroinflammatory response. This will involve secretome proteomics, immunoblotting, cytokine ELISA, qRT-PCR, and cell imaging, combined with autophagy manipulation involving CRISPRi and CRISPRa, to establish the key molecular players acting during neuroinflammatory signalling and their downstream impact on glial biology and neuronal health.

Please note: *This project in collaboration with the University of Bristol and the University of the West of England (UWE) is subject to a* ***joint degree award****. Successful applicants will be registered at both these institutions, and graduates will be awarded a joint degree from these two institutions upon successful completion of the PhD programme.*