3 Year PhD Studentship available for September 2019

**Department:** Genetics and Genome Biology

**Supervisors:** Professors Flaviano Giorgini & Charalambos Kyriacou

**Eligibility:** UK and EU candidates only

**Project Title:** Exploring the pathogenic roles of Rab GTPases in models of taupathy

**Project Description:**

Alzheimer’s disease (AD) is the most common neurodegenerative disorder and the predominant cause of dementia. The main pathological hallmarks of the disease in the brain are the presence of amyloid plaques and neurofibrillary tangles composed of hyperphosphorylated forms of tau (P-tau). While several cellular pathways have been implicated in AD pathogenesis, perturbed membrane dynamics affecting vesicular trafficking, secretion and autophagy likely play a key role in this disease and other neurodegenerative disorders, including Parkinson’s disease (PD) and Huntington’s disease (HD). The Rab GTPase family of monomeric G proteins plays a critical role in regulating membrane trafficking in cells, with several members being linked to these diseases. Several recent studies have highlighted novel links between specific Rabs and tau biology/pathology. Indeed, phosphorylated RAB10 co-localizes to P-tau in AD patient brains, and both RAB1 and RAB7A have been found to modulate tau secretion in neurons, with Rab7A expression upregulated in specific regions of AD brains. Notably, individuals with mutations in RAB39B exhibit intellectual disability with early-onset PD and related pathology, including tau immunoreactivity. Despite these links, modulation of these and other Rab GTPases has not been conducted in animal models of taupathy in order to clarify their roles in pathogenesis and potential therapeutic value.

We have previously employed the fruit fly *Drosophila melanogaster* to functionally interrogate Rab GTPases (e.g. Rab11 and Rab8a) in the context of PD and HD. Here we propose to use similar genetic approaches to explore the pathogenic roles of key Rab GTPases in *Drosophila* and mammalian cell tauopathy models. The student will assess modulation of tau-dependent disease-related phenotypes by candidate Rabs in flies by monitoring viability, lifespan and several behavioural paradigms (e.g. locomotor and circadian activity). Neurodegeneration, synaptic dysfunction and related phenotypes will be studied using biochemical and microscopy approaches in these animals and mammalian cell models. This work will provide important insight into the mechanisms and therapeutic potential of Rab GTPases in AD, and other disorders where tau plays a causative role.
References:


Funding details:

This 3-year studentship is jointly funded by the University of Leicester’s College of Life Sciences and the Department of Genetics and Genome Biology. Tuition and bench fees will be covered and a stipend will be paid at the annual Research Council rate (https://www.ukri.org/skills/funding-for-research-training/).

Entry requirements:

Applicants are required to hold/or expect to obtain a UK Bachelor Degree 2:1 or better in a relevant subject. The University of Leicester English language requirements apply where applicable.

How to apply:

You should submit your application using our online application system.
Apply for a PhD in Genetics
In the funding section of the application please indicate you wish to be considered for a CLS Studentship
In the proposal section please provide the name of the supervisor and project you want to be considered for.

Project / Funding Enquiries: Prof Flaviano Giorgini (fg36@le.ac.uk)
Application enquiries to pgradmissions@le.ac.uk
Closing date for applications: 28 January 2019