A UCL, Department of Genetics, Evolution and Environment, Institute of Healthy Aging Project

PhD Studentship: *"Identifying causes of neuronal cell death in C9orf72 repeat expansion toxicity"*

Applications are invited for a PhD studentship to be hosted in the Institute of Healthy Aging, at UCL, to start September 1st 2025, with funding for 3.5 years.

Project: Neurodegenerative diseases, including ALS, lack effective treatments due to our limited understanding of the molecular cascades causing neuronal death. The most common genetic cause of ALS is a hexanucleotide repeat expansion in the C9orf72 gene (C9). To identify triggers of neuronal cell death at cellular resolution, we conducted single-cell RNA sequencing (scRNA-seq) analysis of the brains of a Drosophila model of C9, throughout disease progression. We identified distinct neuronal populations susceptible to degeneration and obtained the transcriptional profiles of individual neuronal populations undergoing depletion. We will leverage this dataset to identify commonly modulated genes and pathways specific to the temporal trajectory of cell death and screen for modulators of C9 toxicity to gain insights into the underlying mechanisms responsible for neuronal demise.

Given the established link between C9 toxicity and a significant reduction in translation, potentially mediated by the formation of stress granules, we will also examine the role of stress granules in modulating pathogenesis.

Finally, we will validate our findings using human single-cell RNA sequencing data and assess pathway modulation in a murine C9 model, in collaboration with Prof. Adrian Isaacs. This multifaceted approach will provide insights into disease pathogenesis and potential novel targets for therapeutic drug development.

Funding: The studentship is funded by The Motor Neuron Disease Association and will cover UK fees and an annual stipend of £ 22,000 for the first year, raising to £25,000 in the third.

Entry requirements: Applicants should have a strong interest in motor neuron research and have or expect to obtain a 1st or upper 2nd class honours degree in any scientific discipline. Candidates from under-represented minority ethnic backgrounds are especially encouraged to apply.

Candidates short-listed for interview will be required to give a short research presentation.

Informal enquiries: Please email Dr.Teresa Niccoli for further information about the project (t.niccoli@ucl.ac.uk)

Application procedures: Application is by CV and covering letter emailed to: t.niccoli@ucl.ac.uk.

Closing date: 6th January