Rhomboid proteolysis: a novel regulator of synaptic function

Supervisory team:
Main supervisor: Prof Jack Mellor (University of Bristol)
Second supervisor: Dr Adam Grieve (University of Bristol)

Host institution: University of Bristol

Project description:
We are seeking a highly motivated PhD candidate to join our multidisciplinary research team in a project focused on understanding the physiological role of rhomboid proteolysis in neurons. We have recently discovered this novel and important regulatory process and this project aims to explore the molecular mechanisms by which rhomboid proteases regulate neuronal signaling and synaptic function, with potential insights into neurodevelopmental and neurodegenerative diseases.

Rhomboid proteases are a unique class of intramembrane serine proteases that cleave transmembrane proteins, influencing key cellular pathways. Similar proteases such as amyloid secretases have critical roles in neuronal function but we are the first to find a crucial role for rhomboids in regulating mammalian synaptic signalling. Since we've just discovered this, the specific functions and physiological importance of rhomboid proteases in neuronal biology remain largely unknown. In particular, investigating whether rhomboid activity influences synaptic plasticity has never been explored.

The PhD candidate will investigate how rhomboid proteolysis contributes to neuronal function using a unique combination of cell biology, proteomics and advanced electrophysiology techniques. The project will involve:

- Discovering and characterising the substrates of certain rhomboid proteases in neurons, using computational and AI driven approaches, as well as proteomic wet lab screens.
- Investigating the effects of rhomboid-mediated cleavage on synaptic signaling and plasticity.
- Exploring the role of rhomboid proteolysis in synaptic transmission in vitro and in vivo.
- Studying the potential involvement of rhomboid proteases in neurodegenerative conditions.

Key Responsibilities:

- Design and execute experiments using primary neuronal cell culture, molecular biology, proteomic and electrophysiology approaches. This work may extend to model organisms.
- Analyse data and interpret results in the context of rhomboid protease activity in neurons.
- Collaborate with other researchers in the host labs and participate in group meetings.
- Present research findings at conferences and publish in peer-reviewed journals.

Requirements:

- A degree (or equivalent) in Neuroscience, Molecular Biology, Biochemistry, or a related field.
- Strong interest in neurobiology and protease biology.
- Excellent communication and organizational skills.
- Ability to work both independently and as part of a team.

Desirable:

- Hands-on experience with molecular biology techniques, cell culture, and/or proteomics is highly desirable.

For more information, please contact Prof Jack Mellor or Dr Adam Grieve at Jack.Mellor@bristol.ac.uk or adam.grieve@bristol.ac.uk. We look forward to receiving your application!

Our aim as the SWBio DTP is to support students from a range of backgrounds and circumstances. Where needed, we will work with you to take into consideration reasonable project adaptations (for example to support caring responsibilities, disabilities, other significant personal circumstances) as well as flexible working and part-time study requests, to enable greater access to a PhD. All our supervisors support us with this aim, so please feel comfortable in discussing further with the listed PhD project supervisor to see what is feasible.