Investigating the role of neuronal metabolism in excitation/inhibition balance

Supervisory team:
Lead supervisors: Dr Kevin Wilkinson (University of Bristol), Dr Tim Craig (University of the West of England)
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Host institution: University of Bristol
Submit applications for this project to University of Bristol

Project description:
Communication between neurons primarily occurs at specialised junctions called synapses. Neurons can send and receive two types of information at synapses, termed 'excitatory' and 'inhibitory' signals, which instruct the neuron receiving the message to become more or less active, to properly control neuronal activity. The brain therefore relies on a delicate balance of excitatory and inhibitory signaling in order to pass information between neurons and ensure that the right signals are sent at the right time. Indeed, maintaining this balance requires an intricate crosstalk between excitatory and inhibitory pathways, and perturbations in this balance have been implicated in a wide range of neurological conditions, including epilepsy, autism spectrum disorder, and schizophrenia. However, despite its importance, how neurons maintain the correct excitatory/inhibitory balance is poorly understood.

Interestingly, for over 100 years, a ketogenic diet rich in protein and fat, but containing little carbohydrate, has been used as a treatment for some forms of epilepsy, suggesting dietary factors can play an important role in controlling the balance of excitation and inhibition in the brain. Furthermore, it is now appreciated that a high fat diet represents a major risk factor for neurodegenerative disease. However, exactly how dietary factors and neuronal metabolism affect synaptic function is not well understood.

In this project the student will use a variety of molecular, biochemical, cell biological, and proteomic techniques in primary cultured neurons. They will expose neurons to various dietary factors (for example saturated/ unsaturated fatty acids and ketones) to examine how these treatments affect neuronal development, the number of excitatory and inhibitory synapses, and how it affects the delivery of proteins essential for excitatory or inhibitory synaptic function. They will then examine how these different metabolic states regulate the levels and activity of proteins that mediate protein delivery to excitatory and inhibitory synapses, focusing on a complex of proteins called SNX27-retromer, which has been shown previously to play an important role in the delivery of a variety of synaptic membrane proteins.

The student will join the large molecular neuroscience communities at Bristol and UWE and will generate knowledge that will advance our understanding of how neuronal activity is controlled in the brain, and how, on a molecular level, metabolic and dietary factors act to orchestrate this balance. Ultimately, this will contribute to our understanding of how these factors may be used to combat disease and promote healthy ageing.

Please note: *This project is in collaboration with the University of Bristol and the University of the West of England (UWE) and 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.*

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.