Regulation of neuronal energy production by SUMOylation

Supervisory team:
Lead supervisors: Prof Jeremy Henley (University of Bristol), Dr Tim Craig (University of the West of England; UWE)
Dr Kevin Wilkinson (University of Bristol), Prof Myra Conway (University of the West of England; UWE)

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

Project description:
The human brain uses 20% of the body's energy but makes up only 2% of its mass. The 100 billion neurones which make up the functional units of the brain require a constant supply of energy, mostly in the form of glucose, in order to maintain and regulate their membrane potential over their large surface area. Without the constant production of ATP by glycolytic and mitochondrial metabolism, normal brain functions fail, which is a major contributory factor in multiple neurological and neurodegenerative diseases. Surprisingly, however, the regulation of metabolism in neuronal cells is still poorly understood.

Our preliminary data demonstrate that neuronal glycolytic and mitochondrial metabolism are regulated by the post-translational protein modification SUMOylation. A large body of evidence links SUMOylation to the regulation of normal neuronal function, including neurotransmitter release and memory formation, and dysfunctional SUMOylation contributes to the pathology of multiple diseases. Remarkably, however, the roles of SUMOylation in the regulation of neuronal metabolism have not been extensively investigated.

This project will involve genetic manipulation of neuronal cell lines and primary neurones to manipulate SUMOylation at a cellular and individual protein level. The student will be trained in a wide variety of molecular biology techniques, Western blotting, cell culture, confocal microscopy and real-time metabolic analyses.

This combination of techniques will allow us to fully investigate the role of SUMOylation in the regulation of neuronal metabolism, which will greatly advance our understanding of energy homeostasis in the brain. The data generated will provide new and important insights into how SUMOylation and deSUMOylation impact on energy production in healthy and stressed cells.