CircadiAgeing: Clock excitability, circadian rhythms and healthy ageing

Project ID: 268

Supervisory team

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Host institution: University of Bristol

Project description: 24 hour/circadian rhythms are essential for all lifeforms, allowing physiology and behaviour to be optimally aligned to light/dark cycles. Our health and wellbeing depend on appropriately timed circadian rhythms with disruption contributing to ageing and disease. Furthermore, our population is getting older having wider medical and socio-economic consequences with ageing dampening daily rhythms in physiology and behaviour causing poor health in the elderly. About half of elderly population experience chronic circadian and sleep disturbances with neurodegenerative diseases causing more pronounced circadian deficits, with poor sleep contributing to disease pathology. The Nobel prize was awarded to Drosophila researchers determining the fundamental mechanisms of circadian rhythms conserved from flies to humans. This molecular clock consists of clock genes which are rhythmically expressed in clock neurons controlling the circadian expression of genes encoding ion channels/receptors that drive daily changes in electrical activity. This membrane clock is vital for synchronising the molecular clock in different clock cells and communicating time-of-day information to the rest of the brain and body. The molecular clock is well-understood, but there is a lack of research on the membrane clock. You will help address this crucial knowledge gap and the effect of ageing on both clocks.The hypothesis you will test is the membrane and molecular clock become synergistically weaker during the lifespan compromising circadian rhythms and the individual's health during ageing. This predicts that disrupted molecular and membrane clocks significantly contribute to ageing. You will help determine the conserved components and mechanisms of the membrane clock and how it ages by defining: 1) The role of clock neuron excitability in circadian rhythms. 2) The mechanism of the membrane clock and effect of ageing. 3) The relationship between the membrane and molecular clocks. 4) How known ageing signalling pathways interact with the molecular and membrane clock. 5) If interventions designed to reverse age-dependent decline in the molecular and membrane clock promoting healthy ageing. Deciphering the membrane clock is important because it is composed of receptors/channels which are the first/third biggest targets for therapeutic drugs, thereby generating knowledge facilitating the development of chronotherapies for ageing. In contrast to previous studies that are limited to certain aspects of the clocks, you will help address how the clock works as a whole spanning multiple levels from mathematical models to whole organisms across their lifetime, thereby identifying evolutionary conserved interventions to rejuvenate rhythms improving health during ageing.

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.