Unravelling a novel role for the mineralocorticoid receptor in dentate gyrus neurogenesis

Supervisory team:
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Project description:
Why do stressful events have a long-term impact on the brain?

With the tremendous rise in the number of people suffering from stress-related mental disorders finding an answer to this question is more important than ever. Stressful events can have a long-lasting impact which includes the formation of memories of such events. Usually, these memories help the individual to cope with the experience and be better prepared in case of a similar event. However, a mental health problem (e.g. post-traumatic stress disorder (PTSD), major depression, anxiety) can develop if a situation is extremely traumatic or exposure to stress becomes chronic. It is still not clear how the brain processes stressful challenges. It has been well established though that stress-induced glucocorticoid hormones play a key role through their actions on a part of the brain (the hippocampus) that is crucial for responding to stress including the formation of memories of the stressful event itself. Interestingly, the hippocampus is one of the main brain systems where new neurons are incorporated throughout life. Adult neurogenesis, plays a principal role in memory formation of events and places and is sensitive to stress. We recently found that glucocorticoid hormones, through binding to their receptors (the mineralocorticoid and glucocorticoid receptors (Mifsud & Reul, Proc. Natl. Acad. Sci. USA 2016)), influence the expression of more than 60 neurogenesis-associated genes in the hippocampus. This is a significant step forward in the investigation of the effects of stress on the hippocampus in terms of stress coping and memory formation.

The aim of this project is to elucidate the role of glucocorticoids in the effects of stressful challenges on hippocampal progenitor pools and neuronal differentiation and maturation. This multidisciplinary research will be conducted both in stress/behavioural models (stress coping, memory formation in adolescence, adulthood, ageing) in vivo and in primary cell culture/progenitor cell lines in vitro. The successful PhD student will apply various state-of-the-art technologies including epigenetic (chromatin immuno-precipitation (ChIP), bisulfite pyrosequencing (for DNA methylation analysis)), molecular (RNA, genome analysis, gene silencing), neuroanatomical (RNAscope, double/triple immuno-fluorescence), cell culture (primary/progenitor cell lines), experimental animal (behavioural models), and bioinformatics (R, Bioconductor, Ingenuity Pathway Analysis) technologies and methods.

This project will be supervised by Professor Johannes Reul, Dr Oscar Cordero Llana and Dr Karen Mifsud at the University of Bristol and Professor Jonathan Mill at the University of Exeter.