Building bridges between immunity and memory: unveiling novel roles of antimicrobial peptides in neural function.

Project ID: 59

Supervisory team

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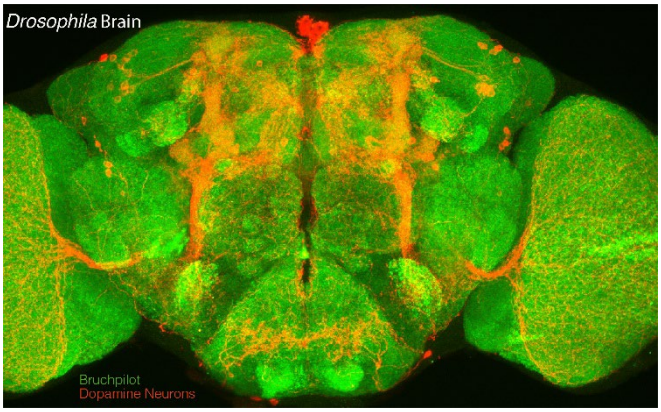
Host institution: University of Bristol



Project description: Both neural and immune systems receive information from external cues and coordinate adequate responses, generating an experience-based outcome for subsequent interactions with said cues. Based on those parallelisms it is not unexpected that immune and nervous systems share functional mechanisms; for example, microglia are resident immune cells in the CNS that also play a role in synaptic function.Another important example are antimicrobial peptides (AMPs). These are molecules involved in combating infections present in all animals. Most AMPs perform antimicrobial roles, but recent evidence involves AMPs in neural function and neurodegeneration. For example, there is upregulation of AMPs in patients with Alzheimer's disease (AD), with evidence that the amyloid peptide itself may be antimicrobial. AMPs have also been linked to dendrite degeneration in invertebrate models. However, how AMPs regulate brain function and deterioration at a mechanistic level is still unknown. This project proposes to investigate the neural roles of a family of AMP genes in Drosophila called Baramicins. Only Baramicin A is immune-induced and may have a neuroprotective role against neurotoxins; while Baramicin B and Baramicin C are enriched in the nervous system. Thus, this family is a promising model to reveal the dual roles of AMP genes in neurology and immunity. The aims of the project are: 1-To investigate the expression of AMPs in the nervous system, in different neural and glial subtypes, using a combination of imaging and connectomic approaches.2-To assess the roles of different AMPs in memory and sensory perception. We will use a panel of existing mutants alongside genetic strategies to downregulate gene expression in glial and neural subgroups during different memory phases (acquisition, consolidation, recall).3-To study the role of AMPs in neurodegeneration. We will manipulate AMP expression in well-established models of AD in Drosophila, addressing the cellular and functional changes that take place in the circuits involved, and leading to a better understanding of AMP modulation of disease pathology. This project tackles a very novel and promising question, combining the expertise of the hosting labs in memory (Boto) and immunity (Hanson) to understand how AMPs regulate brain function in health and disease. The student will acquire expertise in molecular, behavioural and brain imaging techniques, and will become part of thriving neuroscience and immunity communities in the South West. The outcomes of this research will provide insights on how AMPs modulate neural function in higher organisms and on novel therapeutical approaches for neurodegenerative disorders.

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.