Luke Paine, PhD - 'Neuroimmune Interactions in Visceral Pain'

Chronic inflammation of the gastrointestinal tract can give rise to Inflammatory bowel disease (IBD). This multi-factorial disease presents a significant burden on healthcare systems around the globe, predominantly in European and North American populations. Such disorders of the gastrointestinal tract include - Ulcerative colitis and Crohn's disease, and for both, there remains a significant unmet clinical need. Pain is a major detriment to the quality of life of patients with such inflammatory diseases, and the lack of efficacy of current analgesics in the clinic warrants a search for novel pharmacological treatments.

While the relationship between pain and inflammation is well established, much remains unknown about the molecular facets of the interactions of the nervous and immune systems. Neuroimmune interactions within the gastrointestinal tract, such as that of cytokines and sensory neurons, therefore present themselves as exciting avenues of research. Cytokines, such as Interleukins, are small proteins released by immune cells that possess the ability to alter pain signalling. Of particular interest to me is the Interleukin-23 (IL-23) / Interleukin (IL-17) signalling axis. Interleukin 23 is a member of the IL-12 cytokine family and is released predominantly by macrophages and monocytes. This heterodimeric cytokine binds to the IL-23 receptor and augments the Th17 immune response, leading to increased IL-17 release.

IL-17 signalling plays a fundamental role in the pathogenesis of inflammatory pain in psoriasis, and given its receptors are localised on sensory neurons, it is intuitive that this cytokine, downstream of IL-23, also instigates chronic pain in IBD. Utilising ex vivo electrophysiology of the lumbar splanchnic nerve, Ca2+ imaging of dorsal root ganglia neurons, and other molecular and pharmacological approaches, I will thereby endeavour to reveal the intricacies of this signalling axis. My research will contribute to the better understanding of neuro-immune crosstalk in the gut and, in time, may contribute to the development of pharmacological treatments for chronic pain associated with inflammatory disease.