**iCase Project / AY 2023 -2024**

# Neuroimmune regulation of gut function

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**Department/Institute:** Pharmacology

**Industrial Partner:** Metrion Biosciences

**Research area:** Neuroscience

**Project outline:**

Sensory neurones are critical to the detection of environmental and internal stimuli within the gastrointestinal tract mediating physiological responses such as pain and satiety in response to noxious, inflammatory, metabolic and microbial stimuli. In addition to mediating reflex responses along the gut-brain axis, the effector functions of sensory afferents mediated through the release of signalling molecules from the afferent terminals play a key role in shaping localised interactions with the microbiome, immune cells, enteric neurons and barrier function at the mucosal interface.

Data from our recent single cell RNAseq study of colonic neurones has provided comprehensive insight into the previously unrecognised diversity of mediator expression with different sensory nerve populations and opportunity for interaction with a diverse range of cell populations and signalling pathways within the bowel. One clear example of this interaction is bidirectional neuroimmune signalling based on the marked expression of cytokines, chemokines and their receptors in sensory neurons, and control of local immune response, gut-brain signalling, barrier function and host pathogen defence. This is most apparent for the nociceptor subpopulation of sensory neurons and our work has highlighted a key role for transient receptor potential (TRP) channels and downstream signalling via p38MAPK in these events. This project will build on these studies utilising the extensive experience of Metrion Biosciences in ion channel drug discovery to investigate further the role of TRPA1 in the activation of gut nociceptors by cytokines and their bidirectional regulation of gut barrier function in mouse and human tissue and IPSCs.

**BBSRC DTP main strategic theme:** Understanding the rules of life