Microbial metabolites as signals for gut cell communication: mapping epithelial signalling and developing rapid readouts in model systems

Project ID: 289

Supervisory team

Main supervisor: Dr Alexander Greenhough (University of the West of England (UWE)
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Host institution: University of the West of England (UWE)
CASE partner: Vidiia

Project description: This PhD examines how gut microbiome metabolites shape epithelial barrier function and intestinal homeostasis. In parallel, you will develop rapid molecular readouts to monitor epithelial responses in real-time as biomarkers of health, dysregulation and inflammation.The gut epithelium forms the frontline barrier between the body and intestinal microbiota. The gut microbiome releases a stream of metabolites including short-chain fatty acids (SCFAs), succinate, indoles and aromatic monoamines. These act as messengers in continuous dialogue with epithelial cells. Some of these metabolites strengthen barrier function and support balanced immune tone, while others promote cellular stress or inflammation. However, the mechanisms by which epithelial cells sense these metabolites and transduce them into responses remain poorly understood.A key opportunity is to develop rapid methods that capture dynamic signalling responses of epithelial cells to microbial metabolites. RNA-sequencing provides a powerful overview of global changes, and this project will build on these insights by developing rapid assay platforms to track responses in real time.As a PhD student on this project, you will investigate how gut epithelial cells sense and respond to microbial metabolites, focusing on signalling pathways and transcriptional dynamics. Working with intestinal epithelial cell line models and three-dimensional (3D) intestinal organoids, you will:1. Characterise how cells and 3D intestinal organoids respond to defined microbial metabolites and conditioned media from selected bacterial strains.2. Discover the transcriptional programmes triggered by these exposures using RNA sequencing time courses, focusing on genes linked to inflammation, barrier function and receptor pathways.3. Design and validate a panel of reverse transcription loop-mediated isothermal amplification (RT-LAMP) assays targeting key marker genes for rapid, sensitive monitoring of epithelial states.4. Apply this assay panel to map dynamic responses, screen metabolite mixtures, test dose responses, and probe the role of G protein–coupled receptors (GPCRs) in shaping signalling outcomes.You will receive training in cell culture, transcriptomics, molecular diagnostics and receptor biology, alongside opportunities to collaborate with an industry partner. We welcome applications from candidates with diverse backgrounds. Full training in all methods will be provided.By uncovering how microbial metabolites regulate epithelial transcriptional states, this project will deepen our understanding of the molecular language between microbes and host cells. It will also produce a validated toolkit of rapid assays with the potential to evolve into point-of-care applications, while shedding new light on how the microbiota shapes barrier homeostasis and, in some contexts, processes such as inflammation and cancer.

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.