

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

Project ID: 3695

Supervisory team

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Host institution: University of the West of England (UWE)

CASE partner: Vidiia Ltd

Project description: This PhD examines how gut microbiome metabolites shape epithelial barrier function and intestinal homeostasis. Alongside these studies, you will develop rapid molecular readouts of epithelial health, dysregulation and inflammatory responses, linking fundamental biology with future diagnostic applications. The gut epithelium forms the frontline barrier between the body and intestinal microbiota. The microbiome releases metabolites including short-chain fatty acids, succinate, indoles and aromatic monoamines. These act as messengers in a continuous dialogue with epithelial cells, influencing barrier function and cellular signalling. However, how cells translate changing metabolite exposure into transient or sustained responses remains incompletely understood. The project will initially focus on two defined metabolites: butyrate, which epithelial cells can use as fuel and which regulates gene expression; and tryptamine, a bacterial product of tryptophan metabolism with reported effects on epithelial receptor signalling. We hypothesise that receptor activity helps determine the duration of epithelial responses and their consequences for barrier function. Targeted perturbations will distinguish receptor-dependent effects from alternative mechanisms. A key opportunity is to translate these biological responses into practical molecular readouts. RNA sequencing will identify candidate markers, while measurements of barrier permeability, viability and inflammatory responses will establish their biological meaning. Working with Vidiia, you will investigate whether these markers can be measured using simpler, rapid assays suitable for future diagnostic development. Using intestinal epithelial cell lines and three-dimensional (3D) intestinal organoids, you will: 1. Characterise responses to butyrate and tryptamine, establishing how concentration and exposure duration affect signalling, recovery and barrier function. 2. Identify transcriptional programmes using selected RNA-sequencing time courses, then test candidate G protein-coupled receptors through depletion and rescue to determine their contribution. 3. Develop a small panel of reverse transcription loop-mediated isothermal amplification (RT-LAMP) assays to distinguish epithelial states, benchmarking performance against RT-qPCR and functional measurements. 4. Apply the panel to further exposure conditions and selected, chemically characterised bacterial preparations, testing whether it reliably reports epithelial responses beyond the conditions used for its development. You will receive training in epithelial biology, transcriptomics, receptor biology and quantitative analysis, alongside assay development and a placement with Vidiia. We welcome applicants from diverse backgrounds; full training will be provided. By uncovering how microbial metabolites regulate epithelial responses, this project will deepen our understanding of host-microbe communication in health, dysregulation and inflammation. It will also deliver a prototype molecular assay panel, establishing a foundation for future diagnostic and point-of-care applications. Continued on next page.....

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.