

## Microfluidic platforms to study host-microbiome interactions

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About three-quarters of human body surface is exposed to dense microbial population along the gastro-intestinal tract (GIT) that accommodates around 80% of immune cells. The GIT is one of the most critical sites for metabolic and immunologic homeostasis in the body. While large-scale genomic analysis and germ-free mice have been widely used, they are limited to capture the dynamic functional interaction between host-microbiome in a humanized setting. *in-vitro* recapitulation of GIT physiology can be a powerful alternative for hypothesis testing in diseases like IBD and cancer.

As a first step, we developed a simple transwell assembly to closely emulate GIT anatomy and the barrier function in a quantitative and analytical manner. The system enables us to sequentially house bacterial cells, a mucus layer, human intestinal epithelial cells and human peripheral blood mononuclear cells (hPBMCs) in a single co-culture platform. Porcine intestine-derived mucin formed a biophysically relevant barrier and also provided *in-vivo* like biochemical milieu to bacterial cells. Addition of human epithelial cell monolayer on a collagen coated semi-permeable membrane added another level of cellular and biophysical complexity. Finally, by introducing human peripheral blood mononuclear cells (hPBMCs), we simulated host-microbiome interactions and successfully captured responses relevant to gut inflammation. Initial data indicate that bacterial products successfully stimulate hPBMCs. Whereas, mucus and epithelial barriers demonstrated strong immunomodulatory functions. Further investigations are being carried out in order to create models that will incorporate differentiated epithelial cells (villi), physiologically relevant flow and stress conditions along with co-culture of aerobic (mucosal) and anaerobic (luminal) components of the human GIT. Hopefully, these models will enable us to study mechanistic interactions of the microbiome with the host and reveal novel therapeutic targets for diseases associated with the dysregulation of host-microbiome homeostasis in human GIT.

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