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A microfluidic-based *in vitro* model of the gastrointestinal human-microbe interface

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Abstract:

Changes in the human gastrointestinal microbiome are associated with several diseases. To infer causality, experiments in representative models are essential, but widely used animal models exhibit limitations. Here we present a modular, microfluidics-based model (HuMiX, human-microbial crosstalk), which allows co-culture of human and microbial cells under conditions representative of the gastrointestinal human-microbe interface. We demonstrate the ability of HuMiX to recapitulate *in vivo* transcriptional, metabolic and immunological responses in human intestinal epithelial cells following their co-culture with commensal *Lactobacillus rhamnosus* GG (LGG) grown under anaerobic conditions. In addition, we show that the co-culture of human epithelial cells with the obligate anaerobe *Bacteroides caccae* and LGG results in a transcriptional response, which is distinct from that of a co-culture solely comprising LGG. HuMiX facilitates investigations of host-microbe molecular interactions and provides insights into a range of fundamental research questions linking the gastrointestinal microbiome to human health and disease.

Keywords: microfluidics, co-culture, human intestinal epithelial cells, *L. rhamnosus*, *B. caccae*, transcriptional response