HuMiX – The artificial gut

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Human gut is an open system that encounters wide-range of diet-derived compounds and numerous microorganisms making it a complex system to explore. Alterations in intestinal morphology and dysbiosis lead to several gastrointestinal (GI) ailments and other disorders. In the present scenario metagenomics is considered as an important discipline to study the correlation of human microbiome with the health and disease. Although it provides association between microbial species and maladies, it does not help to infer the cause of disease. A thorough knowledge of fundamental molecular mechanism behind the host-microbe interaction is required to study the disease causality which necessitates experimental validation. Animal models have always been the subject of choice but they cannot recapitulate the human systems completely. Moreover the cross-talk between the host and its gut microbiota is host-specific and therefore this requires the model system *i.e.* human gut. However all experiments cannot be performed on human volunteers as it is relatively challenging to manipulate different variables on them. Therefore a system is needed that mimics the intestinal conditions and can represent Gl human-microbe interface.

A microfluidics-based *in-vitro* model of the GI human-microbe interface named HuMiX (human-microbial crosstalk) has been reported in the journal, "*Nature Communications*" *by researchers from the* University of Luxembourg in collaboration with colleagues at the the University of Arizona. This model of human gut consists of three co-laminar microchannels *viz*. a perfusion chamber, which contains media, a human microchamber, which is a human epithelial cell culture microchamber and a microbial microchamber that supports the microbial growth. These microchambers are equipped with an inlet and outlet for the inoculation of cells and management of physicochemical parameters. The microchambers are separated by a porous membrane analogous to healthy epithelial cell layer. Optodes which are the oxygen sensors in the device monitors the dissolved oxygen concentration. Also the specially designed form of device accommodates an electrode to measure transepithelial electrical resistance which depicts the growth and differentiation of cell inside the device.

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The researchers demonstrated the recapitulating ability of HuMiX *in vivo.* They co-cultured human epithelial cells (Caco-2) with GI commensals like *Lactobacillus rhamnosus* GG (LGG) a facultative anaerobe under anaerobic conditions as well as obligate anaerobe *Bacteroides caccae* along with LGG. Transcriptional response resulted were different amongst both the cultures. Results were in accordance to the published *in vitro* and *in vivo* data sets which makes HuMiX an efficient representative model of the GI human-microbe interface. Co-culture of Caco-2 cells with LGG and some strains of other bacterial species like *Lactobacillus rhamnosus*, were found to produce gamma-aminobutyric acic (GABA) a neurotransmitter. This makes HuMiX a suitable tool to study gut-brain axis and communication in future.

Thus HuMiX can be used as a key device to facilitate the exploration of host-microbe interactions and molecular processes behind these interactions. It could possibly be used in various other areas like probiotics, pharmacokinetics, drug discovery and development. It helps to comprehend microbiome impact on the actual gut milieu and in human health and disease onset. According to the authors, HuMiX is considered as a substitute to animal models for first-pass experiments which might help replace the animal testing in future. Similarly, the modular architecture of the regions apart from GI tract can also be designed to explore and study the different human organs. A wider and deeper understanding of the gut and the other regions could open the doors to new research avenues that can help us device personalized treatments and right therapeutic strategy in terms of patient treatment and better patient management.

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