

## **Miniaturized Colon-on-Chip to Recapitulate Normal and Diseased Physiology**

Nancy Allbritton, Department of Bioengineering, University of Washington, Seattle, WA, USA

Organ-on-chips are miniaturized devices that arrange living cells to simulate functional subunits of tissues and organs. These microdevices provide exquisite control of tissue microenvironment for the investigation of organ-level physiology and disease. A 3D polarized epithelium using primary human gastrointestinal stem cells was developed to fully recapitulate gastrointestinal epithelial architecture and physiology. Primary cells are cultured on a shaped hydrogel scaffold to form an array of crypt-like structures replicating the intestinal architecture. Imposition of chemical gradients across the crypt long axis yields a polarized epithelium with a stem-cell niche and differentiated cell zone. Co-culture of pericryptal intestinal fibroblasts also modulates cell compartmentalization along the crypt long-axis. A dense mucus layer patterned in the X-Y-Z directions is formed on the luminal epithelial surface and is impermeable to bacteria. An oxygen gradient across the tissue mimic permits luminal culture of anaerobic bacteria while maintaining an oxygenated stem cell niche. Construction of the crypt array with a porous scaffolding permits the incorporation of stromal immune cells in the model system. This in vitro human colon crypt array replicates the architecture, luminal accessibility, tissue polarity, cell migration, cell types, mucus patterning and cellular responses of in vivo intestinal crypts. Intestinal biopsy samples can be used to populate these constructs to produce patient-specific tissues for personalized medicine and disease modeling. This bioanalytical platform is envisioned as a next-generation system for assay of microbiome-behavior, drug-delivery and toxin-interactions with normal or diseased epithelium.