Abstract

Three-dimensional (3-D) cell culture models of the gastrointestinal epithelium are quickly being adopted for toxicology, drug discovery, and disease modeling. These models provide a biomimetic approach to live and primary cell-based models, including the mimicking of native intercellular crosstalk and importantly, the recapitulation of physiological attributes of the tissue. The MimEX GI model system, when using current 3-D models, such as gastrointestinal organoids, experience difficulties with model variability, toxicity issues, and experimental accessibility. Overcoming these obstacles is paramount for the logistical incorporation of 3-D tissues into high throughput platforms.

MimEX GI tissue is an innovative human tissue model system that utilizes the unique characteristics of adult “ground-state” stem cells to generate 3-D gastrointestinal organ tissue on a 2-D surface. In this paper, we demonstrate that the MimEX GI platform can be used to routinely isolate and expand gastrointestinal organ tissues from specific regions of the adult gastrointestinal tract. Using MimEX GI Differentiation Media, we show that a high-density monolayer of region-specific gastrointestinal cells will differentiate into its respective tissue of origin, ex vivo. This differentiation is uniform and is oriented such that the apical surface of the mucosa is accessible within the well. Finally, using a high throughput accessibility assay, we demonstrate the barrier function of MimEX GI tissue, and its response to different molecules, as evidence for the flexibility of this tissue in high throughput drug screening.

Overview of MimEX™ GI Model System

Progression of Gastrointestinal Tissue Differentiation Using MimEX™ GI Reagents

MimEX™ GI Tissue Contains Cells Characteristic of the Gastrointestinal System

Conclusions

• MimEX™ GI-differentiated tissue mimics the cellular make-up and cytoarchitecture of human gastrointestinal tissue, including apical-to-basolateral polarity and the presence of goblet cells, Paneth cells, enteroendocrine cells, and enteric cell-adhesion.

MimEX™ GI tissue provides a novel platform for the efficient generation of 3-D intestinal tissue ex vivo.

Validation of High Throughput Permeability Experiments using MimEX™ GI Tissue. MimEX™ GI-differentiated human transverse colon tissue was exposed to Dextran (500 µg/mL) to the apical tissue surface and, following a 3 hour incubation, Dextran was measured in media from the basolateral side of the transwell membrane. Untreated (control) or incubated for 24 hours with Latrunculin A (10 nM, 100 nM, 1000 nM) or left untreated, which correspond to a transmembrane passive control (100%). Dextran was either left untreated or incubated for 24 hours with COX2 inhibitor (10 µM, 100 µM, 1000 µM) or left untreated, which correspond to a transcytosis positive control (100%).