TECHNOLOGY

Multicellular Organotypic Tissue Engineering of the Human Intestinal Mucosa

OVERVIEW

The engineering of a three-dimensional (3D) multicellular organotypic model of the human intestinal mucosa has a wide ranging potential as a tool for discovery of both health and diseases, such as interactions with pathogens, antigen trafficking, inflammatory processes, and tissue bioengineering. To more appropriately mimic an in vivo microenvironment, UMB inventors has developed 3D cell culture models with complex cellular architecture and functions that loosely resembles the human intestinal mucosa both structurally and functionally. The present system takes advantage of suspension culture in a rotating bioreactor, allowing for 3D cellular aggregation composed of several different cell types, including epithelial cells and fibroblasts and unlike earlier 3D models incorporate lymphocytes and endothelial cells. Preliminary studies in a model of salmonella typhi infection successfully demonstrated pathogen entry into the cell and production of several cytokines in response to the infection. This 3D culture model allows for the proper study of cell physiology, mechanotransduction, and tissue morphogenesis in vitro, through the construction of a microenvironments that recapitulate critical mechanical and biochemical cues present in the native ECM while facilitating hierarchical processes such as migration and tissue organization.

APPLICATIONS

General -A matrix enriched with gut basement membrane proteins -Integrates multiple cell types in 3-D constructs grown under microgravity Research - A tool to investigate the early events of the host interaction with gastrointestinal pathogens, including invasion, pathogenesis and immune responses. Clinical -A platform for the construction of a final product that would be useful for therapeutic replacements for diseased organs. Industry -Drug discovery

ADVANTAGES

Rotating-Wall Vessel (RWV) system (original concept of the RWV developed at NASA's Johnson Space Center in 1996) -Widely viewed by modeling studies to more closely mimic the conditions in the intestine -Facilitate nutrient and gas exchange -Cultures grown in states of microgravity promote cell-cell interaction by up-regulating various cell-cell adhesion molecules and ECM proteins.

STAGE OF DEVELOPMENT

Data obtained from this 3-D organotypic system confirm: Cellular polarity, tight junctions, desmosomes, and microvilli Expression of tissue-like differentiation markers, including villin, cytokeratin, and mucin Cytokine production upon antigenic stimulation Monolayer organization of gut epithelium Long-term viability

R&D REQUIRED

Future studies include the development of bioengineered blood-vessel like conduits

LICENSING POTENTIAL

UM seeks to develop and commercialize by an exclusive or non-exclusive license agreement and/or sponsored research with a company active in the area.

CONTACT INFO

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Additional Information

INSTITUTION

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PATENT STATUS

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CATEGORIES

- Research Tools, Antibodies, & Reagents

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EXTERNAL RESOURCES

- Engineering of a multicellular organotypic model of the human intestinal mucosa.

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