

Pilot Project Abstracts

Vascularized organotype model of the human intestinal mucosa **PI: Rosangela Mezghanni, University of Maryland, Baltimore**

This proposal describes a research plan based on the expertise of the PI in two key fields, cellular immunology and tissue engineering. This expertise will provide a unique and exciting opportunity for advancing the study of mucosal immunity in humans. The overall research plan is to design an innovative **vascularized *in vitro* three-dimensional (3-D) organotypic construct of the human intestinal mucosa**. Because animals models might not fully recapitulate human immunity and because the studies that can be performed in humans are more restricted by a set of experimental protocols than those that can be performed in animals, there is an ongoing need to develop new technologies that will facilitate human mucosal immunity research. One of these technologies is the generation of *in vitro* tissues by using 3-D *in vitro* cell culture. The first prototypes of these 3-D bioengineered tissues showed that cells growing in a 3-D environment closely mimic native tissues from where they were originated. However, a major limitation in these models is that cell aggregates generated *in vitro* that exceed a few millimeters in size invariably develop hypoxic, necrotic cores. In consequence, the construction of tissues with blood-vessel like conduits that allow efficient transfer of nutrients, drugs and oxygen diffusion is an important goal in 3-D tissue engineering. Additionally, blood-vessel cells are known to release mediators with strong regulatory properties. They have been shown to modulate phenotypic and functional changes in other component cells of the mucosa by cross-talking (e.g., through secretion of chemokines and cytokines). Blood-vessel cells also serve as a “sentinel” cells detecting and responding to the invasion of microorganisms. Thus, **our main research goal** is to generate bioengineered blood-vessel like conduits in an organotypic model of the human intestinal mucosa. Results from these studies are likely to advance the goals of the CCHI by providing an excellent platform for studying human gut mucosa.