SUMMARY

- Realistic in vitro models of the gut barrier are needed to facilitate research on inflammatory bowel disease (IBD)
- The MultiU-Int is a multi-chamber intestine-on-chip system with the Collagen Cell Carrier® as central element that separates the apical and basal compartment and allows for cellular interactions and selected permeability
- The novel, controlled microphysiological system is a next-level in vitro research tool to comprehend immune-system-mediated disorders of IBD and to identify new therapeutic strategies

COLLAGEN CELL CARRIER® IN SUPERIOR INTESTINE-ON-CHIP SYSTEM

Separating compartments and enabling cell interactions in an in-vivo-like intestinal barrier model

THE NEED

The intestinal epithelial barrier (IEB) with its gastrointestinal mucosa is the key site of nutrient uptake, immune sensing and pathogen defense. Complex cellular interactions and molecular signaling are orchestrated to fulfil these essential gastrointestinal tasks.[1] As such, the gut barrier plays a fundamental role in health and in diseases like inflammatory bowel disease (IBD). Previous IBD research have been difficult to correlate across studies. The multifactorial nature of the disease necessitates a reliable and practical experimental model to elucidate its etiology and pathogenesis, and to facilitate research on barrier-restoring therapeutics.

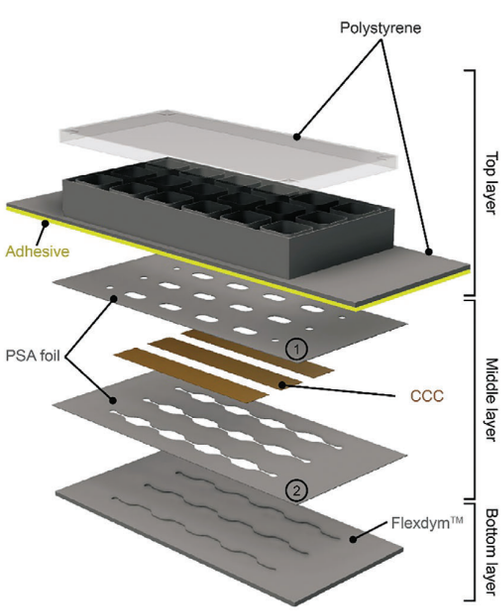
THE SOLUTION

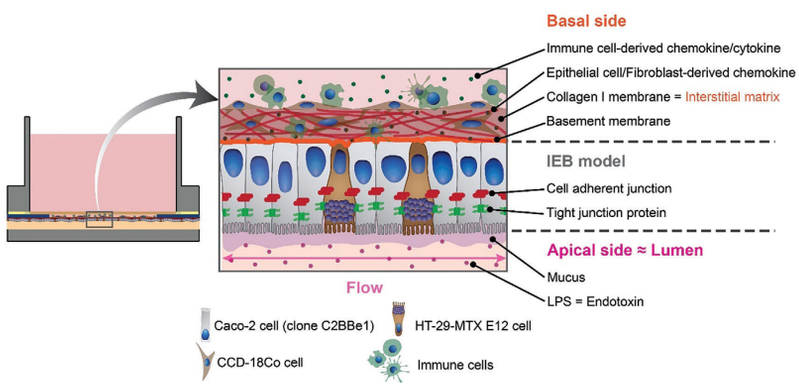
Scientists from the ETH Zurich have developed a novel, multi-chamber intestine-on-chip system (MultiU-Int) as a versatile in vitro intestinal barrier model to study the role of different immune cell populations and factors that contribute to the onset of intestinal inflammation in IBD.[2]

To model the intestinal microenvironment at the onset of IBD in vitro, it is important to incorporate relevant cellular and noncellular components before inducing stepwise pathogenic developments. The novel system includes an array of tight and polarized barrier models formed from intestinal epithelial cells on an in-vivo-like subepithelial matrix within one week.

The Collagen Cell Carrier® (CCC) serves as a key element of the system by separating the apical and basal compartment, similar to in vivo subepithelial stroma in which intestinal fibroblasts and immune cells reside.

Unlike inert plastic membranes, the CCC membrane enables cell migration and bidirectional cell interaction, thereby offering the potential for investigations of other IBD-associated complications, such as fibrosis. The dense collagen I fiber network within the CCC features a selective permeability for the apical-basal passage of substances, which helps to separate the signaling milieus between basal compartments.





Left: *Representation of the individual layers of the MultiU-Int microfluidic chip, their arrangement, and materials. Top layer: Polystyrene multi-well slide. Middle layer: Sandwiched CCC strips between two pressure-sensitive adhesive (PSA) foils, with the upper foil ① featuring oval areas where fibroblasts and, later, immune cells were allowed to interact with the IEB model (fibroblast seeding areas). The lower foil ② featured the same pattern of channel structures that were hot-embossed into the bottom layer of the chip. Bottom layer: Hot embossed elastomer Flexdym.*[2]

Right: *Schematic representation of key structural and cellular components of the in vitro intestinal epithelial barrier model formed within the MultiU-Int microfluidic chips.*[2]

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CASE STUDY

Collagen Cell Carrier® in superior intestine-on-chip system

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THE IMPACT

The new on-chip IEB model represents a physiologically relevant in vitro test system. Its design enables the introduction of various immune cell types and inflammatory stimuli at specific locations in the same barrier model, which facilitates investigations of the distinct roles of each cell type in intestinal inflammation development.

The MultiU-Int can not only mimic inflammatory processes that manifest in an upregulated expression of inflammatory markers and cytokines (TNF-α), but also helps to demonstrate the neutralizing effect of the anti-inflammatory antibody Infliximab on levels of TNF-α and its inducible cytokines.[2]

This controlled microphysiological system is a next-level in vitro tool to comprehend immune-system-mediated disorders of IBD and to identify new therapeutic strategies.

The CCC at the core of the multi-layer device is crucial for the establishment of the apical-basal polarity as well as for the in-vivo-like cellular interactions and signaling mileus of the IEB. The flexible collagen type I membrane represents a natural extracellular matrix scaffold that is suitable as a universal compartment separator in organ-on-chip models in general.

"The CCC is a remarkable material to work with. Its versatility in allowing for co-culturing of cells on both sides, while supporting cell migration and effectively maintaining separation between the cellular compartments, has been a game-changer for our project."

Dr. Oanh T. P. Nguyen,
Department of Biosystems Science and Engineering, ETH Zurich

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