# Gut-on-a-Chip using Microfluidic Devices

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*Primary CNF Tools Used: Object 3D Printer, VersaLaser engraver/cutter, MVD 100, PDMS casting station*

## Abstract:

**Current methods to test genotoxicity and cytotoxicity either use live animals *in vivo*—e.g., a food or drug is administered to a rodent, then monitored for physiological and behavioral changes, histology, and blood results—or we use *in vitro* tests, in which a few bacterial or mammalian cell lines are cultured inside a transwell insert, and then monitored for cell viability. Both have striking limitations. The first one assumes that we can model the pathophysiology of human diseases on animals, an assumption that has led to the costly failure of many clinical drug trials (approximately nine out of ten. It is also unpredictable and fraught with ethical concerns). The second one assumes that a single type of epithelial cancer cell line (i.e., Caco2) inside a transwell insert has the same uptake mechanism and behavior as the diverse microenvironment of the human gastrointestinal tract, which is in fact not composed of only one type of cell but a wide array of crypt stem cells, goblet cells, enterocytes, enteroendocrine cells, tuft cells, Paneth cells, immune cells, and microbiota—all of which influence each other through intricate cross-talking mechanisms such as paracrine and autocrine signaling in order to maintain cell viability.**

## Summary of Research:

**Gut-on-a-Chip.** Current *in vitro* models cannot adequately address the complexity of gut environment because of its rapidly changing nature. Herein, we present a "Gut-on-a-Chip" model system to explain intricate crosstalk in the gut microenvironment, using a microfluidic technique to encapsulate the gut constituent cells in the intestinal microenvironment including organoids, immune cells, and microbiome within microgels. Appling this technique, we decouple contact-independent cell-cell interactions from the contact-dependent effects of soluble mediators. This model can be used to evaluate the effect of biopharmaceutical products and food ingredients on the intestinal cells and microbiome and will be served as a unique approach for pathological threat detection in gut environment.

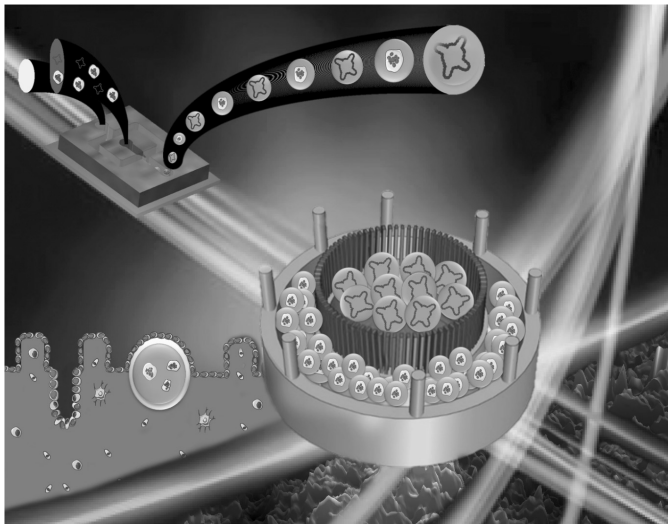

*Figure 1: Schematic of the 3D printed insert for co-culture of organoid-embedded microgels along with Peyer's patch embedded microgels. See full color version on pages xxviii-xxix.*

## References:

[1] Pajoumshariati, S. R., M. Azizi, D. Wesner, P. G. Miller, M. L. Shuler, and A. Abbaspourrad. 2018. Microfluidic-Based Cell-Embedded Microgels Using Nonfluorinated Oil as a Model for the Gastrointestinal Niche. ACS applied materials and interfaces 10:9235-9246.