Title: Modeling the Gut–Brain Axis Using Human Organ-on-Chip Systems

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Abstract: Organ-on-chip technologies are advanced experimental platforms that recreate selected structural, biochemical, and mechanical features of human tissues within controlled microfluidic environments. By integrating human cells, compartmentalized culture, dynamic flow, extracellular matrices, and functional readouts, these systems bridge the gap between conventional two-dimensional cultures and animal models. Their advantages include improved physiological relevance, precise control of intercellular communication, reproducibility, and the possibility of modeling patient-specific disease mechanisms. These features are particularly important in neuroscience, where access to living human neural tissue is limited and many disorders involve interactions between the nervous system and peripheral organs.

The gut–brain axis is one such complex communication network. Intestinal barrier dysfunction, microbial metabolites, and chronic inflammation are increasingly associated with neurological and neurodegenerative diseases. To investigate these mechanisms, we developed complementary human gut–brain-axis-on-chip platforms that reproduce controlled epithelial–neural interactions.

The first platform is a compartmentalized PDMS–glass device containing separate intestinal and neural chambers connected by shallow microgrooves. The intestinal module is formed by a Caco-2/HT29-MTX co-culture, while human neural progenitor cells are differentiated directly in the neural compartment. The microgrooves maintain spatial separation while enabling molecular exchange and guiding βIII-tubulin-positive neurite-like extensions. A second platform incorporates a central hydrogel region separated by micropillars, allowing evaluation of extracellular-matrix-dependent neural growth. Matrigel supported neural penetration and extension, whereas fibrin was less permissive.

Intestinal stimulation with lipopolysaccharide induced epithelial remodeling, including reduced ZO-1 continuity and cytoskeletal reorganization, together with shortening and reorganization of neuronal extensions. These observations indicate that the platforms can capture indirect gut-to-neural effects of inflammatory stimulation.

The systems provide a modular basis for incorporating microglia, patient-derived neural cells, microbiota-associated metabolites, electrophysiological measurements, and biomarker analysis. They may support mechanistic studies of neurodegeneration and preclinical evaluation of therapies targeting the gut–brain axis.

Short Bio: Katarzyna Tokarska, PhD, Eng., is an Assistant Professor in the Medical Diagnostics Department at the Centre for Advanced Materials and Technologies CEZAMAT, Warsaw University of Technology. She received her PhD in chemical sciences from the Faculty of Chemistry at Warsaw University of Technology in 2019.
Her doctoral research focused on polymeric nanomaterials as drug-delivery systems for photodynamic therapy and their evaluation using lab-on-chip platforms.
Her interdisciplinary research combines microfluidics, organ-on-chip technology, cell engineering, biomaterials, and bioanalytical methods to develop human-relevant in vitro models and miniaturized biomedical devices. Her current interests focus on multi-organ microphysiological systems, gut–brain communication, neuroinflammation, neurodegeneration, electrophysiological monitoring, and the integration of biological models with optical and electrochemical sensing.
She is the Principal Investigator of an NCN SONATA 20 project devoted to developing a microbiota–gut–brain-axis-on-chip platform for studying mechanisms associated with neurodegenerative diseases. The project integrates intestinal barrier models, human neural cells, microbiota-related factors, and functional analytical readouts to investigate how intestinal dysfunction and inflammatory signaling affect neural homeostasis.
Her international experience includes a research internship at the Microfluidics and Biomimetic Microsystems Laboratory at Politecnico di Milano, supported through the first edition of the “Best of the Best at WUT” programme. During a research stay at the International Iberian Nanotechnology Laboratory in Braga, her work has focused on developing a vascularized colorectal-cancer-on-chip system for evaluating the efficacy of anticancer therapies.
She has received internal research funding through the Warsaw University of Technology IDUB BIOTECHMED-1 programme and a grant supporting research in the biotechnology discipline. She has also contributed as a researcher to multidisciplinary projects funded by the National Centre for Research and Development, the National Science Centre, the Virtual Research Institute, the Medical Research Agency, and the European Research Council, including the ERC Advanced Grant SFINKS.
Her scientific achievements also include a Best Poster Presentation Award at the 9th International Symposium on Sensor Science. Her work aims to provide physiologically relevant alternatives to conventional cell cultures and animal models and to support mechanistic studies and preclinical testing in neurological and oncological research.

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