OVERCOMING LIMITATIONS OF ORGAN-ON-CHIP (OOC) TECHNOLOGIES TO ADVANCE THE CHARACTERIZATION AND MEDICAL MANAGEMENT OF CHEMICAL AND BIOLOGICAL (CB) THREATS

Donor-matched Multiorgan Microphysiological Systems In Advanced Risk Assessment

Martin Trapecar Johns Hopkins University School of Medicine

Risk assessment and reliable threat characterization relevant to human physiology remain a significant challenge. Both in vivo animal and simplistic in vitro models often fail to provide a clear picture regarding the full scope of dangers and their mechanics associated with unknown agents.
Multiorgan microphysiological systems (MOMPS), mimicking complex human physiology, offer new possibilities to clarify the origins of systemic and mucosal pathology. Controlled interaction of individual human tissues and the scalability of biological complexity in MOMPS, supported by advances in systems biology, hold the key to identifying novel relationships between interorgan crosstalk, immunity, and xenobiotics. The Trapecar lab of Human Biomimetics is integrating 3D bioprinted donor-matched tissues into MOMPS to investigate how i) immune-tissue communication directs complex tissue development and homeostasis and how ii) a disruption thereof leads to acute pathologies. We show that tissue-level interaction between and within the three primary germ layers, ectoderm (neurons), mesoderm (lymphoid), and endoderm (gut and liver), led to increased tissue maturation and increased in vivo-like functionality. In our approach, we reconstruct donor-matched hepatic, gut-mucosal, and neuronal tissue via digital light-assisted bioprinting under fluidic communication and the presence of the donors circulating immune cells. We compare tissue maturation, longevity, and functionality across interacting versus isolated tissue and identify significant contributors to altered performance. We further use the established system to derive how a disruption in immune-tissue signaling contributes to overlapping inflammatory disorders of the gut-liver-brain axis. MOMPS represent a unique opportunity to systematically dissect how an external perturbation alters systemic and local tissue behavior and offer clues to its neutralization.