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Teratology Society Abstract

Human Neurovascular Unit On-A-Chip: Microscale Systems for Tissue-Level Response

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To truly understand the contribution of genetics, environment, drugs, and maternal health to fetal development and resulting birth defects, we need new tools to model and investigate these complex interactions. Animal studies have been invaluable, but in many cases they fail to recreate human physiology, and traditional cell culture models lack the complexity to capture the full disorder. To help bridge this gap and give investigators a new tool in their experimentation arsenal, we are developing organs-on-chips that provide highly accessible – but still complex – cell culture models of a target organ. With these engineered tissues and their accompanying perfusion systems, it is possible to model blood-brain barriers (BBBs), fetal membranes, mammary glands, or other organs. These microfluidic platforms and associated pumps and valves let us create tissue-specific microenvironments and test the effects of drug exposure over time, including immune response (which is often an evolving response), tissue recovery, and repair. In our human Neurovascular Unit (NVU), for example, we have seen BBB disruption soon after toxin exposure but partial recovery after 24 hours, and we have identified compounds capable of preventing BBB disruption. Through ion mobility-mass spectrometry analysis we have also demonstrated that disruptions to the BBB lead to metabolic changes within the NVU. An important challenge will be to address the urgent need to screen the effects of common environmental hazards on fetal development and overall health by adapting our NVU to adequately recapitulate specific stages in the development of the fetal BBB, either as a static system or as one whose temporal development tracks that of the fetus. This should be a feasible goal, given our success with the adult NVU. Research reported herein was supported by Assistance Agreement No. 83573601 awarded by the U. S. Environmental Protection Agency to Vanderbilt University, and by the National Center for Advancing Translational Sciences of the National Institutes of Health under Award Number UH3TR000491. The views expressed in this document are solely those of the authors and do not necessarily reflect those of either agency. EPA does not endorse any products or commercial services mentioned in this publication.