SPRING 2024

Biochemistry and Molecular Biology Brown Bag Series

Eric Reed

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"Impact of Dynamic Oxygen Conditions on a Human Neurovascular Unit-on-a-Chip"

Tuesday, March 26, 2024

11:00 AM

Location 125 Medical Sciences Building

Lab: Tyler Nelson, Ph.D.

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https://science-math.wright.edu/biochemistry-and-molecular-biology

Abstract:

Airman piloting high performance aircraft face a number of environmental stressors during missions that could reduce efficiency and compromise success. One of those stressors is hypoxia. The military has addressed the issue of hypoxia by supplying high levels of oxygen to the pilots. Cognitive symptoms that may be related pilot oxygenation have still been seen, leading to concern over negative impacts directly from hyperoxia or from hypoxia that may be caused by a mismatch between the pilots and the equipment. To study the mechanisms that may be affected we used a Neurovascular-unit-on-a-chip model built in Emulate microfluidic chips, and exposed it to either hypoxia or hyperoxia. To address the potential mismatch between Pilot breathing and oxygen supply from the equipment we also included oscillatory hypoxia and hyperoxia exposures. The bottom channel contained hiPSC-derived brain microvascular endothelial cells. The top channel contained hiPSC-derived dopaminergic neurons, astrocytes, and pericytes (Fujifilm Cellular Dynamics). The chips were matured for 6-7 days on pump at a flow rate of 30/60 ul/hr before the experiment began. At the start of the experiment the media was refreshed, outlets emptied, and Cascade blue dextran was added to the vascular media. Hypoxic or hyperoxic exposures lasted 6 hours followed by 24 hrs of recovery. Media was collected from the outlets before the exposures, after 6 hrs, and after 24 hrs. Chips were either fixed for imaging or harvested for transcriptomic analysis. Confocal imaging was done for ZO1 in the vascular channel (bottom) and β3-tubulin, NG2, and GFAP in the brain channel (top). Media was used for Viability analysis using LDH, permeability analysis by measuring the amount of cascade blue that crossed the BBB, Neuroscience 18-plex ELISA panels, dopamine measurements, and metabolomics. Both hypoxia and hyperoxia were sufficient to disrupt the BBB. Viability was not affected very much by hypoxia or hyperoxia in the vascular compartment. In the brain compartment both hypoxia and hyperoxia appeared to improve viability of the cells. Overall the NVU chips are tolerating both hypoxia and hyperoxia, however function if being negatively impacted and downstream these affects could impact pilot performance.