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Soldier-on-a-chip: Multi-omic Investigation of Staphylococcal Entertoxin B Exposures in Microphysiology Systems

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Microphysiology systems (MPS) are used to mimic human organ systems in order to collect more human-real data. Traditional experiments have relied on either cell cultures, which aren't physiologically accurate, or animal studies, which are very expensive. However, human-relevant data is important in understanding the human host's response to exposures of lethal chemicals (i.e. sarin, VX) and biological organisms (i.e. Bacillus anthracis, Western equine encephalitis). Understanding the molecular response to these threats will allow for further treatments and medical countermeasures to be developed.

In this project, a multi-organ system situated on a single chip was exposed to Staphylococcal enterotoxin B (SEB). SEB is a toxin produced by gram-positive S. aureus bacteria. It is mainly responsible for food poisoning but has the potential to be used as a biological threat agent. This MPS contained three organ systems – lung tissue, cardiac organoids, and skin tissue. These tissues are linked on-chip and share flow through micro-pumps, which is meant to mimic blood flow through a human system. The three tissues were harvested 24 hours after exposure to SEB and prepared for proteomic and metabolomic analysis via Orbitrap mass spectrometry. Data was collected and analyzed via Proteome Discoverer 2.5 and Compound Discoverer 3.2. For proteomic analysis, each tissue type dataset was processed with its respective Human Proteome Atlas database along with the Housekeeping Protein database and the Transcription Regulation database.

Within the three tissue types, between 239 and 340 proteins were found to be significantly changing. In the skin tissue, SUMO-conjugating enzyme UBC9 was significantly downregulated from the PBS-exposed control sample. This enzyme plays a role in sumoylation, a process in with SUMO proteins are covalently attached to specific lysine residues in target proteins and used to regulate various aspects of protein function, like transcription, subcellular localization, DNA repair and cell cycle. Also in skin, the mitochondrial fission 1 protein (FIS1) was significantly upregulated. This protein is part of maintaining functional mitochondria when cells experience metabolic or environmental stresses. Disruptions in this process have been implicated in neurodegenerative diseases. This data reflects previous in vivo observations where mitochondrial defects were observed through microscopy experiments on animal model tissues, though the mechanism of this effect was not previously characterized. Thus, this data indicates a path forward in determining the mechanistic effects of SEB without utilizing animal models.

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