MITIGATION - SCIENCE AND TECHNOLOGY ADVANCES FOR CHEMICAL AND BIOLOGICAL HAZARD MITIGATION

Integrated Human Neurovascular Unit-on-a-chip For Machine Learning-based Prediction Of Neurotoxin Exposure

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The safety and well-being of military personnel, which are crucial for mission efficiency and success, can be compromised by various chemical or biological threats. One such exposure risk is inhalation neurotoxin exposure which has classically been evaluated through animal studies. These studies are generally limited in scope though as they are expensive and time consuming. Therefore, we aimed to develop an advanced platform, including human alveolus-on-a-chip and neurovascular unit-on-a-chip (NerVOC) models, to detect and predict neurotoxin exposures. These models utilize human induced pluripotent stem cells (hiPSC) and provide a controlled, high-throughput approach for assessing exposure. We selected fentanyl as our exposure threat as it has previously been shown to bind opioid receptors in many brain regions resulting in impaired cognitive function and altered neural activity. Acute sub-lethal doses of fentanyl exposure were examined in both alveolar and brain models. The ability of our platforms to evalute sublethal doses of exposure enables the identification of subtle changes that could proceed acute toxicity and more overt symptoms. The effects of sublethal fentanyl exposure were investigated utilizing our alveolus-on-a-chip and NerVOC platforms to examine fentanyl and resulting metabolite transport for their impact on tissue-blood barriers and toxicological responses. Neural activity of hiPSCs after fentanyl exposure was further assessed by microelectrode array (MEA). We are currently applying our collected data, in tandem with neuronal firing patterns from other military relevant exposure risks, to develop computational models and machine learning approaches for the prediction and detection of future exposure scenarios. Future studies are aimed at building a multi-organ-on-a-chip model to include additional relevant organ systems, such as liver or kidney, to enhance our understanding of the molecular and functional effects of neurotoxin exposure. Collectively, our platform contributes to the development of early exposure detection for risk prediction and mitigation towards enhancing the safety of military personnel.