AI/ML AND VIRTUAL HUMAN PLATFORMS FOR THREAT AGENT HAZARD ASSESSMENT AND MEDICAL COUNTERMEASURE DISCOVERY AND DRUG DEVELOPMENT

Human Nmj-based Microphysiological System For Discovery And Evaluation Of Medical Countermeasures Against Chemical Threats

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We apply human motor neurons (MNs) in combination with a 3D complex of muscle fiber tissue to generate functional neuromuscular junctions (NMJs) and identify novel molecular targets for development of broad-spectrum prophylactics and tissue regenerative antidotes to injuries induced by chemical warfare agents. We performed global transcriptome studies on human NMJ responses to cholinergic crisis induced by high doses of the neurotransmitter acetylcholine and the organophosphate neurotoxin paraoxon ethyl. Using the EDGE bioinformatics analytical platform, we streamlined the gene expression profiles into gene ontology pathways and identified key regulators of neuronal and muscle regenerative mechanisms triggered by ion-flux imbalance. Next, from protein–drug interaction databases we identified a set of compounds ranging from natural metabolites, synthetic anticonvulsant drugs, and anti-inflammatory glucocorticoids with known bioavailability and pharmacokinetics that can be repurposed as medical countermeasures (MCMs) to prevent neuronal cell death and muscle atrophy caused by the over-stimulation at the NMJ. We discuss how we can apply SmartTensors AI platform to fuse our global transcriptome data with transcriptomics datasets generated by other research labs investigating the effects of various classes of neurotoxic agents on MN function. This effort holds great potential in the discovery of cellular wiring patterns triggered by various chemical stimulants of cholinergic crisis, extraction of essential features underlying neuronal cell recovery, and prediction of broadly acting MCMs against chemical threats.

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