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

Assessing Computational Toxicology For Applications In Homeland Defense

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To accurately evaluate chemical risk, DHS must identify emergent chemical and biochemical threat agents and understand their physical, chemical and toxicological characteristics. Assessing the existing gaps in toxicity screening and measuring practices can impact DHS capabilities to identify novel chemical and biochemical threat agents. Computational methods have the potential to provide defensible estimates for toxicity values of molecules of interest at a fraction of the traditional time and budget. The ability to easily predict the toxicity of these threat agents can provide accurate estimates for HSE chemical risk assessments while simultaneously providing valuable tools to screen and prioritize emergent threats for future characterization work.

Machine learning (ML) and deep learning (DL) models can predict novel compound toxicity endpoints using their chemical properties and structural features. Though they commonly have high accuracies, they also have limitations including the potential over-fitting, lack of fidelity for minor structural differences significantly affecting receptor binding and thus toxicity, and the fact that many do not account for mechanism of action. Further, to date, most computational toxicology methods have been leveraged primarily for early drug screening and prioritization applications and the regulation of toxic industrial chemicals and pharmaceuticals, with the focus on multiple low-dose exposure, and chronic effects.

DHS S&T is assessing current computational toxicology capabilities, limitations, and gaps from the perspective of calculating acute human toxicity values to HSE-relevant chemicals and individual confidence scores to existing toxicity prediction tools as well. Essential elements from identified tools will be adapted into future workflows and developing a conceptual tool to assess toxicology of HSE-relevant chemicals. Draft toxicological values will receive consensus-based confidence scores and compounds will be ranked for future research based on these factors. Where possible, data supporting potential mechanisms of action will be assessed.
A specific example using skin and brain models to assess toxicity of known opioids and analogues through dermal exposure will be evaluated.

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