THE USE OF AI AND ADVANCED COMPUTER SYSTEMS TO DEVELOP DRUGS AGAINST NEW EMERGING THREATS

Semi-automated Antiviral Discovery With Machine Learning

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The rapid emergence and re-emergence of viral pathogens present a significant challenge to global health security. This talk outlines our efforts towards the semi-automated discovery of antiviral compounds, specifically targeting encephalitic alphaviruses such as Venezuelan, Eastern, and Western equine encephalitis viruses. Starting from a curated list of compounds known for their alphavirus activity, we integrate machine learning, cheminformatics, and iterative experimental testing to target critical biothreats like alphaviruses. We have developed a semi-automated discovery process that optimizes for drug-likeness, non-mutagenicity, and blood-brain barrier permeability while rapidly identifying antiviral compounds. Utilizing a combination of non-negative matrix factorization (NMF), semi-supervised positive-unlabeled learning, and design of experiments (DOE) principles, we efficiently prioritize compounds with favorable properties, refining our selection through successive in vitro experiments under BSL-3 conditions. This iterative loop, now encapsulated within a robust Knime workflow, captures both automated steps and manual data inputs, enhancing reproducibility and scalability. Our results from testing over 20,000 molecules demonstrate the complexity of balancing drug-likeness with functional efficacy, as for instance enhancing blood-brain barrier penetration often reduces antiviral activity. By comparing different ranking strategies, we uncover nuanced insights into the trade-offs involved in targeting viral encephalitis. This talk will explore our advanced methodologies, significant findings, and the implications of our work for rapid response to viral outbreaks.

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