Atomically Yours: Novel DeepGraphDTI Takes Fight Against Future Pandemics to the Next Level

Lim, Wan Qin (School: Hwa Chong Institution)

The World Health Organisation’s Blueprint Priority Disease Nipah henipavirus’ (NiV) deadly pandemic potential has been evidenced by outbreaks across the world. High mortality rates of up to 91% across countries such as India, Malaysia and Philippines renders it distressing as no approved vaccines and therapeutics exist to this date. Current in silico methods to discover a cure rely on molecular docking and dynamics which are computationally intensive and time-consuming. Hence, deep learning Drug-Target-Affinity (DTA) models, able to predict drug-target interactions within seconds, present an attractively accelerated approach to circumvent tedious protein and chemical environment preparations required for simulations. Present DTA architectures encode protein residues for learning, often using Convolutional Neural Networks that neglect structural information. To greatly enhance the predictive prowess of DTA models, this study curates novel Graph Neural Network model DeepGraphDTI, which builds graph representations of proteins from atomic-level properties by converting protein sequences into Simplified Molecular-Input Line-Entry System strings, allowing high-resolution structural attributes to be extracted. DeepGraphDTI surpassed performances of existing state-of-the-art models, proving itself a potent tool for diverse applications in drug discovery such as unearthing novel drugs against emerging pathogens. In this study, DeepGraphDTI identified potential inhibitors against the NiV attachment and fusion glycoproteins from 1,040 drugs in the Global Health Priority Box, Pandemic Response Box and Pathogen Box, which were further verified by molecular docking. 7 promising drugs were thus selected for future in vitro and vivo experimental evaluation.

Awards Won:

Non-Trivial: 10 scholarships for Non-trivial