Abstract No: 101 ***Life Sciences***

LIGAND-BASED VIRTUAL SCREENING OF POTENTIAL DRUG COMBINATIONS AGAINST AMINOGLYCOSIDE RESISTANCE IN BACTERIA

J.P.P.S. Rasangani [1,2] and W.R.P. Wijesinghe[1,3*]

[1]Department of Botany, Faculty of Science, University of Peradeniya, Peradeniya, Sri Lanka.
[2]Genetics and Molecular Biology Unit, Faculty of Applied Science, University of Sri Jayewardenepura, Sri Lanka.
[3]Postgraduate Institute of Science, University of Peradeniya, Peradeniya, Sri Lanka.
[*]priyangaw@sci.pdn.ac.lk

Antibiotic resistance in bacteria is an international crisis estimated to have 10 million annual deaths by 2050. Aminoglycosides (AGs) are becoming inefficient with the widespread of multidrug-resistant bacteria. The resistance mainly occurs due to the enzyme modification or inactivation of AGs, increased expression of efflux pumps that remove AG from the cell, reduced drug permeability or alteration in the drug target site. Many studies have determined that one of the fastest routes to evade AG resistance is restoring the effectiveness of existing AGs by combining them with some chemical compounds. The main purpose of this study was to predict the bioactivity of phytochemicals and a few other drugs against AG resistance using Machine Learning (ML) methods and predict their synergy with existing AGs (Amikacin, Tobramycin), using an efficient and less expensive pipeline. Open-source nodes in KNIME software were used to create a pipeline including Random Forest, Support Vector Machine and Artificial Neural Network ML models and RDKit tools. The ChEMBL site was used to retrieve structural data of 500 phytochemicals, 18 AGs, and 18 Non-antibiotic drugs. The drug likeliness of potential drug candidates was determined using Lipinski's rule of five by the CDK toolkit. The synergies were predicted using the bioactivity data obtained from the PubChem site. Eleven compounds resulted as potential drug candidates by the pipeline: Allicin, Aspartic acid, Fosbretabulin, Myoinositol, Lysine, Alpha-pinene, Acetoside, Linoleic acid, Histidine, Choline and Polymyxin B. Out of them only Fosbretabulin and Lysine respectively having 0.033 and 0.36 individual bioactivities showed a higher synergistic effect only when combined with Tobramycin. The synergy scores are 0.24 and 0.78, respectively. Fosbretabulin is a cancer drug, and not known for having antimicrobial properties. This pipeline can screen many molecules to predict potential drug combinations against AG resistance before laboratory experiments, reducing cost, time and resources

Keywords: Aminoglycosides resistance, Drug Synergy, Ligand-based**,** Machine Learning, Prediction