### **Hybrid Machine Learning Framework for Drug Efficacy Prediction in Breast Cancer: A Multimodal Precision Oncology Approach**

**Sharon Melhi¹ and Dhanashree Bhamare²** ¹Amity University Bengaluru  
 ²Somaiya Vidyavihar University, Mumbai

### **Abstract**

Tumor heterogeneity and inconsistent drug responses amongst clinical subtypes stand as obstacles to personalized breast cancer treatment. We address this by proposing a novel hybrid machine learning-based method-the pharmacogenomic data integrated with clinical and molecular profiles-remotely to predict drug-specific LN\_IC50 inhibitory concentrations for drug selection optimization. Using a stacked ensemble that combines gradient boosting, composed of XGBoost and a deep neural network, our approach was able to achieve a truly excellent prediction performance (RMSE=0.21; R²=0.89), thus showing its robustness across multiple folds of validation.

Our input features include measures of drug potency (MAX\_CONC, MIN\_CONC), tumor stage, treatment history, and patient age. Evidence from SHAP analysis suggested drug AUC values and tumor stage to be the top impactors of drug efficacy, supporting the biological rationality behind a model's insights. To add to this, we presented a visual analytics suite that revealed the following four major conclusions:

* Drug resistance trajectories specific to subtypes informing on molecular subpopulation vulnerabilities;
* A non-linear inverse-country trend between drug dosage and drug response, warning of overmedication;
* Drug amount started to significantly increase with tumor stage, with Stage IV demanding about a 10 percent higher dose compared to Stage I for similar inhibition,
* Feature importance maps to foster transparent, data-based clinical decisions.

These represent some capabilities that are of prime importance in translational clinical oncology - A scalable, interpretable, adaptive platform for dose optimization and cutting down on empirical treatment doses. It is anticipated that model architecture will be expanded in the future with the provision of integrating real-time patient information, thereby creating a feedback loop for continuous learning in precision oncology systems.

**Keywords:** Breast Cancer, Precision Oncology, XGBoost, Deep Learning, SHAP, Drug Efficacy, Clinical Data Integration, Tumor Stage, Pharmacogenomics, Adaptive Therapy