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Enhancing drug response prediction and interpretability through gene ontology and drug target information integration

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As modern precision medicine is receiving more spotlight for its therapeutic efficacy, a need for the accurate prediction of an individual's response to drugs is becoming ever more crucial. However, recent studies of drug response prediction may suffer from low interpretability due to the use of deep neural network (DNN) black-box models, as well as lack of target information since they only use two types of data – gene expression feature and drug SMILES structure – for prediction. To address these challenges, we have come up with a novel approach to improve the interpretability of drug response prediction in transcriptome and biological pathway level by leveraging gene ontology (GO) and drug target information to our neural network. Our model learns functional roles of each cellular subsystem through GO terms and delineates which biological terms are significantly perturbed by drug reaction. Subsequently, we employ drug target information which increments perturbation effects of drug treatment. Our model outperforms state-of-the-art models in regression metrics for drug response prediction. We also demonstrate that potential perturbed biological pathways for each drug can be identified, implying a prospective breakthrough for targeted therapy and personalized treatment strategies.