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DR.DEGMON: Self-explainable deep neural network for drug-induced cell viability prediction incorporating differentially expressed genes and Gene Ontology

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Accurate prediction of cancer drug responses is crucial for advancing cancer treatment and drug development. With the growth of large-scale pharmacogenomic datasets, many deep learning models have been developed to predict cancer drug responses. However, most existing models fall short in providing important biomedical insights, such as revealing the mechanisms of action. To address this, we introduce DR.DEGMON (drug response prediction using differentially expressed genes with multi-layer perceptron integrating gene ontology network), a self-explainable deep learning model designed to predict the cell viability of cancer cell lines in response to drug treatments, utilizing differentially expressed genes.

DR.DEGMON incorporates prior biological knowledge by adopting Gene Ontology (GO) into the hierarchical architecture of a multi-layer perceptron. DR.DEGMON achieved a Pearson correlation coefficient of 0.8568, outperforming existing baseline models. This unique design of DR.DEGMON not only predicts drug responses but also identifies key genes and GO terms involved through layer-wise relevance propagation, offering insights into the mechanisms of action. By integrating GO and layer-wise relevance propagation, DR.DEGMON suggests biological processes potentially associated with drug response, providing both practical utility for drug development and a deeper understanding of cancer biology. This approach enhances the accuracy of drug response prediction and uncover novel biomedical knowledge in cancer pharmacogenomics.