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GCNPath: Decoding Anticancer Drug Sensitivities with Pathway-based Graph Neural Networks

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Drug response prediction (DRP), in the context of inter-tumor heterogeneities can significantly contribute to the anticancer drug discovery and repurposing. For successful DRP, two well-known approaches are pathway-based feature extraction and graph neural networks. The former enhances the interpretability of drug responses while mitigating the risk of overfitting, and the latter considers interactions between genes and proteins. To leverage these strategies, we developed GCNPath, a model that predicts drug sensitivities by incorporating multi-level crosstalk between pathways using graph neural networks. We validated the effectiveness of GCNPath through extensive benchmark tests using various drug response datasets and cell line omics. In addition to showing competitive performances compared to state-of-the-art models, our approach maintained robust predictive powers, particularly in addressing batch effects common in RNA-based omics data through pathway-based feature extraction. We expect that our model could facilitate the exploration of diverse drug sensitivities arising from heterogeneous pathway activation profiles and distinct cancer subtypes.