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Synthetic lethality prediction via attentive knowledge graph neural network in the divergent human cancer cell-lines

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Synthetic lethality (SL), which induces cell death by simultaneously inhibiting individual genes, has emerged as a promising concept in anticancer therapy. Since wet-lab experiments for screening overall gene pairs need high cost and time, deep learning-based computational SL prediction models have been developed to predict the SL interaction in human cancer. Despite the adequate performance, most of them didn't consider the heterogeneous characteristics of cancer cells and depended on the limited biological data. In this paper, we introduce an advanced SL prediction model based on attentive graph convolutional networks across diverse cancer cell lines. To facilitate this prediction, we collect the latest biological relations to construct the updated knowledge graph and conduct a comparative analysis of multiple knowledge graph embedding models, selecting the most appropriate model for pre-training entity embedding vectors. Leveraging multi-omics data from various cancer cell lines, we train a graph attention network-based model specifically designed for the task. Following rigorous optimization through ablation studies, we benchmark our proposed model against state-of-the-art baseline methods and reveal its superior predictive capabilities. Finally, we conduct an in-depth analysis of attention scores for each edge in the graph, elucidating potential gene pairs involved in synthetic lethality and uncovering their underlying mechanisms.