OrphaDRGL: A Novel Graph Deep Learning-based Drug Repositioning Approach for Orphan Diseases

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More than 95% of the approximately 7000 orphan diseases in the world do not have effective treatments, and since orphan diseases are conditions that affect a limited population, there is little incentive to develop novel treatments for them. Thus, drug repositioning, or finding new uses for existing drugs, has become a viable option as it is faster and more economical than traditional de novo drug discovery. To this end, OrphaDRGL was created: a novel computational orphan disease drug repositioning approach utilizing graph deep learning. OrphaDRGL uses open-source disease phenotype, drug side effect, drug chemical structure, and drug-indication data to form a heterogenous network with drug and medical condition nodes. Edges were created using the Tanimoto coefficient of drug side effects and chemical structures, Resnik phenotypic similarity of medical conditions and their phenotypes, and existing drug-indication pairs. Morgan fingerprint bit vectors were assigned as explicit node features for drug nodes. A link concealing algorithm was then applied to emulate orphan disease conditions, and a graph convolutional neural network-based link prediction framework was trained on the network in order to identify potential drug repositioning candidates for orphan diseases. After 10-fold cross-validation, OrphaDRGL achieved an average AUC-ROC score of 0.953. In addition, OrphaDRGL was able to identify both literature-supported and previously unreported drug repositioning candidates for three different orphan diseases. OrphaDRGL is the first of its kind in the scientific literature, and its promising performance helps address the pressing issue of in silico identification of potential drug repositioning candidates for orphan diseases.

Awards Won:
Second Award of $2,000