Drug Repositioning Approach Based on Network Neighborhood Metrics and Transcriptome Data

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Development of new drugs is a complex and very expensive process. Drug repositioning (DR) explores new treatment area to approved drugs. DR provides lower cost, shorter time and risk-free investment compared to traditional drug development processes. For this reason, finding the best possible estimates by computational DR methods is gaining serious importance to reduce the cost in wet-lab experiments. This study aims to develop a novel network-based repositioning approach by integrating functional interaction networks, drug treated transcriptome profiles and disease-causing genes. The proposed DR method was experimented on breast and lung cancers. Drug data sets are obtained from the LINCS Project and disease-causing genes are gathered from the related cancer cohorts in the TCGA Project. We used functional interaction data between proteins as the main network structure. We adapted network neighborhood metrics to compute a similarity (overlap) score between the disease-causing network and the drug-affected network. The Adamic-Adar and neighborhood scoring metrics were adapted to utilize differential gene expressions into the similarity score calculation. Based on the experimental results, Adamic-Adar has ranked 35 of 345 drugs in breast cancer cell line and 5 of 95 drugs in lung cancer cell line with an 0.6 AUC threshold. On the other hand, neighborhood scoring metric proposed 5 and 1 drugs in breast cancer and lung cancer cell line, respectively. Some of these predictions has ongoing clinical trials for these selected cancer types. So, the suggested drugs have potentials to be used in the treatment of these cancers. Although the Adamic-Adar metric has shown more promising results, our method has room for improvement. As a future work, different network scoring metrics would be adapted to improve predictions.

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