In-silico prediction of drug repositioning candidates using an integrated network approach

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With increasing cost of developing novel drugs, drug repositioning (DR) is being actively sought, which is using known drugs for novel indications. Elucidation of new drug-disease links using comparison between biological signatures is efficient way for DR.

Here, we propose an integrative computational approach to identify DR candidates and apply our method to three types of cancer (glioblastoma multiforme, lung and ovarian cancer). Our method is based on the idea that novel drug-disease links can be established by using the similarity of their signatures in terms of genes, biological pathways and chemical structures. An extensive dataset is collected for >40,000 chemicals in total, such as drug targets, chemical signature genes from CMAP, chemical structures as well as gene expression profiles for the target disease. DR candidate chemicals are associated to the target disease by comparing chemical target/signature genes, pathway activity profiles and chemical structures with those for the disease or its 'GOLD STANDARD' drugs. Eight distinct types of drug-disease associations are established as a result of more than 1 billion comparisons in total, which were further integrated by a logistic regression method. Our method consistently shows high accuracy in predicting DR candidates for all the three types of cancers (AUC: 0.88~0.91).

Our integrated approach is shown to be effective in finding chemical-disease associations for targeted drug repositioning.