Unraveling Dynamics of Biological Networks towards Computational Drug Target Discovery

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Abstract

In recent years, much attention has been focused on predicting mode-of-action of a drug as a gene interaction pathway by using genome-scale transcriptome data. Based on the estimated gene interaction pathways, it is believed that increasing therapeutic efficacy of a drug would be achieved by finding signaling pathways that control drug's mode-of-action. Strategic methodology, however, has not been well-established in order to find such signaling pathways, because of the lack of comprehensive protein profiling technology. Here, we present a computational method for finding them by integrating genome-scale transcriptome expression profile data and proteome protein-protein interaction data. The method can identify the drug-affected gene interaction pathways and their dynamic behavior, and find signaling pathways strongly affecting them. The method is applied to elucidate the mode-of-action of an anti-hyperlipidemia drug, fenofibrate, in human endothelial cells. We demonstrate the method by finding a set of signaling pathways that have the potential to increase the efficacy of fenofibrate.

References

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