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From drug repositioning to target repositioning: omics-based prediction of therapeutic targets for a variety of diseases

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The identification of therapeutic targets, biomolecules that lead to therapeutic effects, for treating diseases is vital in drug development [1]. However, most therapeutic targets easily identified using pathological data have been thoroughly investigated. The conventional methods for investigating individual diseases are limited in their ability to discover novel therapeutic targets. Recently, there has been an accumulation of omics data on various diseases. Thus, there is a need to identify novel therapeutic targets by effectively using omics data resources about various diseases.

In this study, we proposed the novel concept of target repositioning, an extension of the concept of drug repositioning, to predict new therapeutic target for a variety of diseases. We developed a novel computational method using genetically perturbed and disease-specific gene expression signatures. We predicted inhibitory and activatory therapeutic targets separately, assuming that gene expression following gene knock-down of inhibitory targets reflects the functions of drugs that inhibit the targets, and gene expression following gene over-expression reflects the functions of drugs that activate the targets. Based on the inverse correlations between the disease-specific and genetically perturbed signatures, we predicted novel therapeutic targets, and performed an integrative analysis taking into account the similarities among the diseases. Our results revealed that the proposed method accurately predicted known inhibitory and activatory targets for diseases. We also made a comprehensive prediction of therapeutic targets for a variety of diseases, suggesting many potential therapeutic targets.

[1] Santos, R. et al. A comprehensive map of molecular drug targets. Nat Rev Drug Discov. 16, 19-34 (2017).