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Estimation of disease preventive drugs and therapeutic targets using clinical big data

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Drug development is the most important issue for medical care. However, it is extremely difficult and it requires a huge amount of time and money. Especially, the depletion of therapeutic targets has become a serious problem in recent drug discovery, and the conventional methods for investigating individual diseases are limited in their ability to discover novel therapeutic targets [1]. Recently, there has been an accumulation of clinical and molecular data on various diseases. Thus, there is a strong need to identify novel therapeutic targets by effectively using various big data resources about various diseases.

In this study, we propose a new computational method to predict therapeutic targets via large-scale analyses of clinical big data on patients with various diseases. First, we estimate the potential preventive drugs that are effective in preventing the onset of the target disease by calculating the reporting odds ratio based on the reports of clinical medication history (more than 40 million reports on drug responses and adverse events). Second, we predict proteins, with which the preventive drugs interact, as candidates for therapeutic targets of diseases of interest based on chemical structures and chemical-protein interactome [2]. We applied the proposed method to various diseases, and evaluated its performance in terms of reproducibility for known therapeutic targets. It was observed that the proteins with high prediction scores tended to correspond to the known therapeutic targets of many diseases at the statistically significant level. For example, in the application to Alzheimer's disease (AD), we confirmed that some of the predicted drugs were reported to be effective against AD in recent literature. We also confirmed that some of the predicted target proteins corresponded to known therapeutic targets of AD. For example, butyrylcholinesterase (BCHE) and acetylcholinesterase (ACHE) were detected with high prediction scores. These results show the validity of the proposed method. Other predicted target proteins are expected to be the potential candidates for therapeutic targets.

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