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Drug profile matching- drug discovery by polypharmacology-based interaction profiling

Zoltan Simon
Eotvos Lorand University, Hungary

Abstract

Most drugs exert their effects via multi-target interactions, as hypothesized by polypharmacology. Here we introduce Drug Profile Matching (DPM) which is able to relate complex drug-protein interaction profiles with effect and target profiles. Structural data and registered effect profiles of all small-molecule drugs were collected and interactions to a series of non-target protein binding sites of each drug were calculated. Statistical analyses confirmed close relationships between the studied 177 effect and 77 target categories and the *in silico* generated interaction profiles of cca.1,200 FDA-approved small-molecule drugs. Receiver Operating Characteristic analysis and 10-fold cross-validation was performed to assess the accuracy and robustness of the method. Based on the found relationships, the effect and target profiles of drugs can be revealed in their entirety, and hitherto uncovered effects and targets can be predicted in a systematic manner.

In order to investigate the predictive power of DPM, three effect categories (angiotensin-converting enzyme inhibitor, cyclooxygenase inhibitor and dopamine agent) were selected and predictions in the set of the FDA-approved small-molecule drugs were verified by literature analysis and experimental tests.

Moreover, a large set consisting of 600,000 drug like molecules was selected from a database of 50 million compounds and their interaction profiles were generated. Based on these profiles, predictions for the same three effect categories were calculated and tested experimentally.

Biography

Zoltan Simon is a biologist who gained his PhD degree in structural biochemistry at Eotvos Lorand University in 2012. His main topic of interest is the application and further perspectives of pattern-based drug design. He is a founding member of Drugmotif Ltd., a Hungarian R&D SME. Besides his scientific interests, he has expertise in research management as coordinator of Hungarian and EU financed research projects. He has 8 publications in international scientific journals and 4 patent applications.