PASS TARGETS: A NEW WEB-SERVICE FOR PREDICTION OF INTERACTIONS BETWEEN THE DRUG-LIKE COMPOUNDS AND HUMAN PROTEIN TARGETS

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Evaluation of interactions between drug-like compounds and molecular targets is critical for drug discovery and toxicity assessment. Using filtered data extracted from the 21st version of the ChEMBL database [1] as a training set and a Bayesian-like method realized in PASS software [2, 3], we developed a computational tool for prediction of interactions between protein targets and drug-like compounds. It allows investigators to narrow the space of opportunities in drug discovery by selection of hits with the high chance of the desirable and little chance of undesirable biological activities. Also, based on PASS Targets prediction, it is possible to identify novel targets for the existing drugs that may be the reason for drug repurposing.

In this study, we present PASS online human targets as the novel component of Way2Drug platform [4]. Key features of our service lay beyond the possibility to predict hundreds of likely protein targets for the organic chemicals of interest with the reasonable accuracy (Average ROC AUC estimated by leave-one-out cross-validation and 20-fold cross-validation exceeded 90 %). These features will help scientists with the different background to select rationally compounds or targets for them, which will meet their expectations.

With the presented tool, we explore the potential targets of known protein kinases inhibitors. Our results indicate some targets for these compounds, which potentially may be related to the adverse reactions and some targets that may provide new indications for this type of therapeutics. The majority of predicted targets were protein kinases including those that were not known as the targets of particular inhibitor previously. These results indicate the need to assess kinase inhibitors against as many kinases as possible to be aware of potential off-targets and beneficial targets besides those that were implied in development initially. Other protein targets with ATP-binding activity also were many hitters in this study. AbCG2 is one example of such targets; this protein is implicated in the efflux of numerous drugs and xenobiotics and contributes to the multidrug resistance phenotype of several cancer cell lines. Thus, according to our results, some kinase inhibitors may be used to fight drug resistance in cancer even on the condition where their known targets are not related to the resistance.

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References

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4) URL [http://www.way2drug.com]