Mining structural knowledge space for target profiling

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Compound promiscuity has several important implications within a drug discovery program: It may help to achieve a higher efficacy through synergistic effects, it may cause adverse effects by targeting proteins in totally unrelated pathways or it may even be useful in order to discover potential new indications (i.e. drug repositioning)[1]. Ideally, knowing the full activity profile of a compound versus all potential targets should provide valuable information to design safer and more effective drugs. Moreover, target profiling is a very useful tool for target identification and target deconvolution in pre-clinical phenotypic assays.

However, systematically producing such experimental profiles is a challenging and usually cost & time prohibitive task. Thus, several computational tools to predict target activity profiles have been developed within the last decade to facilitate and guide a drug design project and/or to help to explain observed biological effects, amongst other applications. There is a wide range of methodologies employed to this purpose, from bioinformatics and statistics based approaches, structure-based methods to ligand-based approaches.

In this work, we present an approach allowing to foster structural knowledge from protein structures to perform target profiling. By combining several well established methodologies with other innovative approaches we show how to estimate compound target profiles using structural information.

Bibliography :

[1] G Rastelli, L Pinzi ; Frontiers in pharmacology 6 (2015) 157