[SC9] Online structure-based screening of purchasable approved drugs and natural compounds: retrospective examples of drug repositioning on cancer targets

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Drug repositioning is the process of identifying and developing new uses for existing drugs with the aim of accelerating and improving the success rate of drug development. [1] It is used in most therapeutic areas and definitively in the field of cancer. Indeed, current development of new anti-cancer drugs suffers of several major difficulties: the process is long and expensive, the success rate in clinical trials is low while poor survival benefits, chemoresistance and adverse effects are observed. [2] Different approaches can be used to perform drug repositioning studies and notably, when the 3D structure of the target is known, structure-based virtual screening (SB-VS) methods. [3] We developed three compounds libraries: Drugs-lib, FOOD-lib and NP-lib that contain approved drugs, food constituents and natural products, respectively, that are optimized for SBVS studies (Figure 1). The three compounds libraries are implemented in the MTiOpenScreen web server [4], this server allows user to perform SB-VS computations on a selected protein target. For drug repositioning endeavours, users will obviously select the Drugs-lib collection. To illustrate the potential of our service, we selected 5 drugs that were successfully repositioned on cancer targets. For each drug, we used the MTiOpenScreen service to screen the Drugs-lib against the corresponding anti-cancer target and we evaluated the ability of our virtual screening protocol to identify the repositioned drug as a hit, i.e. to rank it in the 1500 first compounds. Users get as output the docked poses and the corresponding predicted energy values. The selected compounds can then be ordered or used as input for additional post-processing computations.

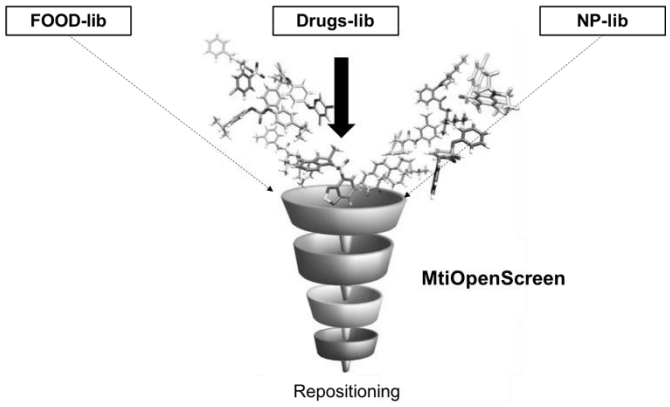

Figure 1: Three virtual screening libraries were constructed to be used for structure-based virtual screening: Drugs-lib, FOOD-lib and NP-lib. These three databases are implemented in the MTiOpenScreen web server. The Drugs-lib can be used to perform repositioning studies.

Bibliography:

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