Probing small-molecule binding to sulfotransferases: an in silico protocol to predict metabolism and inhibition

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Sulfotransferases (SULTs) are enzymes able to metabolize diverse exogenous and endogenous molecules inside the human body. They catalyze the transfer of sulphate groups responsible for some ADMET (Absorption, Distribution, Metabolism, Excretion and Toxicity) properties of drug candidates. Indeed, sulfonation can cause the decrease of the biological activity of drugs (e.g. increasing drug elimination) or in some cases induce toxic effects through the formation of highly reactive intermediates. Thus, the prediction of small molecule binding to SULTs can be useful for *in silico* prediction of such ADMET properties of compounds of therapeutic interest. To this end, we used molecular docking to explore the binding of known ligands within SULTs. We assessed several docking programs in order to correctly reproduce the experimental binding modes of known ligands. Further, previous studies suggest that most of these proteins are extremely challenging in part because of the presence of a large and flexible ligand-binding cavities able to interact with very diverse ligands. Employing molecular dynamics simulations and protein-ligand docking we developed an approach intending to discriminate the binders from non-binders among a large chemical compound library with the goal of predicting molecules potentially transformed by SULTs. Our results show that the developed approach may be useful for prioritizing compounds among a large compound collection.