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Combine molecular docking and QSAR to predict drug metabolism by sultfotransferase1a3 (SULT1A3)

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Sulfotransferase (SULT) catalyzes the reaction of transferring a sulfo group from a donor (most common is 3'-phosphoadenosine-5'-phosphosulfate (PAPS)) to an acceptor, which plays an important role in phase II drug metabolism. In this process, drugs are converted to more polar inactive metabolites and become easier to excrete from organisms. Accurate prediction of whether a drug metabolized by SULT contributes to personalized therapy by optimizing prescription. However, information about drug metabolism by SULT is not well organized online and few predictive models have been reported. Here, by combining quantitative structure-activity (QSAR) and molecular docking, we successfully establish a model to explain and predict the sulphation reaction activity by SULT1A3. We collected Km values of 105 compounds known as SULT1A3 substrates from online database and published papers. Based on the activity and structure of these molecules, we build predictive QSAR models using k-nearest neighbor algorithm. From the best model (R^2=0.75, RMSE=0.47) we found that several descriptors have major contribution to K_m, including diameter and number of basic atoms. Furthermore, in order to explore the 3D interaction between SULT and its substrate, molecular docking is performed and rational poses are selected. We found that the outliers in the QSAR model can be well explained by the docking results and chemistry characters of these molecules. By combining QSAR and molecular docking, at least in our data set, the substrates of the SULT1A3 can be well predicted in our system.

Biography

Zhi Tan got his MD degree from Wuhan University in China and is pursuing his PhD degree in University of Texas MD Anderson Cancer Center. Currently, he is in his third year and is mainly working on polypharmacology, molecular modeling and QSAR.

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