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Specialty training : Research Professional

a few key words to describe the subject of training : Drug metabolism, carboxylesterases, virtual screening, molecular docking, drug-drug interactions

Title of internship: Assessment of CES1 inhibition by drugs that could impact the clinical relevance of treatment.

this subject is a first step towards a thesis: Yes - No

Short texte describing your project

The carboxylesterases belong to the superfamily of alpha/beta-hydrolases and are implicated in the metabolism of a diversity of endogenous and xenobiotic molecules including therapeutic agents. The most prominent members of the human carboxylesterases are carboxylesterase 1 and 2 (CES1 and CES2). Crystal structures of CES1 have been reported and will be used in this project.

The main objective is to apply molecular modeling and machine learning approaches that could help to determine drugs and other xenobiotics that could reduce the function of this enzyme. To do so, we have a large collection of known CES1 substrates and inhibitors that we will use to perform docking and machine learning approaches (RF, SVM...). A virtual screening protocol will be then developed to predict potential CES1 inhibitors based on these predictive models. In a second step, we will consider the impact of some genetic variations in the efficacy of drugs metabolized by CES1 based on docking approach.

This project is in collaboration with some biochemists from the section of forensic chemistry at Copenhagen University that will perform in vitro test for some suggested compounds from our protocol, our internal computational group at the University Hospital at Roskilde and Pr. Olivier Taboureau from the university of Paris Diderot.

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