MASTER « *In Silico* Drug Design »

2ème année

PROPOSITION DE STAGE
Année Universitaire 2020/2021

A envoyer à Mme Pr Camproux
anne-claude.camproux@univ-paris-diderot.fr

Nom du Responsable du Laboratoire ou de l'Entreprise: Pr. Nicolas Leulliot

Affiliation administrative (CNRS, INSERM, …) et Numéro d'affiliation de l'unité :
Inserm U1268 MCTR, UMR 8038 CNRS – Univ. Paris

Adresse précise du Laboratoire :
Fac. de Pharmacie de Paris
4 Av. De l'Observatoire
75006 Paris

Nom du Responsable de l'équipe d'accueil (EA) : Pr. Michel Vidal/ Dr. Maria A. Miteva
E-mail : michel.vidal@parisdescartes.fr, maria.mitev@inserm.fr

---

Nom du Responsable du stage : Dr. Maria A. Miteva

Téléphone : 0170649403
E-mail : maria.mitev@inserm.fr
HDR : oui

Ecole doctorale de rattachement : MTCI

Spécialité du stage : Recherche X☐ Professionnel ☐

Indiquez par quelques mots clés, l'orientation scientifique du sujet :

drug metabolizing enzymes, docking, machine learning, toxicity prediction

---

Titre du stage :

Development of a machine learning approach to predict inhibitors of phase II drug metabolizing enzymes

Ce sujet constitue-t-il un premier pas vers un travail de thèse : Oui

---

Description du sujet (quelques lignes):

Sulfotransferases (SULTs) and UDP-glucuronosyltransferases (UGT) are major phase II drug metabolizing enzymes (DME), which are responsible for the metabolism of many human drugs. The metabolism is a key mechanism for detoxification allowing drugs to be eliminated from the organism. However, in some cases drug metabolites can be toxic or administration of more than one drug can provoke drug-drug interactions via inhibition of drug metabolizing enzymes. This internship will focus on developing original in silico approach to predict inhibitors of SULTs and UGTs integrating knowledge of 3D structures of DME and its dynamic behavior in response to the binding of various inhibitors and machine-learning technics. Our team has already developed several models combining structure-based and machine-learning approaches. During this internship, we will employ homology modeling, docking, and machine learning approaches in order to develop a protocol for prediction of drug or xenobiotic toxicity due to the interactions with phase II drug metabolizing enzymes.

References:

1. Integrated structure- and ligand-based in silico approach to predict inhibition of cytochrome P450 2D6. Martiny VY, Carbonell P, Chevillard F, Moroy G, Nicot AB, Vayer P, Villoutreix BO, **Miteva MA**. Bioinformatics. 2015 Dec 15;31(24):3930-7. doi: 10.1093/bioinformatics/btv486. Epub 2015 Aug 26.

2. MTiOpenScreen: a web server for structure-based virtual screening.
Labbé CM, Rey J, Lagorce D, Vavruša M, Becot J, Sperandio O, Villoutreix BO, Tufféry P, **Miteva MA**.
Nucleic Acids Res. 2015 Jul 1;43(W1):W448-54. doi: 10.1093/nar/gkv306. Epub 2015 Apr 8.

3. AMMOS2: a web server for protein-ligand-water complexes refinement via molecular mechanics.
Labbé CM, Pencheva T, Jereva D, Desvillechabrol D, Becot J, Villoutreix BO, Pajeva I, **Miteva MA**.
Nucleic Acids Res. 2017 Jul 3;45(W1):W350-W355. doi: 10.1093/nar/gkx397.

Retour par e-mail : anne-claude.camproux@univ-paris-diderot.fr