Université Paris 7 - Denis Diderot

MASTER ISDD
M2 - 2ème Année - Année 2018-2019

Fiche de proposition de stage

NOM: Miteva
Prénom: Maria

Adresse Professionnelle
Maria A. Miteva, PhD
Directeur de recherche Inserm
ERL Inserm « Medicinal Chemistry and Translational Research » , UMR CiTCoM
Faculté de Pharmacie de Paris
4 av de l'Observatoire
75270 Paris cedex 06

HDR : oui
Ecole doctorale de rattachement : MTCI
Appartenance Unité, nom et code:
ERL Inserm « Medicinal Chemistry and Translational Research » , UMR CiTCoM
Tel: +331 57 27 83 92 Fax: +331 57 27 83 72 Courriel: maria.mitev@inserm.fr
Spécialité du stage : Recherche ☒
Professionnel ☐

Indiquez par quelques mots clés, l'orientation scientifique du sujet:
Bioinformatique Structurale, Biologie des systems

Titre du stage: **Integrated in silico approach to understand polymorphism and drug side effects related to drug metabolizing enzymes**

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

Description du sujet:
Cytochromes P450 (CYPs), sulfotransferases (SULTs) and UDP-glucuronosyltransferases (UGT) are major drug metabolizing enzymes (DME), which are responsible for the metabolism of about 90% of 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 drug toxicity 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 molecular dynamics simulation, docking, and machine learning approaches in order to develop a computer protocol for prediction of drug or xenobiotic toxicity due to the interactions with 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.