Master Project internship

Project title	**Development of *in vitro* enzymatic assays of cytochrome P450 for the characterization of bioactive compounds**
Laboratory	Biomolecular Screening Facility (http://bsf.epfl.ch/)
Head of Lab **Assistant**	Dr Gerardo Turcatti, MER Dr Marc Chambon
Contact	gerardo.turcatti@epfl.ch (021 693 96 66) marc.chambon@epfl.ch (021 693 17 78)
Starting date	2020

Background

In the frame of drug discovery project, the initial characterization of chemical properties of bioactive compounds through various assays allows to detect the most promising and tractable chemical series. Among early ADME/tox assay panel, evaluation of compounds for cytochrome P450 (CYP450) interaction is critical due to potential drug-drug interaction, drug degradation and toxicity. CYP450 are a large family of enzymes responsible for drug metabolism, especially the 3A4, 2D6, 2C9, 1A2 and 2C19 isoforms.

Aim

The aim of the project is to develop in vitro enzymatic assay for evaluating potential interactions of bioactive chemical compounds for the 5 most important CYP450 (3A4, 2D6, 2C9,1A2 and 2C19) that are known to metabolize more than 90% of marketed drugs. In a first time, assay amenable to high throughput format and based on the inhibition of the enzymatic activity monitored through a specific fluorogenic substrate has to be developed for each isoform. A lower throughput secondary assay based on conventional substrate degradation could also be established by LC/MS approach. Validated assays will be applied to characterize compounds detected as hits in different previous screening campaigns (e.g. natural products inhibiting cyclooxygenase activities), as well as to evaluate degradation properties of some specific chemical libraries like the academic Swiss Chemical Collection. Additional chemical analysis like partition coefficient determination could also be perform in order to better characterize physico-chemical properties of the compounds.

Requirement:

The student should be interested in working in a multidisciplinary industrial-like environment and have a good background in analytical biochemistry and ideally in enzymology.

Biomolecular Screening Facility

EPFL SV BSF
Dr. Gerardo Turcatti, M.E.R.
AAB 003 - Station 15
CH - 1015 Lausanne

Phone : +41 21 693 96 66
Fax : +41 21 693 94 75
E-mail : gerardo.turcatti@epfl.ch
Website : bsf.epfl.ch