McGill Biochemistry Department | Département de biochimie

BIOC 462/491 Internship Position in Industry

Winter 2024

Restrictions

Open only to Honours Students enrolled in BIOC 462/491 during the winter 2024 semester

Company

REPARE THERAPEUTICS

Repare Therapeutics,
7171, Rue Frederick Banting, Building 2
Ville Saint-Laurent, QC H4S 2A1
https://www.reparerx.com/

Project Title: Detection, characterization, and synthesis of metabolites of interest

Background

Most xenobiotics are transformed by metabolizing enzymes into more polar and stable metabolites. The identification and quantitation of these metabolites (Met ID) is important at different stages of drug discovery. LC-HRMS is commonly used to identify, quantify, and elucidate the chemical structure of different metabolites. There are cases in which is necessary to synthesize metabolites of interest and to unequivocally assign their chemical structure. Different kits are commercially available to help identify the best conditions for the synthetic scale-up of the metabolite of interest. One of the scopes of this project is to establish the best experimental conditions for the scale-up of metabolites.

Some xenobiotics undergo metabolic activation to generate reactive electrophiles that can bind to DNA and other biomolecules. The binding of reactive metabolites to biomolecules may alter biological processes and further result in direct toxicities. Different nucleophiles are used to trap electrophiles and form adducts that are stable. The second objective of the project is to optimize experimental conditions for the trapping of reactive metabolites and for their detection by mass spectrometry.

Objectives

1. Optimize and validate different commercial kits to synthesize metabolites of interest.
2. Optimize and validate an experimental protocol for reactive metabolite screening.

The student will learn:

- Overview of drug metabolism and disposition
- Incubation of cellular fractions (Microsomes, recombinant enzymes)
- Best practices on laboratory safety and data recording.
- Use of biosafety cabinets
- LC-MS sample preparation, operation and data analysis using various software
- The student will be exposed to daily operations and experiments conducted within the DMPK group.

Contact Information

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