LIFE SCIENCES / EPFL
Master Project internship

To be hosted under: Bioengineering - Biomedical Technologies

Project title
Characterization of the molecular mechanism of action of anti-inflammatory compounds

Laboratory
Biomolecular Screening Facility (http://bsf.epfl.ch/)

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Starting date
Beginning of 2015 academic term

Background:
Nonsteroidal anti-inflammatory drugs are a major class of drugs that provides analgesic (pain-killing), antipyretic (fever-reducing) and anti-inflammatory effects. The cyclooxygenase of type 2 (COX2) is the main therapeutic target of this class of drugs. We recently performed a large primary screening of natural products that allowed us to identify some active compounds. Many hits inhibiting inflammatory response have been confirmed through interference filtering assays and concentration dependent behavior in in vitro enzymatic COX2 activity assay, and/or, cell based assay measuring the production of prostaglandinE2 by Homogeneous Time Resolved Fluorescence.

Aim:
The aim of the project is to valuate some hits by characterizing at a molecular level their mechanism of action, like determining if compounds exhibited competitive inhibition with respect to the COX2 substrate site, and studying their time-dependence behavior to discriminate tight-binder from promiscuous inhibitor. Additional chemical analysis like solubility determination could be performed at the same time.

For compound acting at cellular level without inhibiting directly the COX2 activity, additional investigations related to the target could be performed to precise the mode of action, like direct inhibition of downstream enzyme (microsomal ProstaglandinE2 synthase) or effect on induced COX2 expression, as well as evaluating permeability properties.

Requirement:
The student should be interested in working in a multidisciplinary industrial-like environment and have a good background in biochemistry (ideally in enzymology) and in cell biology.