



PhD proposal in organic synthesis

PhD project title: Molecular probes for the study of PIMs biosynthesis

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GlycoBio&Chemistry Team, <http://www.icoa.fr/en/content/glycobiochemistry>

Project:

This project consists in designing and synthesizing molecular probes for the study of PIMs biosynthesis (Phosphatidyl-*myo*-Inositol Mannosides). These molecules are essential constituents of the cell wall of mycobacteria, responsible for tuberculosis, one of the most deadly infectious diseases in the world. The treatment of tuberculosis is difficult and requires the daily use of two to four drugs for several months. In addition, resistance to these treatments is becoming increasingly common. The search for alternative drug therapies is therefore essential and these molecules could allow in the long term the discovery of new drugs to fight against this disease.

In this thesis project, we will focus on two essential enzymes of the mycobacterial cell wall synthesis: PimA and PatA. Innovative molecules, designed as analogues of substrates or inhibitors of these enzymes, will be synthesized using methodologies already mastered within Dr. Gallienne's team at ICOA. The affinity and inhibitory activity of these molecules will then be evaluated by the PhD student on the two enzymes in the Structural Glycobiology Laboratory of Professor Marcelo Guerin in Spain. Structural biology studies will also be carried out in this laboratory, in order to highlight the interactions of the molecules with the enzymes and to improve the understanding of the substrate recognition mechanism. These studies will allow us to refine the structure of the synthesized molecules. In parallel, these molecules will be tested on the pathogen *M. tuberculosis* at the Pasteur Institute of Lille, which will allow us to identify potential drug candidates.

Funding: ANR MolPropIMS

PhD start date: September or October 1, 2021

Candidate profile:

The candidate must be a **chemist with an M2 or MSc in organic chemistry with strong practical and theoretical knowledge in organic synthesis and a great interest in the chemistry/biology interface**. Experience in glycochemistry would be appreciated, but is not required. Application should include a CV, a motivation letter, M1, M2 or MSc grades (if available) as well as a recommendation letter (M1, M2 or MSc internship supervisor).

Deadline for application: April 30, 2021