Master 2 Internship in Organic Chemistry, Institut de Chimie de Clermont-Fd (ICCF)

Design, synthesis and conformational study of fluorinated peptoid-type peptidomimetics

In the fight against bacterial infections, the emergence of resistance is not the only serious threat to patients. Infections associated with specific bacterial lifestyles, such as biofilm formation or intracellular localization, are also difficult to treat with currently available antibiotics. In this context, natural antimicrobial peptides (AMPs) are a major source of inspiration for the development of new generations of effective and safe antimicrobial agents. An important area of study is the development of peptidomimetics that mimic the amphipathic structure and mechanism of action of AMPs, and peptoids (*N*-substituted glycine oligomers) are among the most promising antibacterial peptide mimics.[1] In this context, our group has developed triazolium-based peptoids with potent and selective activities on Gram-positive bacteria.[2]

The present project aims to design and synthesize a novel class of fluorinated peptoid oligomers with particular folding properties and cell-penetrating capacities for the development of innovative anti-bacterial peptidomimetics. The introduction of fluorine atoms is a well-established strategy in drug development[3] for notably modulating hydrophobicity, membrane permeability and metabolic stability that are crucial parameters to access efficient antimicrobials. To reach these objectives, this project will be developed in collaboration with Pr. Grégory Chaume (BIOCIS, Cergy University), an expert in the design and synthesis of enantiopure fluorinated amines and aminoacids.[4]

The internship will be devoted to the development of robust synthetic route to peptoid oligomers incorporating one or several fluorinated side-chains on solid-support and/or in solution. Two strategies will be explored, one relaying on a submonomer approach using chiral or achiral fluorinated amines or a SPPS-like monomer approach using *N*-fluoroalkylated amino acids. The work will include the design and synthesis of short peptoid oligomers (up to 12 residues), their characterization by classical techniques (NMR, Mass spectrometry, HPLC) and the study of their propensities to adopt well-defined secondary structures (Circular dichroism, NMR, X-ray diffraction). Biological evaluations will be performed in collaboration.

Keywords: Organic synthesis, Solid-phase synthesis, Peptidomimetics, Secondary structures, Antibacterials

This internship is funded by the CY initiative project FLUOPEPTO and the work will be carried out in the team “Organic and Medicinal Chemistry” (PEPTOID group) at the Institute of Chemistry of Clermont-Ferrand (ICCF UMR 6296). Period of internship: 6 months starting from January 2026

To apply: Please send CV, cover letter and Master 1 grades to: sophie.faure@uca.fr and olivier.roy@uca.fr

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