Available PhD position in Organic/Medicinal Chemistry

<u>Subject</u> : Fluorinated alkenes as peptide surrogates towards medicinal applications

A PhD position in collaboration between our « Fluorinated Biomolecules Synthesis » research group, located at UMR 6014 COBRA-CNRS, Normandie University, and Pr Pierre-Luc Boudreault head of Laboratoire de Chimie Médicinale at Université de Sherbrooke (UdS) is now available.

The development of therapeutic peptides has growing up due to their safety and their high specificity. However, they have two major drawbacks which are a poor membrane permeability and a poor *in vivo* stability. The replacement of the peptide bond by appropriate mimics should be able to overcome these drawbacks. In this context we aim to develop and use fluorinated alkene moieties as peptide bond surrogates in the design of biopeptides with improved properties. Indeed, some fluorinated alkenes are recognized as stable, isosteric and isoelectronic mimics of amide/peptide bond.

In such a context, this PhD project aims at developing new fine fluorinated molecular tools in order to obtain pseudopeptides with a fluorinated alkene replacing the central peptide bond. These fluorinated peptides with original properties will be then exploited in medicinal chemistry. Indeed, the Canadian partner being a specialist in peptide chemistry, is particularly interested in G-protein coupled receptor (GPCR) ligands and their signaling profile. The targeted biopeptides display high affinity for their receptor and are *in vivo* biologically active in cardiovascular and analgesic assays. However, their peptide nature also leads to low proteolytic resistance and pharmacokinetic (PK) profile as well as balanced signaling profiles, activating several pathways and leading to undesirable side effects. Our new fluorinated alkenes modifications might lead us to discover new signaling profiles allowing for better understanding of the intricacies of GPCR ligand-receptor interactions and their downstream effects. By implementing this new chemical modification, we expect to improve their stability and pharmacokinetic properties, as well as the potential to fine-tune their signaling pathways. The Ph.D. student will spend 18 months at COBRA laboratory in France and 18 months at Laboratoire de Chimie Médicinale in Canada. An additional scholarship would be granted to the candidate in order to help him to move from Rouen to Sherbrooke.

The ideal candidate for this position should be highly motivated, must hold a master degree in organic chemistry/medicinal chemistry and have a strong background in organic synthesis. Moreover, the candidate should be dedicated, curious, have good communication skills and a good team spirit. An experience in fluorine chemistry is not required.

Application should be sent to Dr. Samuel Couve-Bonnaire (samuel.couve-bonnaire@insa-rouen.fr), Dr. Thomas Castanheiro (thomas.castanheiro-matias@univ-rouen.fr) and Pr. Pierre-Luc Boudreault (Pierre-Luc.Boudreault@USherbrooke.ca) and include:
- A detailed CV with at least two referees, able to be contacted
- A cover letter
- Master or engineer school grades

<u>Start of PhD:</u> October 1, 2024 (gross monthly salary around 2044 euros)