



Laboratoire d'Innovation Thérapeutique
UMR 7200 CNRS-Unistra
Université de Strasbourg, Faculté de Pharmacie



PhD position available

New metabolically stable fluorocarbon conjugates and fluorogenic probes derived from peptides to develop potential analgesic compounds in non-opioid pain pathways.

Laboratory for Therapeutic Innovation, IMS, EURIDOL, University of Strasbourg
<https://medchem.unistra.fr/chimie-biologie-integrative-et-pharmacognosie-cbip/>

Key words: Organic synthesis, fluorine chemistry, medicinal chemistry, peptide, fluorescence, GPCR, pain

Context: Chronic pain is a major health issue in our society that clearly impacts quality of life. 30-40% of the population in the United States, and equivalent in Europe, suffer from chronic pain and its total cost has been estimated at 560-635 billion dollars annually [1]. Opiates still represent the gold standard analgesics to treat pain but their use is clearly associated with numerous adverse side effects.

Objectives: Based on a novel FluoroPEP technology recently developed by our team [2], the goal of the thesis is to design and to synthesize new metabolically stable peptides targeting G protein-coupled receptors (GPCR) to develop potential analgesic compounds of which mechanisms of action are not related to the opioid system. The first part of the thesis will be dedicated to the structure-activity relationship studies around fluorinated peptides. The second part will be focused on the design and the synthesis of specific and potent innovative fluorescent fluorogenic probes [3] derived from these peptides to perform live-cell and *in vivo* imaging.

Scientific context: The thesis will be carried out at the Laboratory for Therapeutic Innovation (UMR 7200 CNRS-University of Strasbourg) within the Integrative Chemical Biology and Pharmacognosy team which focuses on developing chemical tools and drug candidates targeting GPCR. The *in vitro* and *in vivo* evaluation of new compounds will be performed within the team of Dr. Frédéric Simonin (ESBS, Illkirch) which is involved in the characterization of novel GPCRs in the context of pain modulation. Both teams are part of the Institut du Médicament de Strasbourg (IMS) and the Ecole Universitaire de Recherche Interdisciplinaire sur la Douleur (EURIDOL) which study pain and novel innovative treatments.

Financial support: EURIDOL ; **Starting date :** 1st October 2021

Expected skills: Multi-stage organic synthesis and standard characterization techniques (NMR, mass spectrometry); candidate willing to work at the interface of chemistry and biology; knowledge in peptide chemistry and fluorescence will be a plus.

Application/further information : dominique.bonnet@unistra.fr.

References :

[1] Breivik, H. *et al. BMC Public Health*, **2013**, *13*, 1229; [2] (a) Bonnet, D. *et al.* patent WO2016102648; (b) Gerbier, R. *et al. FASEB J.* **2017**, *31*, 687-700; (c) Flahault, A. *et al. Nat. Commun* 2021, 305; [3] (a) Karpenko, I.A. *et al. JACS*, **2015**, *137*, 405-12; (b) Esteouille, L. *et al. Chem. Sci.* **2020**, *11*, 6824-29; (c) Bonnet, D. *et al.* Patent EP20305479.6, 12-05-2020.