

**Master 2 internship project  
Year 2020-2021**

**Laboratory/ Institute:** IBS  
**Team:** Channels

**Director:** Winfried Weissenhorn  
**Head of team:** Michel Vivaudou

**Name and status of scientist in charge of the project:** Michel Vivaudou **HDR** yes  no   
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**Program of the Master's degree in Biology:**

- Immunology, Microbiology, Infectious Diseases     Integrative Structural Biology  
 Physiology, Epigenetics, Differentiation, Cancer     Neurosciences and Neurobiology  
 Planta International

**Title of project: Novel regulation of potassium channels by opioid receptors**

Objectives

The study of novel regulatory pathways linking opioid receptors and G-protein activated potassium channels.

Abstract

This project concerns the mechanisms of the receptor regulation of G-protein activated potassium channels (called GIRK or Kir3 channels). These important channels are activated by the G-proteins released by G-Protein Coupled Receptors (GPCR) upon binding of their ligands. We have discovered that opioid GPCRs can modulate these channels by two pathways, the classical G-protein dependent pathway and a new pathway independent of G-proteins. Our results suggest that distinct signalling modes may be associated with distinct homomerization states of the receptors. The goal of the project will be to understand the molecular basis of this novel regulation using advanced biophysical and protein engineering techniques. The work will be conducted in close collaboration with a third year PhD student.

Methods

Protein engineering (modeling, mutagenesis, PCR, etc.). Heterologous expression and functional characterization by electrophysiological techniques using manual and robotic devices (patch-clamp, microelectrodes).

Relevant publications of the team

Moreau CJ, Dupuis JP, Revilloud J, Arumugam K, Vivaudou M (2008) Coupling ion channels to receptors for biomolecule sensing. *Nature Nanotech* **3**:620-5

Vivaudou M, Todorov Z, Reyes-Mejia GC, Moreau C (2017) Ion Channels as Reporters of Membrane Receptor Function: Automated Analysis in *Xenopus* Oocytes. *Methods Mol Biol.* **1635**:283-301

Moreau CJ, Revilloud J, Caro LN, Dupuis JP, Trouchet A, Estrada-Mondragón A, Niescierowicz K, Sapay N, Crouzy S, Vivaudou M (2017) Tuning the allosteric regulation of artificial muscarinic and dopaminergic ligand-gated potassium channels by protein engineering of G protein-coupled receptors. *Sci Rep.* **7**:41154

Requested domains of expertise

Experience or interest in molecular biology and biophysics. English is the working language of the team.