UFR de Chimie et de Biologie
UNIVERSITÉ Grenoble Alpes

Master's degree in Biology – Chemistry-Biology Department

Master 2 internship project
Year 2019-2020

Laboratory/ Institute: IBS
Director: Winfried Weissenhorn
Team: Channels
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: Design of light-gated potassium channels

Objectives

The goal of this project is to optically manipulate the gating of potassium channels to better understand their physiological role in various organs and to provide tools for optical control of cell excitability.

Abstract

Optogenetics is based on the optical control of light-sensitive elements expressed in cells with high spatial and temporal resolution. We are currently focusing on two ubiquitous channels, ATP-sensitive potassium (K-ATP) channels and G-protein-gated inward rectifying K^+ (GIRK) channels. K-ATP channels couple cell metabolism to membrane excitability while GIRK channels are activated by G proteins, released upon activation of G protein-coupled receptors.
The strategy is the photoswitched tethered ligand (PTL) approach, whereby a photosensitive blocker or opener is grafted onto cysteines introduced at key positions. These positions, suggested by molecular modeling, are verified by mutagenesis and functional assessment using electrophysiological techniques. Significant results have been obtained already but they need to be refined and extended.
The work will be conducted in close collaboration with a second 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.