Grenoble Alliance for Integrated Structural & Cell Biology

INTERNSHIP PROPOSAL

Institute and Group: IBS / Channels

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Research project title: Design of light-gated potassium channels

5 Keywords to describe the project: optogenetics; potassium channel; protein engineering; electrophysiology

Description of the project (aims, experimental techniques, recommended background):
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 characterization using electrophysiological techniques. Significant results have been obtained already but they need to be refined and extended.

Justification that the internship's subject fits with the general theme of GRAL:
The project is focused on of membrane channel proteins and combines protein engineering based on structural analysis and functional analysis using biophysical techniques. The light-controlled channels will be useful tools in cell biology research as they allow to control and study cell signalling.

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