



Grenoble Alliance for Integrated  
Structural & Cell Biology

## GRAL MSc RESEARCH SCHOLARSHIP 2020-2021 RESEARCH INTERNSHIP PROPOSAL

### Institute / Group

IRIG / IBS - CHANNELS

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### Research Project Title

Design of light-gated potassium channels

### Description of the project

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<sup>+</sup> (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 with the design of the first light-inhibited Kir3.4 and Kir6.2 channels. These results need to be refined and extended to other members of the Kir family. The core of the internship will be to engineer Kir2.1 channels light-sensitive mutants through molecular biology and electrophysiology.

Appropriate Masters: Integrative Structural Biology, Neurosciences, Neurobiology, Nano-biosciences.

### Keywords

Optogenetics, potassium channel, protein engineering, electrophysiology

### 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

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

Zabelskii D, Alekseev A, Kovalev K, Oliviera AS, Balandin T, Soloviov D, Bratanov D, Volkov D, Vaganova S, Astashkin R, Chizhov I, Yutin N, Rulev M, Popov A, Rokitskaya T, Antonenko Y, Rosselli R, Rodriguez-Valera F, Armeev G, Shaitan K, Bueldt G, Vivaudou M, Kirpichnikov M, Koonin E, Bamberg E, Gordeliy V (2020) Viral channelrhodopsins: calcium dependent Na<sup>+</sup>/K<sup>+</sup> selective light-gated channels. (under review)