Soutenance

THESE

Jeudi 21 Avril 2022 à 09h

Visioconférence

Institut de biologie structurale - 71 avenue des Martyrs CS 10090 38044 Grenoble Cedex 9 - T.+33 (0)4 57 42 85 00

www.ibs.fr

par **Ana Sofia Oliveira**

Institut de Biologie Structurale

Groupe Transporteurs Membranaires

Electrophysiological studies of (1) the regulation of G protein-gated potassium channels by δ-opioid receptors and (2) the function of viral rhodopsins

Thèse de Doctorat de l'Université Grenoble Alpes

Two projects were conducted using heterologous expression in Xenopus oocytes and electrophysiological characterization. During this work, we also developed XenoGlo, a non-destructive technique using nanoluciferase to precisely quantify surface expression in single oocytes.

Dual regulation of G protein-gated potassium channels (GIRK) by δ-opioid receptors (DOR):
Our data disclose an unreported inhibition of GIRK channels by DOR. Opioid agonists acting through DOR activate GIRK channels at nM concentrations but inhibit them at higher concentrations. Notably, inhibition of GIRK channels was revealed at high levels of expression of DOR. Control experiments performed with the closely related μ-opioid receptor did not show any sign of inhibition.
Unlike channel activation, inhibition does not require receptor activation of G proteins, implying that these are two independent signaling pathways. Further experiments show that this fast inhibition cannot be attributed to already described mechanisms involving GPCR kinases or arrestins.
These observations highlight another level of complexity in the regulation of GIRK by OR, with mechanistic and physiological implications that remain to be fully elucidated.

Shedding light on the function of Viral Rhodopsins: Viral rhodopsins (VR) are a monophyletic group of proteins from viral origin within the superfamily of rhodopsins. While several VR structures have been solved, their function remains elusive.
We found, using Ca-activated ion channels as reporters, that VR accumulate intracellularly and that their activation by light induces dose-dependent calcium release from intracellular stores. This finding was reproduced in mammalian cultured and native cells.
Because the release of calcium from intracellular stores mediates a large panoply of cellular processes such as gene expression, neurotransmitter release, or muscle contraction, VR are great candidates as novel optogenetic tools, with potential applications in the manipulation of intracellular calcium.

Cette soutenance sera retransmise par visioconférence :
https://cnrs.zoom.us/j/95581538850?pwd=eTZGMmR5Zk1NQkYwWC9rUDZUNW01dz09
(Meeting ID: 955 8153 8850, Passcode: aJy4Ux)