Séminaire

CONFÉRENCIER INVITÉ

Vendredi 06 Juillet 2018 à 14h

Salle des séminaires

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 **Catherine Vénien-Bryan**

Université Pierre et Marie Curie, Paris

Institut de minéralogie, de physique des matériaux et de cosmochimie

Structural and dynamics studies of the human potassium channel kir2.1 and disease-associated mutants

Inwardly rectifying potassium (Kir) channels are transmembrane proteins that regulate membrane electrical excitability and K+ transport in many cell types generating and controlling the membrane resting potential. The function of this channel although simple is primordial for physiological processes such as the creation and the propagation of the neuronal action's potential, the regulation of cellular volume, the muscular contraction and the cardiac pulse. Their physiological importance is highlighted by the fact that genetically inherited defects in Kir channels are responsible for a wide-range of channelopathies including Andersen's syndrome a pathology that can cause periodic paralysis or serious heart problems. To elucidate how channel function becomes defective in the disease state requires a detailed understanding of how the channel goes from the open to the closed states. This will allow the identification of the most suitable regions for the binding of small correctors or drug, which could influence the conformation of intracellular gating elements

In this work we are focusing on the Kir2.1 channel and three important mutations (G144S, C154Y, R312H), which are responsible for dysfunction of the channel leading to the rare disease Andersen syndrome. The atomic structures of the open states KirBac3.1 (bacterial homologue of the human Kir2.1) and several of its mutants were solved by our team. These structures suggested that a rotation of the cytoplasmic domain could be associated with the opening of the channel. MDeNM (Molecular Dynamic Excitations Normal Modes) simulations were performed along with experimental mass spectrometry H/D exchange (HDX-MS) in order to test this "twist to open hypothesis".

In addition, I will present our latest biochemical functional and structural studies on the human Kir2.1 WT.

The structural studies of the channel were performed using either x-ray crystallography, single particle cryo-EM but also 2D electron crystallography. During my talk, I will present CRACAM, a robot dedicated to the production of 2D crystals or possibly 3D nano-crystals, which can be exploited by electron crystallography.

Hôte : Waï-Li Ling (IBS/Groupe de Microscopie Electronique et Méthodes)

L'accès au campus EPN nécessite un avis de rendez-vous

Contactez O. Cavoret (au moins 48h à l'avance) - T. 04 57 42 87 04 - email : ibs.seminaires@ibs.fr