Laboratoire PPSM – UMR CNRS 8531

Photochimie et Photophysique Supramoléculaires et Macromoléculaires

Séminaire PPSM

Vendredi 16 novembre 2018 - 11h00

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«Pentameric ligand-gated ion channels gating mechanism using a bacterial prototype»

Pentameric channel-receptors, including nicotinic acetylcholine, glycine and GABAA receptors, play a key role in fast excitatory and inhibitory transmission in the nervous system and are the target of numerous therapeutic and addictive drugs. They carry several neurotransmitter binding sites which govern the opening of a transmembrane ion channel. Extensively expressed in animals, they were found in several bacteria, especially the homolog from the cyanobacteria Gloeobacter violaceus (GLIC) which functions as a proton-gated ion channel. The simplified architecture of this archaic homologue, as well as its prokaryotic origin, helped solving its X-ray structure in two closed and one open conformation. To investigate the dynamics of the protein, we further engineered multiple fluorescent/quencher pairs that report on the protein conformation. Our data show that, upon activation by protons, the protein first undergoes a rapid (faster than a ms) and global pre-activation transition, followed by a more local channel opening. Mapping of the titrable residues also identify the key protein domains mediating proton activation. These data collected on a model pLGIC help understanding the mechanism of functioning of neurotransmitter-gated channel for which intermediate conformation also contribute the activation transition pathway.

Selected recent references from the lab:

Nemecz et al, *Neuron*. 2016 **90**:452-70
Menny et al, *eLife* 2017 **6**:e23955.
Nemecz et al, *PLoS Biol.* 2017 **15**:e2004470.

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