Seminar/Talk

Optical probing and optogenetic of TREK channels physiology

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Ion channels generate the electrical signals with which the nervous system uses to sense the world, process information, create memories and control behavior. One of the most diverse family of ion channels, the K2P channels, serves as a hub for the generation and regulation of the negative resting membrane potential and neuronal excitability. K2P channels also play a central role in the response of cells to diverse extracellular and intracellular signals, such as GPCR signaling, pH and membrane stretch. The members of the TREK channel subfamily, TREK1, TREK2 and the more distantly-related TRAAK channel are widely expressed in the nervous system and are involved in several physiological and pathological functions, including pain perception, depression and PUFA-dependent neuroprotection against ischemia. In this seminar, I will first describe the molecular basis for TREK1 and TREK2 channel pH-sensitivity and I will show how these channels can be oppositely regulated by pH. Then, I will present single-molecule imaging data demonstrating that TREK channels can heteromultimerize to increase functional diversity, and I will discuss the development of a novel optical imaging method to probe interactions of a channel s isolated intracellular domain with the plasma membrane. In the case of TREK, we showed that the interaction between the C-terminus and the plasma membrane is involved in the TREK channel gating and the regulation by GPCRs and the antidepressant fluoxetine. Finally, I will show you how we created light-gated versions of members of K2P family and an important new method for optogenetics, which we call the photoswitchable conditional subunit method (TREK1-PCS), which makes it possible to endow native (unmodified) channels with light sensitivity. TREK1-PCS allows us to show that TREK1, typically considered to be only a leak channel, contributes actively to the hippocampal GABAB response which breaks with conventional idea that hippocampal GABAB is mediated only by GABAB-GIRK coupling. In addition, by using this tool we have shown how phospholipids act specifically on TREK channels and how small molecules, such as ethanol, can specifically modify TREK channel functions.

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Mondi Seminar Room 3, Central Building

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