SFB 1078

Protonation Dynamics in Protein Function

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Webex

Link via e-mail

Colloquium

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Mechanisms of Sensory Transduction by Ion Channels

Ion channels control cellular electrical signaling by opening and closing pores for ionic flux across cell membranes in response to tremendously diverse stimuli. In this talk, I will discuss recent efforts from my lab that leverage structure, electrophysiology, and pharmacology to understand mechanisms of ion channel function in animals and microbes. First, I will present studies on vertebrate two-pore domain K+ channels (K2Ps) regulated by mechanical and chemical cues. For the mechanosensitive K2P TRAAK involved in action potential propagation, structures and single channel recordings of gain-of function mutants (including those that cause in the human neurodevelopmental disorder FHEIG) reveal distinct leak and mechanically-activated open states and lead to a model for how membrane tension gates the channel. For the pH-regulated K2P TASK2 involved in breathing regulation, cryo-EM structures reveal novel channel gates for intracellular and extracellular inhibition by protons. pH-regulation of the K2P TWIK1 involved in heart rhythm generation is found to involve a distinct selectivity filter gate that could contribute to its unusual sodium permeability in hypokalemic conditions. These studies provide insight into the diversity of sensing and gating mechanisms among K2Ps. Finally, I will discuss ongoing efforts to understand gating of the microbial light-gated channelrhodopsin ChRmine and the SARS-CoV-2 viroporin ORF3a.

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