生命科学セミナー

Charm of the structure-function study of ion channels

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Fri. 24th October 2025, 15:15-16:15

KUIAS Main Building, 2F Seminar Room

(Kyoto University Campus map #77)

Abstract:

Ion channels are membrane proteins that play fundamental physiological roles, including the regulation of excitability in neurons and muscles. Since the cloning of ion channel cDNAs, structure-function studies in heterologous expression systems have elucidated the functioning mechanisms, and recent advances in structural biology have greatly accelerated this progress. In this seminar, I will present two studies that illustrate the “charm” of ion channel research.

[A novel ion-conducting pathway in an inherited GIRK mutant (J Physiol, 2022)]

G protein-gated inwardly rectifying K^+ (GIRK) channels are critical regulators of membrane excitability in the brain, heart, and other organs. K^+ channels are highly selective for K^+ over Na^+, a property conferred by the selectivity filter in the central pore. Mutations in and around the GIRK selectivity filter are associated with some inherited human diseases. It is widely assumed -without direct evidence- that the pathophysiology arises from impaired selectivity caused by deformation of the central permeation pathway. We showed that this is not necessarily the case: in some mutants, a distinct secondary ion-conducting route exhibiting abnormal ion selectivity is formed alongside the central pore.

[An extracellular K^+-gated Cl^- channel, DmAlka (unpublished)]

Extracellular K^+ strongly influences membrane excitability by setting the K^+ equilibrium potential, yet membrane proteins directly regulated by the binding of extracellular K^+ have not been described in animals. DmAlka, a Cys-loop receptor type anion channel expressed in the Drosophila nervous system, has been characterized as an extracellular pH-sensitive channel. We serendipitously discovered that DmAlka is directly regulated by extracellular K^+ within the physiological range, and mutational analysis identified a candidate K^+-binding site consistent with direct gating.

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