

特別講演 (基盤医学持論)



Well-being in ASIA

2016年10月11日(火) 17:00-18:30

医学系研究科 基礎研究棟 1F 会議室1 (学務課前)

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タイトル : A molecular movie of the Excitation- Contraction Coupling

【講義内容】

The voltage-gated sodium and calcium (Na_v and Ca_v) channels and the intracellular high-conductance calcium channel RyRs collectively control the rapid release of Ca^{2+} from sarcoplasmic reticulum to cytoplasm, an event that subsequently triggers the excitation-contraction (E-C) coupling of skeletal and cardiac muscles. In recent years, we have determined the crystal structure of a bacterial Na_v channel Na_vRh as well as the near atomic-resolution cryo-EM structures of the mammalian $\text{Ca}_v1.1$ and RyR1. We were able to capture the structures of RyR1, which represent the largest ion channels known, in multiple closed conformations and one open state. These structural characterizations provide important clue to understanding the long-range allosteric gating of RyRs. Furthermore, classification of the EM particles of the $\text{Ca}_v1.1$ complex yielded multiple reconstructions that reveal pronounced conformational changes. These studies shed light on the molecular understanding of E-C coupling. In addition, the atomic model of the $\text{Ca}_v1.1$ complex provides a three-dimensional template for molecular interpretations of the function and disease mechanism of Ca_v and Na_v channels.

【掲載主要論文】

• *Nature* 2016;537:191-196

“Structure of voltage-gated calcium channel *Cav1.1* at 3.6 Å resolution.”

• *Cell* 2016;165:1467-1478

“Structural Insights into the Niemann-Pick C1 (NPC1)-Mediated Cholesterol Transfer and Ebola Infection.”



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