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(理研 和光キャンパス 脳科学中央研究棟 1階セミナー室)

Title: Molecular mechanism of channelrhodopsin and structure-guided development of useful optogenetics tools

チャネルロドプシンの分子機構と構造に基づく光遺伝学ツールの開発

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Channelrhodopsins (ChRs) are light-activated cation channels that mediate cation permeation across the cell membrane upon light perception. We first solved the high-resolution crystal structure of ChR (C1C2), and based on the structure, many ChR variants are made and utilized in optogenetics. We designed by QM/MM simulation and developed blue-shifted variant. Among these variants, red-shifted (650 nm) channelrhodopsins are particular important, because the longer wavelength light allows penetration into deeper tissues. However, the molecular mechanism of the red-shifted absorption has not been elucidated so far. Here we report the crystal structure of the most red-shifted channelrhodopsin, Chrimson, at 2.6 Å resolution. The structure revealed unique molecular architectures to achieve its highly red-shifted absorbance; hydrophobicity around the retinal Schiff's base and the biased distribution of the polar residues and the rigidity in the retinal binding pocket. The structural comparison revealed that Chrimson has several structural features that resemble the light-activated proton pump, bacteriorhodopsin, while retaining the similarity to other channelrhodopsins around the ion channel pore, indicating that Crimson is a primitive variant during molecular evolution from the prokaryotic ancestors. Based on these mechanistic insights, we engineered ChrimsonSA, a mutant with an about 20 nm red-shifted maximum activation wavelength and accelerated closing kinetics. When expressed in hippocampal neurons, ChrimsonSA allowed selective action potential generation with red light, and thus it is ideally suited for dual color optogenetic applications. To uncover the mechanism how ChR opens the channel upon perception of blue light, we performed time-resolved crystallography using XFEL in SACLA. I will talk about the light activation mechanism of ChR.

<References>

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