OIST SEMINAR

Hosted by Cellular & Molecular Synaptic Function Unit

Speaker: Associate Prof. Masayuki Mori

Kyoto University

DATE: Tuesday, September 29
TIME: 16:00 - 17:00
VENUE: Meeting Room D014, Level D, Lab1

Title:

" **Molecular insight into Ca^{2+}/Calmodulin-dependent regulations in TRPC channels** "

Abstract:

Calmodulin (CaM) contributes a variety of ion channels gating regulation in response to cellular $Ca2^{+}$ concentration ($[Ca^{2+}]_i$) changes. However, the information is still missing about the molecular basis of CaM-mediated regulation of mammalian TRP channels which generate receptor-operated cation (Ca^{2+} and Na^{+}) currents. For understanding of its molecular mechanism, we examined CaM binding to the C-terminal region of TRPC6 by Ca^{2+}-dependent FRET system. FRET due to CaM binding to the C-terminal region of TRPC6 demonstrated a bell-shape response curve with respect to $[Ca^{2+}]_i$. This Ca^{2+}-dependence was distinctive compared to those of IQ-domain of voltage-gated Ca or Na channels. The bell-shape response curve changed to a simple grow by a mutation in either N- or C-lobe domain of CaM. Intriguingly, the mutant in the N-lobe of CaM delayed the decay of receptor-operated currents of TRPC6, indicating the lobe-specific function of CaM. From these results, the Ca^{2+}-dependent regulation of TRPC6 may be explain by the bell-shape response curve of CaM binding which is probably caused by a competitive binding between the both lobes of CaM. Our results provide a unique molecular basis for CaM to terminate ion channel activity, which may play critical roles at the down-stream of vasoconstrictors, releasing transmitters and growth factors.

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