CDB SEMINAR

Speaker: Masaru Ishii

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Title: "Physiological regulation of heterotrimeric G protein signaling in intact cells: An unexpected finding from electrophysiological measurement."

Date: Friday, June 18
Time: 16:00 -17:00
Place: 7th floor Conference Room of Building A,CDB

Summary:

Over the past decades, enormous amounts of signal molecules have been identified and various kinds of signaling pathways have been proposed. However, their physiological relevance has not been fully examined so far. Electrophysiological measurements, such as patch-clamp experiment, enable us to grasp the real function of cell signaling *in vivo* with high temporal resolution. In recent successive studies I have revealed a physiological mode of regulation in heterotrimeric G protein signaling in native cardiomyocytes. A cardiac potassium channel which is activated by heterotrimeric G protein βγ subunits has been known to exhibit a characteristic temporal behavior, called as "relaxation". Upon depolarization the channel current is inhibited which is slowly recovered by the repolarization of the plasma membrane. Because the channel is essentially voltage- and time-independent, the molecular basis of this curious behavior has been an enigma for a long time. Ensemble of electrophysiological and biochemical techniques has revealed that this behavior is attributable to the temporal regulation of G protein cycle. This regulation includes depolarization-induced elevation of intracellular calcium concentration, resultant formation of Ca^{2+}/calmodulin complex and facilitation of a negative regulator of G protein signaling (RGS) by removing its endogenous inhibitory phospholipid, PtdIns(3,4,5)P_3. This result unexpectedly provides us with a novel principle that "G protein cycle is dynamically regulated by membrane depolarization" *in vivo*. Electrophysiology is not only an essential method for investigating ion channel function but also, when coupled to other biochemical and imaging techniques, this is a powerful tool for elucidating physiological signal reaction which is orchestrated by diverse signaling molecules.

Host: Shin-Ichi Nishikawa <Stem Cell Biology, CDB>
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