【Integrated Science and Innovative Science（Comprehensive fields）】

Study of IP_3 receptor/Ca^{2+} signaling in neural plasticity and brain development and differentiation

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【Outline of survey】

Biophysical and biochemical studies of the molecular properties of IP_3Rs helped us realize that various mechanisms contribute to the fine-tuning of IP_3R-mediated Ca^{2+} signal. These mechanisms equip different isoforms, assemble various IP_3R-associated molecules, or dynamically change in the subcellular localization of the signal. The discovery of many kinds of binding partners suggests that IP_3Rs form a macro signal complex and function as a center of multiple signaling cascades. The diversity of Ca^{2+} signaling patterns and/or subcelullar distribution mechanisms of IP_3Rs most likely are a product of the components of IP_3Rs-signaling complex, which can differ from cell to cell, and even from subcellular space to subcellular space.

Our final goal is to understand the precise role of IP_3R-mediated Ca^{2+} signaling in recognition, learning and memory, and consciousness. By focusing our study on the regulation of IP_3R-mediated Ca^{2+} signaling by these various mechanisms described, we will elucidate the molecular basis of IP_3R function in a series of brain development process and brain function. To achieve this, our approach to the study of IP_3Rs needs to remain diverse, especially when looking at IP_3Rs as in a signaling complex.

【Expected results】

We will focus on uncovering the function and physiological roles of IP3Rs, to understand the role of IP3Rs-mediated Ca^{2+} signaling in recognition, learning, and memory. Using the latest imaging methods, (e.g. fluorescent resonance energy transfer (FRET), Quantum Dots, a single molecule imaging technique), we will clear the relationship of dynamics of molecular interaction and biological phenomena. We also expect that we understand the molecular mechanism of diseases caused by abnormality of influx along the elucidation of physiological function of IP_3 receptor.

【References by the principal investigator】

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- Shirakabe, K., Priori, G., Yamada, H., Ando, H., Horita, S., Fujita, T., Fujimoto, I., Mizutani, A., Seki, A. & Mikoshiba, K.: IRBIT specifically binds to and activates pancreas-type Na^+/HCO_3^- cotransporter 1, pNBC1. **Proc. Natl. Acad. Sci.** 103(25) 9542-9547 (2006)

【Term of project】 FY2008− 2012

【Budget allocation】
159,700,000 yen (direct cost)

【Homepage address】 Under construction