CDB SEMINAR

Speaker: Mitsuhiko Ikura

<Ontario Cancer Institute, University of Toronto>

Title:

" Structural basis for inositol 1,4,5-trisphosphate receptor mediated calcium release from the endoplasmic reticulum "

Date:	**Thursday, November 18**
Time:	**16:00 -17:00**
Place:	**7F Conference Room of Building A,CDB**

Summary:

A central mechanism for calcium (Ca^{2+}) signaling in eukaryotic cells involves release of Ca^{2+} from the intracellular endoplasmic reticulum (ER) Ca^{2+}-stores into the cytoplasm. This process is mediated by the ER membrane-associated Ca^{2+} release channel, inositol 1,4,5-trisphosphate receptor (IP_3R) which requires IP_3 and Ca^{2+} for its channel gating activity. Ca^{2+} also acts as a negative regulator of the receptor at the very high concentration *via* the Ca^{2+}-calmodulin pathway. IP_3R has been shown to play a crucial role in the control of cellular and physiological processes as diverse as cell division, cell proliferation, apoptosis, fertilization, development, behavior, memory and learning. In order to understand the mechanism by which the ion channel is regulated by the two key intracellular messengers, we have undertaken structural studies of the protein by X-ray crystallography and NMR spectroscopy. We have recently determined a crystal structure of the IP_3 binding core of the mouse type I IP_3 receptor at 2.2 Å (Bosanac et al. Nature 420, 696, 2002). The asymmetric, boomerang-like structure consists of an N-terminal ®-trefoil domain and a C-terminal ⟨-helical domain containing an armadillo repeat fold. The cleft formed by the two domains exposes a cluster of arginine and lysine residues that coordinate the three phosphoryl groups of IP_3. Putative Ca^{2+} binding sites were identified within the ligand binding core. The talk will discuss the current status of our knowledge on the structure-function relationship of IP_3R.

Host: **Masatoshi Takeichi** **<Cell Adhesion/Tissue Patterning, CDB >**

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