Principal Researcher	Katsuhiko Mikoshiba	**Number of Researchers**	1
Research Institution • Department • Title	Professor, The Division of Molecular Neurobiology, The Institute of Medical Science, The University of Tokyo	**Location of Institution**	Minato-ku, Tokyo

Title of Project	Study of the IP_3 receptor/Ca^{2+} signaling in neural plasticity and brain development and differentiation
Abstract of Research Project	When cells receive external stimuli, they produce intracellular Ca^{2+} wave and oscillation in a spatio-temporal pattern resulting in various physiological phenomena. In this project, we investigate how the Ca^{2+} dynamics are involved in basic mechanisms in brain development, growth, differentiation, and also higher neural activity such as neural plasticity. We plan to analyze 1) the Ca^{2+} wave and oscillation in neurons and glial cells in a real time scale, 2) the real time visualization of the dynamic movement of functional molecules in neural cells, 3) the activity-dependent dynamic movement of functional molecules and cytoskeletal proteins in real time scale during LTP and LTD, 4) the molecular mechanism of neuralization during morphogenesis. We discovered IP_3 receptor as a developmentally regulated P400 protein and cloned whole cDNA of IP_3 receptor (Nature 1989). We found that it works as a channel by lipid bilayer experiments (J.B.C. 1991). We also found that it works as a Ca^{2+} oscillator (Science 1992) and that IP_3 receptor is essential in fertilization (Science 1992), dorso-ventral axis formation (Science 1996), neurite extension (Science 1997), coupling with the Ca^{2+} channel on the plasma membrane (PNAS 1999). IP_3 receptor deficient mice (Nature 1996) have given an information of the important role in higher brain function and neural plasticity (Nature 2000). In addition, we recently succeeded in solving 3D structure of IP_3 binding domain at 2.2 Å (Nature 2002). As described above, we have a strong background of the research and are intensively working by leading the IP_3 receptor / Ca^{2+} signaling research.
References	1)Furuichi, T., Yoshikawa, S., Miyawaki, A., Wada, K., Maeda, N. & Mikoshiba, K.: Primary structure and functional expression of the inositol 1,4,5-trisphosphate-binding protein P400. Nature 342 32-38 (1989) 2) Saneyoshi, T., Kume, S., Amasaki, Y. & Mikoshiba, K.: The Wnt/Calcium pathway activates NF-AT and promotes ventral cell fate in *Xenopus* embryos. Nature 417 295-299 (2002)
Term of Project	Fiscal years 2003-2007 . (5years)

Budget Allocation (in thousand of yen)	FY2003	FY2004	FY2005	FY2006	FY2007	TOTAL
	20,000	18,600	18,600	17,700	17,700	92,600

Homepage Address	http://www.ims.u-tokyo.ac.jp/kagaku/mikoshibalab.html http://www.brain.riken.go.jp/japanese/bj_rear/b4_jlob/b4_jtop.html