Special Issue in Honor of Professor Katsuhiko Mikoshiba

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Published online: 26 May 2011
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Katsuhiko Mikoshiba

It is our great pleasure to organize this special issue in honor of our dear friend and former boss, Professor Katsuhiko Mikoshiba.

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One editor, Professor Hideyuki Okano, began his training under Professor Mikoshiba in 1979. Back in those days he was an undergraduate medical student, and Professor Mikoshiba was an Assistant Professor. In physiology lectures at the Keio University School of Medicine Hideyuki recalls how Professor Mikoshiba always talked about his research with great joy and shining eyes. Since Hideyuki was just an undergraduate student, he couldn't grasp everything Professor Mikoshiba talked about in detail. But

one thing he understood well was his professor's great zest for his research. In fact, Hideyuki was so taken by these passionate lectures that he vowed to become a basic researcher like Professor Mikoshiba. The other editor, Professor Kazuhiro Ikenaka joined Professor Mikoshiba's lab at Osaka University in 1985. He had never been involved in the field of brain science, but shortly after working together with Professor Mikoshiba, became so enchanted by Mikoshiba-ism, that he has been working in the field of neurochemistry ever since. Both editors worked with Professor Mikoshiba as faculty members when he started his own lab at the Institute for Protein Research at Osaka University. They've shared both tough (back then) times and beautiful (at present) times together. Back in those days Professor Mikoshiba lived alone, while his family remained back in Tokyo. He worked tirelessly from 7 am until past midnight, and ate three meals a day at the cafeteria on campus. It was our great fortune that he spent to so much time at work because we were able to spend countless hours of valuable time with him. Professor Mikoshiba's family's loss was our gain.

Professor Mikoshiba graduated from the Keio University School of Medicine in 1969, joined Professor Yasuzo Tsukada's lab in the Department of Physiology at Keio University where he received his Ph.D. in 1973. He remained there as an instructor, first as an assistant professor, then later as an associate professor, until 1985, when he moved to Osaka University as a full professor. During this period, from 1976 to 1977, he spent 1 year at the Pasteur Institute in France, working with Dr. Jean-Pierre Changeux. In 1992 he moved to The Institute of Medical Science at The University of Tokyo, eventually retiring from there in 2007. He currently serves as a team leader at the RIKEN Brain Science Institute. What is special about Professor Mikoshiba (at least in Japan) is that he has often been appointed as the professor or group director in separate organizations at the same time, and usually ran more than two labs. Thus he was a professor at the National Institute for Basic Biology from 1986 to 1991, Chief Scientist, Group Director or Team Leader in RIKEN from 1992 to the present, and Project Leader of the Mikoshiba Calciosignal Net Project (Exploratory Research for Advanced Technology—ERATO) from 1995 to 2000. Over the years he has worked together with about 230 scientists, including graduate students, postdocs and faculty members in his labs, of whom nearly 100 received their Ph.D. under his instruction. All of his lab members will tell you that they've been enchanted and drawn in by his enthusiasm for science. Professor Mikoshiba was often

heard to say, "Let us do research in an unexplored field, if we do it at all!" or "You have to be at the top of the world!" and "Do not follow fashion, make the fashion!" His attitude toward science can be represented by his saying, "Do not finish your research with only gene research! What is most important is the research of connecting genes, cells, tissue, organs and organisms. For this purpose, you can utilize mutant mice and connect the genes with the organism and its behavior!" He said this long before we began to produce transgenic animals, therefore, at that time, mutant animals were the only source for this purpose. He kept nearly 10 mutant mouse strains in his lab. It was an enormous surprise to us that animal behavior could be so drastically changed by only one defective gene. Much of his work has originated from the analysis of mutant animals, such as: (1) The neuron-glial interaction project has immersed from the *shiverer* mouse; (2) the developmental neuroscience project from the *reeler* mouse; and (3) the intracellular signaling project from the *staggerer*.

All three of these projects grew to be Professor Mikoshiba's major scientific fields of interest. In particular, he gained worldwide fame by cloning and identifying an important Ca^{2+} channel known as the inositol 1,4,5-trisphosphate receptors (IP_3Rs) through his project #3. Professor Mikoshiba also identified the Ca^{2+} store with which the IP_3R is associated—the endoplasmic reticulum, and directly demonstrated its role as a Ca^{2+} channel that produces all of the important Ca^{2+} oscillations. More recently he identified a new Ca^{2+} store in possession of IP_3Rs —the acidic Ca^{2+} Store. The role of the IP_3R is not confined to Ca^{2+} signaling. In fact recent studies from the Mikoshiba lab identified many new IP_3R binding partners including Na^+ , K^+ -ATPase, 4.1N, ERp44, and IRBIT (**I**nositol **P**rotein released with **I**nositol 1,4,5-**T**risphosphate). This discovery of IRBIT is particularly important, as it represents a new signaling pathway. These exciting findings indicate that the IP_3Rs expand the roles they play in Ca^{2+} signaling to include their diverse roles as a signaling hub.

To honor his numerous outstanding achievements, Professor Mikoshiba has received around 20 noteworthy awards, starting with the Erwin von Balz prize in 1974 to the very recent, 2011 Honorary Doctorate of Medicine from Karolinska Institutet in Sweden.

In this special issue, all of his three major fields are well covered by many of his colleagues. We are proud to present this publication in tribute to Professor Mikoshiba's extraordinary lifetime of achievement.