



PERSONAL

Retirement

Professor FUTAKI, Shiroh
Division of Biochemistry
– Biofunctional Design-Chemistry –



On March 31, 2025, Dr. Shiroh Futaki retired from Kyoto University and was honored with the title of Professor Emeritus of Kyoto University.

Dr. Futaki graduated from the Faculty of Pharmaceutical Sciences, Kyoto University in 1983. He received his master's degree from the Graduate School of Pharmaceutical Sciences, Kyoto University in 1985 and his Ph.D. in Pharmaceutical Sciences from Kyoto University in 1989. He became a research associate and associate professor at the Faculty of Pharmaceutical Sciences, Tokushima University in 1987 and 1993, respectively. Meanwhile, he spent 16 months (1989–1991) in the United States as a Postdoctoral Associate in the Department of Biochemistry, Rockefeller University. In 1997, he became an associate professor at the Institute for Chemical Research, Kyoto University, and was promoted to full professor in 2005. In addition, from 2010 to 2015, he served as Vice Director of the Institute for Chemical Research, Kyoto University.

Dr. Futaki has made significant contributions to peptide science, particularly in the area of design and functional analysis of membrane-interacting peptides. These include: (1) discovery of cell membrane permeability of arginine-rich peptides and analysis of membrane interaction and permeation mechanism; (2) intracellular delivery using arginine-rich cell-penetrating peptides and membrane permeabilizing peptides; (3) creation of peptides that affect cell membrane curvature, lipid packing, and tension; and (4) potentials of macropinocytosis in intracellular delivery.

Dr. Futaki is best known for (1) and (2). The idea of cell-penetrating peptides has opened a new stream in chemistry-based cellular studies and drug development. He is one of the pioneers in this field of research. Initially, he was motivated to understand the mystery of membrane permeability of HIV Tat-derived cationic segment (TAT peptide). After studying the cell permeation behavior of a number of RNA-binding peptides, he realized that membrane permeability is ubiquitously shared among arginine-rich peptides. This also shed light on the fundamental role of arginines in the TAT peptide.

Dr. Futaki was also interested in analyzing the internalization mechanisms of arginine-rich cell-penetrating peptides. He reported that cellular uptake of arginine-rich peptides involves macropinocytosis, which is an actin-driven, clathrin-independent fluid-phase endocytosis. At that time, macropinocytosis was considered to be only a specific form of endocytosis associated with host infection by some viruses. However, subsequent studies by the research group

and others have revealed the importance of macropinocytosis in the cellular uptake of a wide variety of extracellular materials.

Regarding the transport of substances/materials across cell membranes, the membranes have mostly been considered as canonical lipid bilayers without lipid packing defects. However, Dr. Futaki proposes the conceptual importance of lipid packing defects for membrane translocation, which can be induced by peptide-membrane interaction. Through the development of curvature-inducing peptides, he realized that dynamic structural changes of cell membranes are accompanied by lipid packing defects. This eventually allowed membrane translocation of arginine-rich peptides. He also developed a peptide capable of delivering antibodies (IgG) into cells. The sequence was originally from a lytic peptide derived from a spider venom, but the lytic activity on the cell surface was ingeniously attenuated by the placement of negatively charged Glu residues in the potentially hydrophobic face of the peptide. However, later studies have shown that this also has activity to induce membrane ruffling, lipid packing defects and transient permeation of membranes.

As a result of the above work, he has published more than 290 original papers and 55 reviews. He has served as Principle Investigator of PRESTO, SORST and CREST programs of Japan Science and Technology Agency (JST). His honors also include Visiting Professor, Université Pierre et Marie Curie in Paris in 2010 and Honorary Member of the Hungarian Academy of Sciences since 2019. He was awarded by The Pharmaceutical Society of Japan (PSJ) Award in 2020, The Akabori Memorial Award, which is given to scientists who have made significant contributions to the advancement of research in peptide science in the world, in 2022, and The Naito Memorial Award for the advancement of science, in 2024. He served as co-chair of the 10th International Peptide Symposium/55th Japanese Peptide Symposium, which was held in Kyoto in 2018. He also held the positions of trustee of the Japanese Biochemical Society and head of the Kinki Branch, vice president and trustee of the Japanese Peptide Society, and trustee of the Pharmaceutical Society of Japan and head of the Kansai Branch.

His contribution to Kyoto University and the Institute for Chemical Research through his scientific, teaching, and administrative activities is greatly appreciated. His warm and sincere personality will remain in the hearts of his colleagues and students.