Yoshimi Kakinuma, Ph.D.

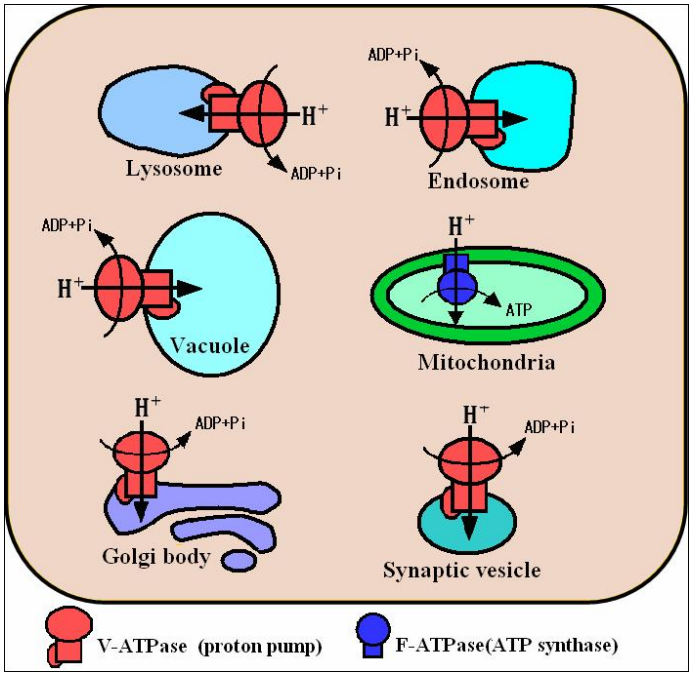
Professor, Laboratory of Molecular Physiology and Genetics, Faculty of Agriculture, Ehime University; Professor, Integrated Center for Science, Ehime University

Dr. Yoshimi Kakinuma is a biochemist in the field of membrane bioenergetics. His general interest is to demonstrate at the molecular level the physiology of a variety of transporters distributed from microorganisms to mammals. In the beginning of his study, he characterized V-ATPase from the yeast vacuole as a new proton-translocating ATPase. In 1990, he discovered another new ATPase, sodium-translocating V-ATPase in an enterococcus and confirmed this ATPase as the first eukaryotic V-ATPase homologue in bacteria by gene cloning. Based on these pioneering activities on V-ATPase research, he received The Pharmaceutical Society of Japan Award for Young Scientist 1996, and he has been frequently invited to the important international meetings in bioenergetics. Topics on V-ATPase are now covered in many international textbooks on biochemistry. His focus is now the 3D structure and molecular mechanism of V-ATPase as the ion-translocating rotary motor and the significance of ATPase and other transporters in cellular ion homeostasis of the persistent toxic substances originated from environmental pollution as the target molecules.

Molecular Basis for Estimating the Action of Persistent Pollutants as Disrupters of Cellular Ion Homeostasis

The maintenance of the intracellular concentration of various ions and metabolites at relatively constant levels, known as “homeostasis”, is indispensable for all living organisms. However, the toxic effects of persistent substances originated from environmental pollution on cellular ion homeostasis and risk assessment are not well investigated. We are interested in the molecular mechanism of regulation of the intracellular concentration of cations, such as K^+, Na^+, Ca^{2+}, Mg^{2+}, especially the pH (pH homeostasis) and associated energy metabolism. Eukaryotic cells contain highly differentiated single membrane organelles including Golgi body, endosomes, lysosomes, synaptic vesicles and vacuoles (in plant cells). These endomembrane organelles are involved in important cellular processes such as sorting of proteins and lipids, receptor-mediated endocytosis, protein degradation and processing, and neural/hormonal signal transduction. They are also essential for particular functions of specialized tissues or cells such as antigen presentation, blood clotting, bone remodeling, and regulation of growth factors and hormones. One of the common features of these organelles is their luminal acidic pH that is indispensable for their functions.

The luminal acidification is carried out mainly by the vacuolar-type, proton–translocating ATPase (V-ATPase). V-ATPase and transporters of these acidic organelles might be the important targets of pollutants during the disruption of cellular ion homeostasis. Although our current work is structural biology and nanoscience of sodium-translocating enterococcal V-ATPase, which is the eukaryotic V-ATPase homologue, as the ion-translocating rotary motor, we are now planning to investigate the influence of various pollutants on the cellular functions of V-ATPase and transporters. Our goal is to understand the action of persistent pollutants as disrupters of cellular ion homeostasis at the molecular level.



Distribution of V-ATPase and F-ATPase in organelles