Lessons from Yeast
- Autophagy as a Cellular Recycling System -

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Every cellular event is achieved through a balance between synthesis and degradation of its constituents such as protein. The cellular degradation is highly regulated and plays crucial roles in cell physiology. Autophagy is a major pathway of intracellular degradation of cytoplasmic components within lysosome/vacuole.

In 1988 I first found under a light microscope that the yeast *S. cerevisiae* induces massive protein degradation in the vacuole under nutrient starvation. Electron microscopy revealed that membrane dynamics during this process are principally the same as macroautophagy in mammals. Taking advantage of the yeast system, many autophagy-defective mutants were obtained. Now we know that 18 *ATG* genes are essential for starvation-induced autophagy. Those Atg proteins concertedly function in the sequestration process of cytoplasmic constituents into the autophagosome. These proteins consist of six functional units, including an Atg1 kinase complex, the PI3 kinase complex and two unique ubiquitin-like conjugation systems. Soon our group found that *ATG* genes are well conserved from yeast to mammals and plants. The identification of *ATG* genes had completely changed the landscape of autophagy research. Genetic manipulation of the *ATG* genes in various organisms and cell types unveiled a truly broad range of physiological functions of autophagy. Autophagy plays critical roles not only in nutrient recycling, but also intracellular clearance through the elimination of harmful or damaged proteins and organelles. It is becoming clear that autophagy is relevant to many diseases and has become one of the most popular field in cell biology.

Recent structural and physiological analyses of Atg proteins revealed the molecular details of the unique membrane dynamics during autophagy.
I will present our current stage of Atg protein research. We are also trying to

answer about physiological roles of autophagy in yeast. We show that autophagy plays important roles in the intracellular ion homeostasis and RNA degradation via autophagy. We are also trying to comprehend details of degradation process in the vacuole and identify final degradation products and their physiological impacts by taking advantage of yeast system.
I would like to discuss about future perspective of autophagy research.