

Special Lecture

June 8 (Fri) 11:15-12:15 Room A

Chairperson: Tamotsu Yoshimori (Osaka Univ.)

SL 11:15-12:15 Looking back on my 30 years of autophagy research
Yoshinori Ohsumi (Tokyo Tech.)

Intracellular degradation is highly regulated and active processes, and plays critical roles in cell physiology. Under nutrient starvation recycling of own cellular constituents via autophagy becomes crucial for survival. Since discovery of lysosome and coining autophagy as a self-eating process by C. de Duve, for long time not much progress had been made about its molecular details and physiological role.

I used to work on the yeast vacuole and found active transport system and v-Type ATPase on the membrane. In 1988 I decided to launch to lytic function of the vacuole, and first found the yeast, *S. cerevisiae*, induces massive protein degradation in the vacuole under nitrogen-starvation by light microscopy. Then electron microscopy revealed that membrane dynamics during the process is topologically the same as known macroautophagy in mammals, indicating yeast provides a good model system for molecular dissection of autophagy. Taking advantage of the yeast system, we succeeded in isolation of many autophagy-defective mutants. We proposed that 18 *ATG* genes are essential for starvation-induced autophagy which encode the proteins essential for the sequestration of cytoplasmic constituents by forming a specialized membrane structure, the autophagosome. They consist of six functional units, which sequentially are recruited to the autophagosome formation site. Soon we found that these *ATG* genes are well conserved from yeast to mammals. The identification of the *ATG* genes completely changed the landscape of autophagy research. By genetic manipulation of *ATG* genes in various organisms and specific organ or cell type, revealed so broad range of physiological functions of autophagy.

Currently we are challenging to fundamental questions such as degradation process and physiological function of autophagy in yeast. The historical landmarks underpinning the explosion of autophagy research are presented with a particular focus on the contribution of yeast as a model organism.