Title of Project : Multidisciplinary research on autophagy: from molecular mechanisms to disease states

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【Purpose of the Research Project】

In order to create living organisms, and keep them functional and of good quality, it is important to not only synthesize but also degrade their constituents. The cell contains proteins, lipid, sugar, nucleotides, and organelles. Intracellular degradation systems play essential roles in removal and recycling of these components. Autophagy is one of the major degradation systems, which delivers cytoplasmic materials to the lytic organelle, 'lysosome' (Figure 1). Japanese researchers have contributed greatly to this field through the identification of autophagy-related genes and the understanding of physiological roles of autophagy. It has become evident that autophagy is essential for various pathophysiological processes such as the maintenance of the amino acid pool during starvation, early embryonic development, the prevention of neurodegeneration and cancer, degradation of invading bacteria, and regulation of immune responses.

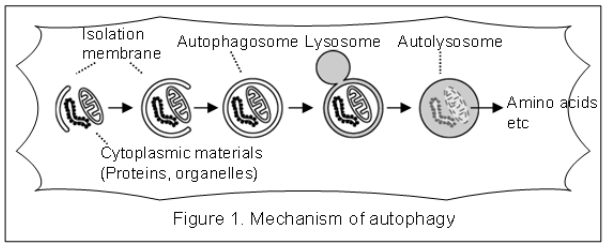

Figure 1. Mechanism of autophagy

Autophagy research is now entering the next important phase, which should address more comprehensive understanding of molecular mechanisms of autophagy, and its relationship with human diseases. In this Project, we will pursue multidisciplinary research on autophagy using *in vitro* reconstitution systems, structural and cell biological techniques, various model organisms, and human genetics.

【Content of the Research Project】

A01: Molecular mechanisms and membrane dynamism of autophagy. Using *in vitro*, yeast, and mammalian culture systems, our focus will be on the molecular function and structure of autophagy-related proteins, and the mechanism of autophagosome formation, elongation of the isolation membrane, and autophagosome-lysosome fusion.

A02: Physiology and pathology of autophagy. In this project, we will investigate novel functions of autophagy particularly focusing on metabolism, cellular renovation, selective degradation, and human diseases. We will also explore novel types of autophagy.

As a multidisciplinary group, the two common topics of “selective autophagy” and “autophagy-modulating compounds” will be investigated both in A01 and in A02

We will establish a web-based discussion forum “Autophagy Forum”, where papers from our groups or outside researchers are introduced and discussed. We will also collaborate with “Autophagy Database” (http://www.tanpaku.org/autophagy/index.html)

【Expected Research Achievements and Scientific Significance】

As autophagy is closely related to many research fields such as cell biology, biochemistry, metabolism, developmental biology, neurology, immunology, oncology, inflammation, and anti-aging medicine, this Innovative Area researches will provide novel insights and techniques in these basic, applied, and clinical areas.

【Key Words】

Lysosome: An intracellular organelle that contains more than 60 hydrolytic enzymes.
Autophagy: A cellular process that deliver cytoplasmic materials to the lysosome for degradation.

【Term of Project】 FY2013-2017

【Budget Allocation】 1,232,300 Thousand Yen

【Homepage Address and Other Contact Information】

http://proteolysis.jp/autophagy/