Horning cell self-digestion: Autophagy wins the 2016 Nobel Prize in Physiology or Medicine

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**A B S T R A C T**

Autophagy is an evolutionarily conserved process by which eukaryotic cells eliminate intracellular components via the lysosomal degradation process. This cell self-digestion process was first discovered and morphologically characterized in the late 1950s and early 1960s. The genetic screen studies in baker’s yeast in the 1990s further identified the essential genes functioning in the autophagic process. In the past two decades, the detailed molecular process involved in the completion of autophagy was delineated. Additionally, autophagy has been implied to function in many aspects of biological processes, including maintenance of organelle integrity, protein quality control, regulation of the stress response, and immunity. In addition to maintain cell homeostasis, autophagy has recently been shown to be modulated and to participate in the pathogenesis of human diseases, such as pathogen infections, neurodegenerative diseases, and tumor development. Overall, the breakthrough in autophagy research relies on the discovery of autophagy-related genes (ATGs) using a genetic screening approach in Saccharomyces cerevisiae, which was established by Yoshinori Ohsumi. This year the Nobel Committee has awarded Yoshinori Ohsumi the Nobel Prize in Physiology or Medicine for his remarkable contribution to autophagy research.

The term “autophagy” is derived from the Greek words for eat (“phagy”) and oneself (“auto”) and was coined in the early 1960s by Christian de Duve, the 1974 Nobel Laureate in Physiology or Medicine, who discovered lysosomes and peroxisomes [1]. In response to stresses, such as nutrient deprivation, protein unfolding and aggregation, or invasion of pathogens, autophagy is activated to regulate a variety of biological pathways to counteract these adverse stimuli, thus maintaining cellular homeostasis [2,3]. The entire process of autophagy involves a stepwise membrane rearrangement process. At the initial step, the particular membranous structure, the so-called isolation membrane (IM)/phagophore, is first originated...
from various organelles, such as endoplasmic reticulum (ER) [4,5], plasma membrane [6], mitochondria [7], and Golgi apparatus [8]. Then, the IM/phagophore further elongates and envelopes the cargo to form a double-membraned autophagosome. Autophagosomes sequester the cargo and fuse with lysosomes, forming autolysosomes in which the engulfed materials are degraded and recycled for further use by cells [2,3]. Although autophagy has been long considered a non-selective bulk degradation process, mounting evidence shows that autophagy can selectively degrade damaged organelles and infecting pathogens [2,3]. The cargo receptors of selective autophagy specifically recognize the polyubiquitinated cargo and subsequently target them to autophagic degradation via interacting with ATG8 family proteins [9,10].

Uncovering of autophagy-related genes (ATGs)

Autophagy was first characterized in the late 1950s by transmission electron microscopy observation of dense bodies that sequester the digestive mitochondria and ER and deliver them to be eliminated by lysosomal proteases in monkey kidney tissue and rat hepatocytes [11–14]. Later, at the 1963 Ciba Foundation symposium on lysosomes, Christian de Duve defined these sequesterating vacuoles that contain cytoplasmic components and lysosomal degradation enzymes as a cell self-lytic process and named it “autophagy” [1]. Soon afterwards, several studies noted that hormones can activate or repress autophagic process due to a loss of autophagic vacuoles in yeast cells [23]. Yoshinori Ohsumi also defined these sequestrating vacuoles that contain cytoplasmic components and lysosomal degradation enzymes as a cell self-lytic process and named it “autophagy” [1].

In the past decade, autophagy has been shown to play functional roles in the development of human diseases [2,48,49]. Hence, modulation of autophagic activity by a specific enhancer or inhibitor has therapeutic potential as a new strategy for curing human diseases. New findings and concepts regarding the regulation and function of autophagy are still growing. Additionally, several fundamental questions for autophagy, such as the origin of preautophagosomal structure and the molecular mechanism responsible for membrane regeneration of vacuoles, are still unanswered and require further investigations. Nevertheless, Yoshinori Ohsumi’s tremendous contribution to autophagy research presents a hallmark for how to utilize baker’s yeasts in biomedical research and has clinical implications for understanding the pathogenesis of human diseases.

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

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