EDITORIAL

The word *autophagy* originates from the Greek words *auto-*, meaning "self", and *phagein*, meaning "to eat". Thus, autophagy denotes "self-eating". This concept emerged during the 1960's, when researchers first observed that the cell could destroy its own contents by enclosing it in membranes, forming sack-like vesicles that were transported to a recycling compartment, called the *lysosome,* for degradation. Difficulties in studying the phenomenon meant that little was known until, in a series of brilliant experiments in the early 1990's, Yoshinori Ohsumi used baker's yeast to identify genes essential for autophagy. He then went on to elucidate the underlying mechanisms for autophagy in yeast and showed that similar sophisticated machinery is used in our cells.

Ohsumi's discoveries led to a new paradigm in our understanding of how the cell recycles its content. His discoveries opened the path to understanding the fundamental importance of autophagy in many physiological processes, such as in the adaptation to starvation or response to infection. Mutations in autophagy genes can cause disease, and the autophagic process is involved in several conditions including cancer and neurological disease. The Belgian scientist Christian de Duve was awarded the Nobel Prize in Physiology or Medicine in 1974 for the discovery of the lysosome.

During the 1970's and 1980's researchers focused on elucidating another system used to degrade proteins, namely the "proteasome". Within this research field Aaron Ciechanover, Avram Hershko and Irwin Rose were awarded the 2004 Nobel Prize in Chemistry for "the discovery of ubiquitin-mediated protein degradation". The proteasome efficiently degrades proteins one-by-one, but this mechanism did not explain how the cell got rid of larger protein complexes and worn-out organelles. Could the process of autophagy be the answer and, if so, what were the mechanisms?

Yoshinori Ohsumi was born in 1945 in Fukuoka, Japan. He received a Ph.D. from University of Tokyo in 1974. After spending three years at Rockefeller University, New York, USA, he returned to the University of Tokyo where he established his research group in 1988. He is since 2009 a professor at the Tokyo Institute of Technology.

The 2016 Nobel Prize in Physiology or Medicine is awarded to Yoshinori Ohsumi for his discoveries of mechanisms for autophagy.

This year's Nobel Laureate discovered and elucidated mechanisms underlying *autophagy*, a fundamental process for degrading and recycling cellular components.

Autophagy removes long-lived proteins, large macro-molecular complexes and organelles that have become obsolete or damaged. Autophagy mediates the digestion and recycling of non-essential parts of the cell during starvation and participates in a variety of physiological processes where cellular components must be removed to leave space for new ones. In addition, autophagy is a key cellular process capable of clearing invading microorganisms and toxic protein aggregates, and therefore plays an important role during infection, in ageing and in the pathogenesis of many human diseases.

Autophagosome is transient and only exists for ~10-20 minutes before fusing with the lysosome, making morphological and biochemical studies very difficult. Different subtypes of autophagy can now be distinguished depending on the cargo that is, degraded macroautophagy degrades large portions of the cytoplasm and cellular organelles. Non-selective autophagy occurs continuously, and is efficiently induced in response to stress, e.g. starvation. In addition, the selective autophagy of specific classes of substrates-protein aggregates, cytoplasmic organelles or invading viruses and bacteria-involves specific adaptors that recognize the cargo and targets it.

Microautophagy, involves the direct engulfment of cytoplasmic material via inward folding of the lysosomal membrane, and chaperone-mediated autophagy.

Autophagy removes long-lived proteins and is the only process. Thus, autophagy plays an essential role in the maintenance of cellular homeostasis. Moreover, autophagy participates in a variety of physiological processes, such as cell differentiation and embryogenesis.

Autophagy participates in a variety of physiological processes, such as cell differentiation and embryogenesis that require the disposal of large portions of the cytoplasm. The rapid induction of autophagy in response to different types of stress underlies its cytoprotective function and the capacity to counteract cell injury and many diseases

associated with ageing because the deregulation of the autophagic flux is directly or indirectly involved in a broad spectrum of human diseases, autophagy is a particularly interesting target for therapeutic intervention.

Autophagy is linked to physiological processes including embryogenesis and cell differentiation, adaptation to starvation and other types of stress, as well as pathological conditions including neurodegenerative diseases, cancer and infections.

The capacity of autophagy to eliminate invading microorganisms, a phenomenon called xenophagy, underlies its key role in the activation of immune responses and the control of infectious diseases.

The discovery of autophagy genes, and the elucidation of the molecular machinery for autophagy by Yoshinori Ohsumi have led to a new paradigm in the understanding of how the cell recycles its contents. Because of his pioneering work, autophagy is recognized as a fundamental process in cell physiology with major implications for human health and disease.

Autophagy controls important physiological functions where cellular components need to be degraded and recycled. Autophagy can rapidly provide fuel for energy and building blocks for renewal of cellular components, and is therefore essential for the cellular response to starvation and other types of stress. After infection, autophagy can eliminate invading intracellular bacteria and viruses. Autophagy contributes to embryo development and cell differentiation. Cells also use autophagy to eliminate damaged proteins and organelles, a quality control mechanism that is critical for counteracting the negative consequences of aging.

Disrupted autophagy has been linked to Parkinson's disease, type 2 diabetes and other disorders that appear in the elderly. Mutations in autophagy genes can cause genetic disease. Disturbances in the autophagic machinery have also been linked to cancer. Intense research is now ongoing to develop drugs that can target autophagy in various diseases.

Anju Jain