

The 2016 Nobel Prize in Physiology or Medicine

The Nobel Prize in Physiology or Medicine for 2016 was awarded to Yoshinori Ohsumi (Japan) for his work on autophagy. Autophagy, meaning 'self-eating', is the process where the cell content like large macromolecule complexes or organelles are fused with the lysosome for degradation and recycling. While other processes like the ubiquitination are usually targeting single and short-lived proteins, autophagy has the ability to target complexes of longer-lived macromolecules for recycling. Autophagy is a normal process in the cell, necessary for maintaining a healthy working cell. The autophagy process occurs more commonly in resting, stressed or starving cells, and is a survival strategy for the cell. Autophagy is tightly regulated, and cells with access to an abundance of nutrients are inhibited by the Class III PI(3) kinase – mTOR pathway.

The discovery

As early as 1963, the concept of autophagy was suggested by Christian de Duve (1974 Nobel Laureate). But, the details of the autophagy process were not revealed until Y. Ohsumi developed a yeast (*Saccharomyces cerevisiae*) model system with visible autophagic bodies. By studying random mutations and phenotypic changes in the yeast cells, he was able to identify 15 genes (ATG1-15) involved in the autophagy process [1, 2]. The genes were later cloned and their involvement in the process was shown. The process of autophagy occurs in an ordered and controlled manner where various components are integrated into the forming autophagosome in a cascading manner, very much like the complement cascade.

The benefit of the discovery

The discovery of autophagy has shown us how evolutionary conserved and important this process is for a healthy cell function. Autophagy is important in many aspects of health and disease and is involved in embryogenesis and also helping to clear intracellular infectious agents. On the other hand, failing to successfully perform autophagy or impairment of regulation of the process properly may lead to disease. Mutations in autophagy-associated genes may increase the risk of developing breast and ovarian cancer. A non-functioning autophagy process lacks the ability to remove misfolded proteins, which in turn may cause neurodegenerative disease.

Conclusion

The discovery of autophagy has revealed fundamental processes in cells and also explains the mechanisms for certain diseases. The mapping of the various phases and regulation of the autophagy process has given us the potential to intervene therapeutically in these diseases.

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References

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- 2 Tsukada M, Ohsumi Y. Isolation and characterization of autophagy-defective mutants of *Saccharomyces cerevisiae*. *FEBS Lett* 1993;333:169–74.