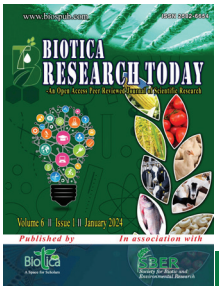
Bio. Res. Today 2024, 6(1):30-32



Biotica Research Today

e-ISSN: 2582-6654

January, 2024

Article ID: RT1549 Popular Article

Autophagy: Versatility and Essentiality in Cellular Homeostasis and Beyond

Berryish Metha, C.[1*], Eniya A.[2] and Samuel P.[1]

[1]*Dept. of Plant Biotechnology, Centre for Plant Molecular Biology and Biotechnology, Tamil Nadu Agricultural University, Coimbatore, Tamil Nadu (641 003), India*

[2]*Dept. of Agricultural Entomology, Centre for Plant Protection Studies, Tamil Nadu Agricultural University, Coimbatore, Tamil Nadu (641 003), India*

Open Access

Corresponding Author

Berryish Metha, C.

: berryishmethac@gmail.com

Conflict of interests: The author has declared that no conflict of interest exists.

How to cite this article?

Berryish *et al*., 2024. Autophagy: Versatility and Essentiality in Cellular Homeostasis and Beyond. *Biotica Research Today* 6(1), 30-32.

Abstract

Autophagy, governed by autophagy-related genes (ATGs), is essential for cellular homeostasis. It impacts diverse cellular functions, including development, reproduction, metabolism, hormone signaling, cell death, senescence, and stress responses. The article delves into macro-autophagy, micro-autophagy, and chaperone-mediated autophagy (CMA), emphasizing cargo specificity. Bulk autophagy engulfs cellular constituents indiscriminately, while selective autophagy targets specific proteins or organelles. In plants, stress-induced selective autophagy involves regulators like BES1 and TSPO. The intricate machinery of macro-autophagy in plants, driven by ATG proteins, participates in lipid transfer, phagophore formation, and autophagosome-vacuole fusion. Initiation mechanisms, including ATG9 vesicles, ATG2-ATG18 complexes, and phosphatidylinositol synthase-enriched ER subdomains, are explored. The review scrutinizes autophagy's role in virus infection, emphasizing its protective function against cell death and its dual impact on anti-viral and pro-viral responses. Silencing ATG genes compromise plant immunity, while certain viruses exploit autophagy for infection. Understanding autophagy's regulation informs therapeutic interventions and agricultural applications, highlighting its versatility and essentiality.

Keywords: Autophagy machinery, Autophagosome, Programmed cell death, Plant-virus interactions

Introduction

Autophagy, an intracellular degradation mechanism, is critical for maintaining cellular homeostasis in a wide range of organisms. While vacuoles serve as key components in yeast and plant cells, lysosomes function similarly in mammalian cells. Underlying cellular homeostasis is the basal level of autophagy, which involves the ongoing elimination of unneeded or damaged cellular components. This process is governed by autophagy-related genes (ATGs), ensuring the recycling of materials and providing anabolic substrates for cellular functions.

Autophagy proves to be multifaceted and employs its influence on various aspects of cellular physiology. It significantly contributes to developmental processes, reproduction, and metabolic regulation. Additionally, autophagy plays a pivotal role in hormone signaling, influencing cellular responses to different hormonal cues. The pathway is intricately involved in programmed cell death, senescence, and responses to both abiotic and biotic stresses. Under stressful conditions, autophagy is induced to remove damaged components and recycle materials, thereby supporting cellular survival and adaptation. In essence, autophagy emerges as a versatile and essential mechanism, influencing diverse cellular functions across different organisms (Yang *et al.*, 2020).

Classes of Autophagy

Autophagy comes in three different forms: macro-autophagy, micro-autophagy, and chaperone-mediated

Article History

RECEIVED on 18th January 2024 RECEIVED in revised form 24th January 2024 ACCEPTED in final form 25th January 2024

autophagy (CMA). Mammals are the only animals that can engage in chaperone-mediated autophagy (CMA), in which HSC70 recognizes particular cytosolic proteins with targeting patterns. This complex binds to LAMP-2A on lysosomes, inducing multimerization and facilitating substrate crossing of lysosomal membranes (Chen *et al.*, 2021). Micro-autophagy involves the association of cytoplasmic materials with the vacuolar surface, leading to engulfment through tonoplast invagination. Membrane fission, which releases autophagic bodies, occurs next. The most well-known type of autophagy, known as macro-autophagy, involves the sequestration of cellular constituents in an autophagosome - a double-membrane-bound structure. The mature autophagosome is delivered to the vacuole for degradation, involving phagophore formation, expansion, and fusion with the lysosome (Kalamgi and Larsson, 2016).

Autophagy Depending on Cargo Specificity

The kind of autophagy is determined by cargo specificity. Cellular constituents are ingested by non-selective bulk autophagy without being given preference for destruction. Conversely, receptors mediate the particular engulfment of certain proteins or organelles during selective autophagy. Selective autophagy responses in plants under stress involve key regulators such as BES1 in the brassinosteroid pathway and TSPO, a stress-induced membrane protein. BES1, targeted to the autophagy pathway under stress, interacts with DSK2 and ATG8. TSPO exemplifies how plants utilize selective autophagy mechanisms to respond to environmental stressors (Yang *et al.*, 2020).

The Autophagy Machinery in Plants

Plant macro-autophagy shows how ATG proteins facilitate the transfer of lipids from the endoplasmic reticulum (ER) to the developing phagophore, causing it to enlarge and close (Yang *et al.*, 2020). The ATG8-phosphatidylethanolamine (PE) system, along with other complexes, contributes to autophagosome formation and subsequent fusion with the vacuole for degradation. Autophagy-related genes (ATGs) sequentially regulate the fusion of autophagosomes with vacuoles. The double-membraned autophagosomes, central to the autophagy machinery, originate from the phagophore assembly site (PAS), a cup-shaped structure derived from the ER.

Autophagosome Formation

Initiation of autophagosome formation requires the presence of ATG9 vesicles at the PAS. Deficiency of ATG9 leads to outgrowth from an ER subdomain, with progression within the ER and involvement of ATG18a trafficking. ATG9 mediates the initiation of autophagosome formation at phosphatidylinositol synthase-enriched ER subdomains. ATG2's interaction with the PI3P-binding protein ATG18 facilitates the PAS's expansion and results in a complicated localization to the tonoplast. The growth of autophagosomes and the location of PAS depend on ATG18's PI3P-binding function. The PAS is tethered by the ATG2-ATG18 complex, which localises to the autophagosome's opening edge. ATG2 is also thought to mediate direct lipid transfer between membranes, according to recent research (Yang *et al.*, 2020).

Autophagy during Virus Infection

Plants and viruses can interact in ways that lead to hypersensitive response (HR) and programmed cell death (PCD). Autophagy prevents PCD from spreading beyond the sites of pathogen infection. Silencing autophagy-related genes, such as Beclin1/atg6, results in unrestricted PCD even in uninfected regions. Autophagy induction during virus infection plays a protective role against cell death, restricting PCD to infectious sites.

Compatible interactions, where disease development is suppressed, are observed in atg5 and atg7 mutant Arabidopsis plants infected with Cauliflower mosaic virus (CaMV). These mutants exhibit heightened disease symptoms, premature senescence and tissue necrosis (Zvereva and Pooggin, 2012).

Anti-viral Autophagy

Silencing ATG genes compromises the plant's immune response against DNA and RNA viruses. Turnip mosaic virus (TuMV), tomato yellow leaf curl virus (TYLCV) and cotton leaf curl Multan virus (CLCuMuV) are among the viruses that autophagy combats. This selective autophagy process serves as a defense mechanism against viral infections (Zvereva and Pooggin, 2012).

Pro-viral Autophagy

Pro-viral autophagy involves the promotion of viral infection by blocking and manipulating autophagy. Viruses use specific proteins to block the normal autophagic processes within host cells. For example, the γb protein of the Barley Stripe Mosaic Virus (BSMV) obstructs ATG7, preventing autophagy. Turnip mosaic virus (TuMV) proteins obstruct autophagy that is dependent on NBR1, which facilitates the growth of the virus (Wu *et al.*, 2022).

Conclusion

The dynamic interplay between autophagy and various cellular processes underscores its versatility and essentiality in maintaining cellular homeostasis across organisms. Understanding the intricate regulatory mechanisms and the impact of autophagy on diverse physiological functions provides valuable insights for therapeutic interventions and agricultural applications.

References

Chen, X., Wang, J., Tahir, M., Zhang, F., Ran, Y., Liu, Z., Wang, J., 2021. Current insights into the implications of m6A RNA methylation and autophagy interaction in human diseases. *Cell & Bioscience* 11, 147. DOI: https://doi.org/10.1186/s13578-021-00661-x.

Kalamgi, R.C., Larsson, L., 2016. Mechanical signaling in the pathophysiology of critical illness myopathy. *Frontiers in Physiology* 7, 23. DOI: https://doi.org/10.3389/fphys.2016.00023.

Wu, W., Luo, X., Ren, M., 2022. Clearance or hijack: Universal interplay mechanisms between viruses and host autophagy from plants to animals. *Frontiers in Cellular and Infection Microbiology* 11, 1345. DOI: https://doi.org/10.3389/fcimb.2021.786348.

Yang, M., Ismayil, A., Liu, Y., 2020. Autophagy in plant-virus interactions. *Annual Review of Virology* 7, 403-419. DOI: https://doi.org/10.1146/annurev-virology-010220-054709.

Zvereva, A.S., Pooggin, M.M., 2012. Silencing and innate immunity in plant defense against viral and non-viral pathogens. *Viruses* 4(11), 2578-2597, DOI: https://doi.org/10.3390/v4112578.