Decoding the Spatiotemporal Dynamics of Autophagosomal Membrane Elongation in Response to Endoplasmic Reticulum Stress

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Abstract. This study elucidates the cellular mechanisms underlying autophagosomal membrane elongation triggered by ER stress. Utilizing advanced live-cell imaging and quantitative proteomics, we identified key regulatory proteins modulating membrane dynamics. Our findings reveal a novel interaction between ER-associated degradation pathways and autophagic processes, providing insights into potential therapeutic targets for diseases characterized by dysfunctional autophagy.

Keywords: autophagosome biogenesis, endoplasmic reticulum stress, live-cell imaging, quantitative proteomics, cellular homeostasis

Introduction

Autophagy, a lysosome-mediated degradation pathway, is crucial for cellular homeostasis and adaptation to stress. The autophagosomal membrane elongation is a vital stage in the autophagic process, particularly under conditions of endoplasmic reticulum (ER) stress, which is implicated in numerous pathological states including neurodegeneration, cancer, and metabolic disorders. The precise molecular mechanisms orchestrating the formation and elongation of autophagosomes remain incompletely understood, warranting further investigation. Recent studies have highlighted the endoplasmic reticulum's pivotal role in serving as a membrane source for autophagosome biogenesis. However, the dynamic interaction between ER stress responses and autophagosomal membrane dynamics is yet to be fully elucidated. This gap in knowledge represents a significant hurdle in the development of targeted therapies aimed at modulating autophagic responses in disease. In this article, we employ state-of-the-art live-cell imaging techniques and quantitative proteomics to investigate the protein networks involved in autophagosomal membrane

elongation during ER stress. We characterize the interactions between ER-associated degradation pathways and autophagic processes, providing novel insights into the regulatory mechanisms that could potentially be exploited for therapeutic benefit. The paper is structured as follows: Section 2 details the methodology employed in our study, including imaging and proteomic analysis techniques. Section 3 presents our findings, with a discussion on the implications of these results for understanding autophagic dynamics. Finally, Section 4 offers a conclusion and potential directions for future research.

References

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