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Tracking Mitochondria-ER Interactions: Advances in Signal-Integrating Reporter Development

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INTRODUCTION

Mitochondria-endoplasmic reticulum (ER) contacts play a crucial role in various cellular processes, including calcium signaling, lipid metabolism, and apoptosis. The close proximity between these organelles facilitates the exchange of metabolites, ions, and signaling molecules, contributing to cellular homeostasis and function. Monitoring the dynamics of mitochondria-ER contacts is essential for understanding their physiological significance and their role in health and disease. Recent advancements in reporter technology have led to the development of signal-integrating reporters capable of visualizing and quantifying mitochondria-ER interactions with high spatiotemporal resolution. Mitochondria and the endoplasmic reticulum are two essential organelles involved in numerous cellular functions, each with distinct roles and functions. However, emerging evidence has highlighted the significance of their physical and functional interactions, particularly at specialized regions known as mitochondria-ER contact sites or mitochondria-associated membranes (MAMs). These contact sites serve as platforms for inter-organelle communication and coordination of various cellular processes.

DESCRIPTION

One of the challenges in studying mitochondria-ER contacts lies in the dynamic and transient nature of these interactions. Traditional methods for monitoring organelle interactions, such as electron microscopy and fluorescence microscopy, provide valuable insights but are often limited by their spatial and temporal resolution. Moreover, these techniques may not capture the dynamic changes in mitochondria-ER contacts in living cells over time. To address these limitations, researchers have developed signal-integrating reporters that enable real-time visualization and quantification of mitochondria-ER interactions in living cells. These reporters typically consist of fluorescent proteins or luminescent probes targeted to specific subcellular compartments, such as mitochondria and the ER, coupled with complementary protein domains that undergo specific interactions at mitochondria-ER contact sites. One approach to developing signal-integrating reporters involves the use of split fluorescent proteins, where the fluorescent protein is divided into two non-fluorescent fragments that reassemble and fluoresce upon interaction at mitochondria-ER contact sites. By fusing each fragment to proteins localized to mitochondria and the ER, respectively, researchers can visualize and quantify the extent of mitochondria-ER contacts based on the reconstitution of fluorescent signal at these sites. Another strategy for developing signal-integrating reporters involves the use of Förster resonance energy transfer (FRET)-based probes, where fluorescent proteins or dyes are paired with compatible donor-acceptor pairs that undergo energy transfer upon close proximity. By targeting these probes to mitochondria and the ER, researchers can measure changes in FRET signal as an indicator of mitochondria-ER contacts in living cells. Recent advancements in reporter technology have enabled the development of Genetically Encoded Calcium Indicators (GECIs) targeted to mitochondria and the ER, which can be used to monitor calcium dynamics at mitochondria-ER contact sites.

CONCLUSION

The development of signal-integrating reporters for monitoring mitochondria-ER contacts has opened up new avenues for studying the dynamic interplay between these organelles in living cells. These reporters provide valuable tools for investigating the molecular mechanisms underlying mitochondria-ER interactions, as well as their physiological significance in cellular homeostasis and disease. By combining advanced imaging techniques with genetically encoded reporters, researchers can gain unprecedented insights into the dynamic nature of mitochondria-ER contacts and their role in cellular function and dysfunction.

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