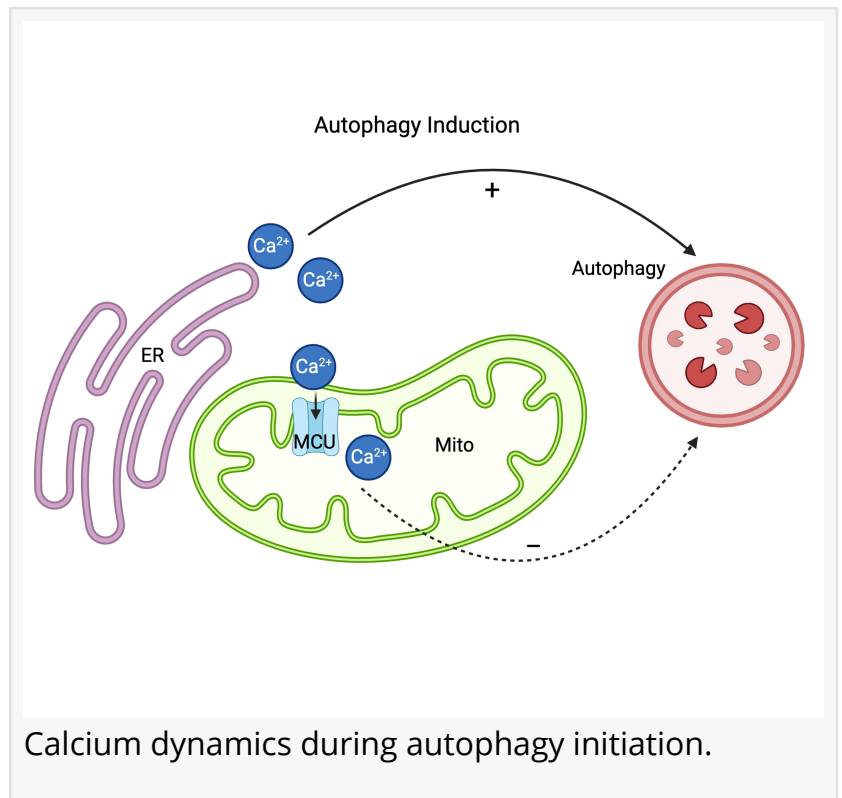


Modulation of cellular recycling by calcium ion dynamics across cellular compartments

USA, March 12, 2024

/EINPresswire.com/ -- This study discovers that upon induction of different autophagy processes, mitochondria immediately import calcium and calcium concentrations at the ER membrane start to fluctuate. The major calcium import channel in the inner [mitochondrial](#) membrane, mitochondrial calcium uniporter (MCU), is required for mitophagy-inducer-initiated mitochondrial calcium uptake. Inhibiting MCU accelerates mitophagy. In neurons derived from a Parkinson's patient, mitophagy-inducer-triggered mitochondrial calcium influx is faster, which may slow the ensuing mitophagy.



Autophagy is a self-eating process for recycling and rejuvenating cellular organelles and components. Intracellular calcium dynamics has been shown to be essential for the initiation of the autophagy process. Mitochondria are a major calcium store within the cell and mitochondria import cytosolic calcium when its level is elevated. However, whether and how mitochondria import calcium during autophagy initiation and whether the uptake of calcium by mitochondria impinges on the autophagy process are not well explored. The answers to these questions could have significant physiological and pathophysiological relevance and shed light on disease mechanisms.

In a new study (<https://doi.org/10.1016/j.mitoco.2024.01.002>) published in the KeAi journal Mitochondrial Communications, a team of researchers from Stanford University School of Medicine examined acute mitochondrial and endoplasmic reticulum (ER) calcium transport responses to various autophagy inducers across different cell types. They aimed to elucidate the relationship between mitochondrial calcium uptake and mitophagy.

Through live monitoring of calcium ions using multiple imaging techniques, the team observed rapid calcium influx into mitochondria upon autophagy induction, coinciding with fluctuations in calcium concentrations at the ER membrane.

"The mitochondrial calcium uniporter (MCU), the primary calcium import channel in the inner mitochondrial membrane, plays a crucial role in mediating mitochondrial calcium uptake triggered by mitophagy inducers," explains Xinnan Wang, senior and corresponding author of the study.

Additionally, the researchers examined mitochondrial calcium transport in induced pluripotent stem cell (iPSC)-derived neurons from a Parkinson's disease (PD) patient and the corresponding control. They discovered faster mitochondrial calcium influx in neurons from the PD patient upon mitophagy induction.

Wang notes, "Given the known influence of cytosolic and ER membrane calcium dynamics on autophagy initiation, our findings suggest a possibility: mitochondria import calcium to regulate mitophagy velocity, and inter-organelle calcium signaling may modulate intricate cellular processes."

"Our study sheds light on the nuanced interplay between mitochondrial calcium dynamics and autophagy, offering insights into potential therapeutic avenues for diseases characterized by dysfunctional autophagy, such as Parkinson's disease," concludes Wang. Top of Form Bottom of Form

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