Rewiring of organelle dynamics and metabolic adaptation during nutrient stress

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Eukaryotic cells contain a variety of membrane-bound compartments called organelles that mediate the important biochemical functions necessary for life. Rewiring organelle dynamics is essential for cells to appropriately react to altering environments such as nutrient deprivation. How such dynamics are rewired on a cell-wide scale remains unknown. I show that, during nutrient starvation, early endosomal signaling lipid turnover by MTM1, a phosphatidylinositol 3-phosphate [PI(3)P] 3-phosphatase mutated in X-linked centronuclear myopathy in humans, controls mitochondrial morphology and function by reshaping the endoplasmic reticulum (ER). Starvation-induced early endosomal recruitment of MTM1 impairs PI(3)P-dependent contact formation between tubular ER membranes and early endosomes, resulting in the conversion of ER tubules into sheets, the inhibition of mitochondrial fission, and sustained oxidative metabolism. This study unravels an important role for early endosomal lipid signaling in controlling ER shape and, thereby, mitochondrial form and function to enable cells to adapt to fluctuating nutrient environments.

References:

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