Advances in microscopy have revealed specific contact points between the ER and other organelles, forming regulated pathways for interorganelle communication crucial for cellular homeostasis. One well-studied example is the interaction between ER and mitochondria, forming mitochondria-associated ER membranes (MAMs). MAMs are involved in various cellular functions, including mitochondrial metabolism, lipid exchange, apoptosis, and Ca2+ and ROS signaling. The ER is a major intracellular calcium store, and calcium release from the ER can affect mitochondrial function. Ca2+ exchange between the ER and mitochondria is closely linked to redox signaling, and ER stress can influence signaling in MAMs, impacting cell fate. During ER stress, changes in MAMs lead to increased Ca2+ influx from the ER to mitochondria, triggering mitochondrial ROS generation and the opening of mPTPs, resulting in cell death. NOX4, enriched in MAMs, promotes pro-survival signaling in response to stress in cardiomyocytes by inhibiting ER-mitochondrial Ca2+ influx and mPTP-dependent necrosis. Redox regulation of MAMs plays a role in cardiac remodeling in response to hypertension and other cardiovascular diseases. MAM-related proteins accumulate in cardiomyocytes during the initial stage of cardiac hypertrophy. MAMs are also involved in inflammation of the rostral ventrolateral medulla (RVLM), contributing to sympathetic hyperactivity in stress-induced hypertension. Reduced expression of sigma-1R (s-1R), an ER chaperone enriched in MAMs, in the RVLM during stress-induced hypertension leads to decreased ER-mitochondria contact. Administration of SKF10047, an s-1R agonist, reduces mitochondrial ROS production and RVLM neuroinflammation, ameliorating sympathetic hyperactivity in hypertensive rats.

Summarized by © lakhasly.com