OPEN ACCESS Freely available online

ISSN: 2167-7662
Bioenergetics: Open Access

Perspective

Effects of Cholesterol Depletion on Mitochondrial Function and Cellular Energy

Bem Rosenbaum*

Department of Molecular Bioenergetics, University of Vienna, Vienna, Austria

DESCRIPTION

Mitochondria, recognized as the powerhouse of cells, play a central role in maintaining cellular health and functionality. They govern processes including energy production, signaling pathways and apoptosis. Central to these functions is the composition of mitochondrial membranes, which determine both structural integrity and functional efficacy. Cholesterol, though often associated with cellular membranes in general, exists in limited concentrations within mitochondrial membranes. Despite its modest presence, mitochondrial cholesterol plays a vital role in regulating mitochondrial structure and bioenergetic functions. The depletion of cholesterol in mitochondrial membranes has been observed to lead to substantial disruptions in these areas, impacting not only the energy balance within cells but also influencing wider cellular health.

While most cellular membranes contain a high concentration of cholesterol, the mitochondrial membrane contains relatively lower levels. Cholesterol's distribution is not uniform across cellular compartments and this disparity reflects the unique functions and requirements of different cellular organelles. Cholesterol in mitochondrial membranes contributes to membrane fluidity and influences the activity of membrane-bound proteins, including enzymes integral to bioenergetic processes. For instance, cholesterol impacts the function of electron transport chain complexes, which are essential in the process of oxidative phosphorylation, the primary pathway for ATP generation in cells. ATP, in turn, provides energy that fuels various cellular activities. Therefore, cholesterol is an integral component of mitochondrial structure and bioenergetics, even though it is present in modest amounts.

The mechanisms behind mitochondrial cholesterol depletion involve various factors, including cellular signaling processes, alterations in cholesterol transport proteins and external stressors. Cholesterol is transported to mitochondria through specialized proteins like the Steroidogenic Acute Regulatory Protein (StAR) and Translocator Protein (TSPO), which facilitate its import across mitochondrial membranes. Disruptions in these transport pathways can result in cholesterol depletion in mitochondria. Additionally, metabolic stress or alterations in cellular lipid metabolism can influence cholesterol content within mitochondrial membranes. Understanding the mechanisms of mitochondrial cholesterol depletion is essential to grasp the subsequent effects on mitochondrial structure and bioenergetic functions.

Cholesterol's role in maintaining mitochondrial structure becomes evident when cholesterol levels are depleted. Mitochondrial membranes, both the Outer Mitochondrial Membrane (OMM) and Inner Mitochondrial Membrane (IMM), are impacted by cholesterol concentration. Cholesterol influences membrane fluidity and alterations in its levels lead to significant changes in membrane properties. Cholesterol depletion can result in increased membrane permeability, which disrupts the balance of ions and molecules across mitochondrial membranes. This disturbance compromises the mitochondrial membrane potential, a critical element for ATP production and cellular survival.

Additionally, cholesterol depletion can result in morphological changes in mitochondria, including alterations in mitochondrial cristae. Mitochondrial cristae are folds in the inner mitochondrial membrane where electron transport chain complexes are located. These structures are crucial for efficient ATP production as they increase the surface area available for oxidative phosphorylation. Changes in cholesterol levels can lead to a loss of cristae integrity and density, which directly impacts the capacity of mitochondria to produce ATP. The structural changes brought about by cholesterol depletion, therefore, have a profound effect on mitochondrial function and, by extension, cellular health.

Cholesterol plays a direct role in modulating the bioenergetic functions of mitochondria and its depletion can disrupt these processes. Mitochondria are responsible for producing ATP through oxidative phosphorylation, a process that relies on the

Correspondence to: Bem Rosenbaum, Department of Molecular Bioenergetics, University of Vienna, Vienna, Austria, E-mail: bem@rosenbaum.au

Received: 27-May-2024, Manuscript No. BEG-24-27423; **Editor assigned:** 29-May-2024, PreQC No. BEG-24-27423 (PQ); **Reviewed:** 12-Jun-2024, QC No. BEG-24-27423; **Revised:** 19-Jun-2024, Manuscript No. BEG-24-27423 (R); **Published:** 26-Jun-2024, DOI: 10.35248/2167-7662.24.12.260

Citation: Rosenbaum B (2024). Effects of Cholesterol Depletion on Mitochondrial Function and Cellular Energy. J Bio Energetics. 12:260.

proper functioning of the electron transport chain. Cholesterol is essential for maintaining the structural integrity of electron transport chain complexes and any disruption in cholesterol content can lead to inefficiencies in these complexes. When mitochondrial cholesterol is depleted, the stability of these complexes is compromised, leading to reduced ATP production and overall bioenergetic efficiency.

Moreover, mitochondrial cholesterol depletion can influence Reactive Oxygen Species (ROS) production. Under normal conditions, ROS are by-products of oxidative phosphorylation and are regulated by antioxidant mechanisms within cells. However, cholesterol depletion can exacerbate ROS generation, leading to oxidative stress. Elevated ROS levels can damage mitochondrial components, including lipids, proteins and DNA. This damage, in turn, further compromises mitochondrial function and accelerates cellular aging and degeneration. The effects of cholesterol depletion on bioenergetics thus extend beyond ATP production, affecting broader aspects of mitochondrial and cellular health.

The depletion of mitochondrial cholesterol does not only affect mitochondria but has far-reaching implications for cellular health. As mitochondria are involved in various cellular processes, including apoptosis, calcium signaling and metabolic regulation, disruptions in mitochondrial structure and function due to cholesterol depletion can lead to cellular dysfunction. For example, alterations in calcium handling within mitochondria, which is influenced by cholesterol, can disrupt cellular calcium homeostasis. Calcium ions play a role in numerous cellular signaling pathways and any imbalance can have cascading effects on cellular health.