

Mitochondrial Activity in Immune Cells: An Essential Component of Health

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Abstract

Mitochondria, the powerhouses of the cell, play a critical role in maintaining immune cell health and promoting optimal immune responses. Beyond their primary function of energy production, mitochondria contribute to a range of vital cellular processes in immune cells, including calcium signaling, reactive oxygen species (ROS) generation, metabolic reprogramming, and cell fate decisions. Proper mitochondrial function is essential for immune cell activation, differentiation, proliferation, and effector functions. Dysregulation or impairment of mitochondrial function in immune cells has been associated with immune-related disorders such as autoimmune diseases, chronic inflammation, and immunodeficiency syndromes. This article provides an overview of the multifaceted roles of mitochondria in immune cells and emphasizes their significance in preserving immune health. Understanding the interplay between mitochondria and immune cells holds promise for developing novel therapeutic strategies to modulate immune responses and combat immune-mediated diseases.

Keywords: Mitochondria; Immunodeficiency syndromes; Mediated diseases; Immune system

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Introduction

The immune system is a complex network of cells and molecules that defends the body against invading pathogens and maintains tissue homeostasis. Among the diverse cellular components of the immune system, mitochondria, the powerhouse of the cell, play a crucial role in orchestrating immune responses. Mitochondrial function in immune cells is not limited to energy production but extends to influencing cellular signaling, metabolic reprogramming, and cell fate decisions. This article explores the vital role of mitochondria in immune cells and highlights their contribution to maintaining immune health [1-4].

Energy Production and Immune Cell Activation

One of the primary functions of mitochondria is to generate adenosine triphosphate (ATP) through oxidative phosphorylation. In immune cells, such as T cells, B cells, and macrophages, ATP is required for diverse processes, including cell activation, migration, and effector functions. Mitochondrial ATP production provides the necessary energy for immune cell activation and supports their ability to mount effective immune responses [5].

Mitochondria and Calcium Signaling

In addition to energy production, mitochondria contribute to

calcium signaling in immune cells. Calcium is a crucial signaling molecule involved in immune cell activation, cytokine production, and cell survival. Mitochondria uptake and release calcium ions, thus modulating intracellular calcium levels. This intricate interplay between mitochondria and calcium signaling influences immune cell functions and helps regulate immune responses.

Reactive Oxygen Species (ROS) Generation

Mitochondria are known to be a major source of reactive oxygen species (ROS) within cells. ROS, including superoxide and hydrogen peroxide, have both beneficial and detrimental effects in immune cells. While ROS act as signaling molecules for immune cell activation and pathogen killing, excessive ROS production can lead to oxidative damage. Maintaining a balance in mitochondrial ROS production is critical for immune cell function and overall immune system health [6].

Metabolic Reprogramming and the Warburg Effect

During immune cell activation, metabolic reprogramming occurs to meet the energy demands of immune responses. Mitochondrial function and dynamics play a pivotal role in this process. Immune cells shift their metabolic pathways to favor glycolysis, a process known as the Warburg effect. This metabolic switch not only

supports energy production but also influences immune cell differentiation, effector functions, and cytokine production [7].

Cell Survival and Apoptosis

Mitochondria are closely involved in regulating cell survival and apoptosis (programmed cell death) in immune cells. Mitochondrial dysfunction or imbalances in cellular energy metabolism can lead to cell death or impaired immune responses. Maintaining healthy mitochondrial function is crucial for ensuring the survival and proper functioning of immune cells.

Implications for Health and Disease

Dysregulation or impairment of mitochondrial function in immune cells has been implicated in various immune-related disorders. Autoimmune diseases, chronic inflammation, and immunodeficiency syndromes have all been associated with mitochondrial dysfunction. Understanding the role of mitochondria in immune cells and their interactions with immune signaling pathways holds significant potential for developing novel therapeutic strategies to modulate immune responses and treat immune-mediated diseases [8].

Methods

Cellular Isolation and Culture

Immune cells, such as T cells, B cells, macrophages, and dendritic cells, can be isolated from peripheral blood, lymphoid tissues, or specific organs using established protocols.

Cells can be cultured in appropriate growth media supplemented with necessary nutrients and growth factors to support their survival and proliferation (Table 1).

Measurement of Mitochondrial Membrane Potential

Mitochondrial membrane potential is an indicator of mitochondrial function.

$\Delta\psi_m$ can be measured using fluorescent dyes, such as tetramethylrhodamine methyl ester (TMRM) or JC-1, and analyzed by flow cytometry or fluorescence microscopy [9].

ATP Measurement

Cellular ATP levels can be assessed as a measure of mitochondrial energy production.

ATP quantification assays, such as luciferase-based bioluminescence assays or ATP detection kits, can be used to measure ATP content in immune cells.

Mitochondrial Calcium Imaging

Mitochondrial calcium dynamics can be visualized using calcium-sensitive fluorescent dyes, such as Rhod-2 AM or Fluo-4 AM.

Live-cell imaging techniques, such as confocal microscopy or multiphoton microscopy, can be employed to monitor mitochondrial calcium uptake and release in response to immune cell activation (Table 2).

Reactive Oxygen Species (ROS) Detection

ROS production by mitochondria can be assessed using fluorescent probes, such as dihydroethidium (DHE) or MitoSOX Red, which specifically target mitochondria [10].

Flow cytometry or fluorescence microscopy can be used to quantify ROS levels in immune cells.

Metabolic Profiling

Metabolic reprogramming in immune cells can be evaluated by analysing key metabolites using techniques like mass spectrometry-based metabolomics.

Measurements of glucose consumption lactate production and oxygen consumption rates can provide insights into metabolic alterations associated with immune cell activation [11].

Table 1. Key functions of mitochondria in immune cells.

Function	Description
Energy Production	Generates adenosine triphosphate (ATP) through oxidative phosphorylation
Calcium Signaling	Participates in intracellular calcium dynamics, influencing immune cell activation
Reactive Oxygen Species (ROS) Generation	Produces ROS as byproducts of mitochondrial respiration
Metabolic Reprogramming	Facilitates the metabolic switch from oxidative phosphorylation to glycolysis
Cell Survival and Apoptosis	Regulates cell survival and apoptosis in immune cells

Table 2. Techniques for studying mitochondrial function in immune cells.

Cellular Isolation and Culture	Isolate immune cells from peripheral blood or tissues for in vitro studies
Measurement of Mitochondrial Membrane Potential ($\Delta\psi_m$)	Assess mitochondrial membrane potential as an indicator of mitochondrial function
ATP Measurement	Quantify ATP levels to evaluate mitochondrial energy production
Mitochondrial Calcium Imaging	Visualize mitochondrial calcium dynamics using fluorescent dyes
Reactive Oxygen Species (ROS) Detection	Measure mitochondrial ROS production using fluorescent probes
Metabolic Profiling	Analyze metabolites to study metabolic reprogramming in immune cells
Mitochondrial DNA (mtDNA) Analysis	Assess mtDNA content, mutations, or deletions in immune cells
Functional Assays	Perform functional assays to evaluate immune cell responses and viability
Genetic Manipulation and Pharmacological Interventions	Modify mitochondrial function using genetic or pharmacological approaches

Mitochondrial DNA (mtDNA) Analysis

Quantitative PCR or DNA sequencing can be employed to assess mtDNA copy number and detect mutations or deletions in mitochondrial genes in immune cells.

Changes in mtDNA content or mutations can indicate mitochondrial dysfunction.

Functional Assays

Functional assays, such as immune cell activation assays, cytokine production assays, or cell viability assays, can be performed to evaluate the impact of mitochondrial modulation or dysfunction on immune cell function.

These assays can include ELISA, flow cytometry, or other appropriate methods to measure immune cell responses.

Genetic Manipulation and Pharmacological Interventions

Genetic manipulation techniques, such as gene knockout or knockdown using CRISPR/Cas9 or RNA interference, can be used to investigate the specific roles of mitochondrial proteins or regulators in immune cell function.

Pharmacological interventions, such as the use of mitochondrial-targeted antioxidants or modulators of mitochondrial function, can be employed to assess the effects on immune cell behavior [12-15].

Discussion

The discussion section focuses on the significance of mitochondrial function in immune cells and its implications for maintaining immune health. It highlights the key findings from the research on mitochondrial involvement in immune cell biology and its potential therapeutic implications for immune-related disorders.

Mitochondria, as the powerhouses of the cell, are known for their role in energy production through oxidative phosphorylation. However, emerging research has revealed that mitochondrial function in immune cells extends beyond energy metabolism and plays a critical role in various aspects of immune cell biology. The findings discussed in this article emphasize the multifaceted roles of mitochondria in immune cells and their importance in maintaining immune system integrity.

One of the notable findings is the impact of mitochondrial function on immune cell activation. Proper energy production by mitochondria is essential for immune cell activation and effector functions. Mitochondrial ATP generation fuels processes such as cell proliferation, migration, and cytokine production,

enabling immune cells to mount effective immune responses. Dysfunctional mitochondria can impair these processes, leading to compromised immune cell function and decreased immune responsiveness [14, 15].

In addition to energy production, mitochondrial calcium signaling is another crucial aspect of immune cell function. Calcium signaling plays a pivotal role in immune cell activation and regulation of immune responses. Mitochondria, through their calcium uptake and release mechanisms, contribute to intracellular calcium dynamics, influencing immune cell activation, cytokine secretion, and cell survival. Deregulated calcium signaling due to impaired mitochondrial function can disrupt immune cell functionality and contribute to immune dysregulation.

Furthermore, the discussion highlights the role of mitochondrial reactive oxygen species (ROS) in immune cell biology. ROS, produced as byproducts of mitochondrial respiration, have dual roles in immune cells. Moderate levels of ROS act as signaling molecules, promoting immune cell activation and pathogen clearance. However, excessive ROS production can lead to oxidative damage and contribute to inflammation and tissue damage. Maintaining a balance in mitochondrial ROS generation is crucial for immune cell function and immune system homeostasis.

Metabolic reprogramming, characterized by a shift towards glycolysis, is a hallmark of immune cell activation. Mitochondrial function and dynamics play a critical role in this metabolic switch, known as the Warburg effect. By adapting their metabolism, immune cells can meet the increased energy demands for activation and effector functions. Understanding the intricate relationship between mitochondria and metabolic reprogramming in immune cells is essential for developing therapeutic strategies that modulate immune responses and potentially treat immune-related disorders.

Conclusion

Mitochondria are not mere energy generators; they play a pivotal role in immune cell function and overall immune system health. From energy production to calcium signaling, ROS generation to metabolic reprogramming, and cell survival to apoptosis, mitochondria influence various aspects of immune cell biology. Further research into the intricate interplay between mitochondria and immune cells will provide valuable insights into the mechanisms underlying immune responses and open new avenues for therapeutic interventions in immune-related disorders. By harnessing the power of mitochondrial function, we can strive towards maintaining a healthy and robust immune system.

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