



Mammalian Inorganic Polyphosphates and their Impact on Cellular Bioenergetics

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DESCRIPTION

Metabolism is a complex network of biochemical reactions that are crucial for the proper functioning of living organisms. Among the various metabolic processes, bioenergetics, which involves the conversion of nutrients into energy, plays a fundamental role in sustaining cellular functions. In recent years, emerging research has analysed on the involvement of mammalian Inorganic Polyphosphates (polyP) in bioenergetic metabolism.

Inorganic Polyphosphates (polyP) are chains of phosphate groups linked by high-energy phosphoanhydride bonds. While initially considered rare in mammalian cells, recent studies have revealed their presence and essential roles in various biological processes. Mammalian cells can synthesize and store inorganic polyphosphates, which can range in length from a few phosphate groups to several hundred.

Bioenergetic metabolism and ATP synthesis

Bioenergetic metabolism primarily revolves around the generation of Adenosine Triphosphate (ATP), the universal energy currency of cells. ATP is produced through two main pathways: substrate-level phosphorylation and oxidative phosphorylation.

Substrate-level phosphorylation involves the direct transfer of a phosphate group from an organic substrate to ADP, resulting in the formation of ATP. This process occurs during glycolysis and the Tricarboxylic Acid (TCA) cycle.

Oxidative phosphorylation takes place in the mitochondria, where electrons from reduced carriers, such as NADH and FADH₂, are passed through the Electron Transport Chain (ETC). This electron flow generates a proton gradient across the mitochondrial inner membrane, which drives ATP synthesis through ATP synthase.

Roles of mammalian inorganic polyphosphates in bioenergetics

ATP Generation and Storage: Mammalian inorganic polyphosphates can directly contribute to ATP synthesis by acting as phosphate donors during substrate-level phosphorylation. Additionally, polyP can serve as a reservoir of high-energy phosphate groups, readily available for ATP synthesis when needed.

Mitochondrial function: PolyP has been shown to modulate mitochondrial bioenergetics. It influences the activity of key enzymes involved in the TCA cycle, oxidative phosphorylation, and mitochondrial membrane potential. PolyP can enhance ATP synthesis by promoting electron flow through the ETC and maintaining mitochondrial membrane integrity.

Cellular signaling: Mammalian inorganic polyphosphates also play a role in cellular signaling, which can indirectly affect bioenergetic metabolism. PolyP has been implicated in regulating intracellular calcium levels, protein phosphorylation, and gene expression, all of which can impact energy metabolism and cellular homeostasis.

Regulation of mammalian inorganic polyphosphates and bioenergetics

Several factors influence the levels and metabolism of mammalian inorganic polyphosphates, ultimately affecting bioenergetic processes.

Enzymatic regulation: Enzymes such as polyphosphate kinases and phosphatases control the synthesis, degradation, and remodeling of polyP. Modulating the activity of these enzymes can impact the availability and utilization of polyP for bioenergetic metabolism.

Cellular stress and energy demand: Cellular stressors, such as nutrient deprivation or oxidative stress, can modulate polyP levels. Under conditions of high energy demand, polyP can be rapidly hydrolyzed to release phosphate groups for ATP synthesis.

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Implications for human health and disease

The intricate relationship between mammalian inorganic polyphosphates and bioenergetics has important implications for human health and disease.

Mitochondrial dysfunction: Mitochondrial dysfunction is a hallmark of numerous diseases, including neurodegenerative disorders, metabolic disorders, and cardiovascular diseases. Understanding the role of polyP in mitochondrial bioenergetics may provide insights into therapeutic strategies for mitigating mitochondrial dysfunction-associated pathologies.

Cellular energetics and aging: Declining bioenergetic capacity is a hallmark of aging. Dysregulation of polyP metabolism may contribute to age-related declines in ATP synthesis and cellular energy balance. Exploring interventions targeting polyP metabolism could potentially restore cellular energetics and slow down the aging process.

Metabolic disorders: Disruptions in bioenergetic metabolism contribute to metabolic disorders such as obesity, diabetes, and

metabolic syndrome. Understanding the role of polyP in energy production and storage may provide novel targets for therapeutic interventions aimed at improving metabolic health.

The emerging field of mammalian inorganic polyphosphates and bioenergetics holds great potential for showing the intricate mechanisms of cellular energy metabolism. Further research is needed to elucidate the precise molecular mechanisms by which polyP influences bioenergetic pathways and to explore their therapeutic implications.

In conclusion, mammalian inorganic polyphosphates are emerging as crucial regulators of bioenergetic metabolism. Their involvement in ATP synthesis, mitochondrial function, and cellular signaling highlights their importance in sustaining cellular energy production and maintaining overall cellular homeostasis. Further investigations into the roles of polyP in health and disease may open new avenues for therapeutic interventions targeting bioenergetic metabolism.