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Commentary

Role of Coenzymes in Citric Acid Cycle

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DESCRIPTION

Coenzymes are major elements of the numerous metabolic processes that keep life alive at the cellular level. A coenzyme is an organic molecule that binds to certain enzyme active sites to help in reaction catalysis. Coenzymes, in particular, can operate as intermediate carriers of electrons during these activities or be transported between enzymes as functional groups. Several coenzymes like free CoA, thiamine pyrophosphate (TPP), lipoic acid (LA), flavin adenine dinucleotide (FAD), oxidized nicotinamide adenine dinucleotide (NAD) and reduced nicotinamide adenine dinucleotide (NADH), are required during the conversion of pyruvate to acetyl co A. Coenzymes, which are typically vitamins or vitamin derivatives, thereby play a critical role in the regulation of most enzyme activities. Apart from the coenzymes involved in the generation of the energy molecule adenosine triphosphate (ATP), various other coenzymes are considered to be necessary for the survival of all living cells [1].

These include oxidized nicotinamide adenine dinucleotide phosphate (NADP+) and its reduced counterpart, NADPH, and other energy coenzymes such as adenosine diphosphate (ADP) and adenosine monophosphate (ADP) (AMP). Several coenzymes, including oxidized glutathione (GSSG) and reduced glutathione, work as antioxidants to remove reactive oxygen species (ROS) (GSH). Glucose is necessary within the body for the synthesis of ATP, which serves to store and distribute energy to cells throughout the body. Glucose can be metabolized either anaerobically (through glycolysis) or aerobically (by the citric acid cycle) [2].

Although glycolysis does not require the addition of oxygen to make ATP, it is restricted in its capacity to extract a considerable quantity of ATP from glucose. In comparison, the citric acid cycle, which requires oxygen input, may create more ATP molecules than glycolysis and so provide more energy to support the numerous metabolic activities necessary to sustain life. However, the citric acid cycle, in association with oxidative phosphorylation, generates more than 95 percent of the energy required by aerobic cells in humans. As previously stated, the citric acid cycle, also known as the Krebs cycle or the tricarboxylic acid cycle (TCA), is critical to all metabolic activities that occur within the cell. TCA is formed when the coenzyme acetyl-CoA condenses to form citrate. Citrate is subsequently dehydrated to make cis-Aconitate, which is rehydrated to form isocitrate [3]. In a two-step process mediated by the enzyme isocitrate dehydrogenase, isocitrate is converted to a-ketoglutarate. As a result of these irreversible reactions, NADH and carbon dioxide are produced (CO_2). Following the formation of a-ketoglutarate, it undergoes an oxidation-reduction process to create succinyl-CoA, a four-carbon molecule, while simultaneously converting NAD+ to NADH. Succinyl-CoA has then transformed to succinate into an energy-saving mechanism that involves phosphorylating guanosine diphosphate (GDP) to guanosine triphosphate (GTP) [4]. GTP quickly converts its terminal phosphate group to ADP, resulting in the production of a new ATP molecule. Other metabolic functions that occur within the mitochondria include programmed cell death, calcium homeostasis, reactive oxygen species (ROS) production, and oxidative stress. Coenzyme dysfunction, like that of any other mitochondrial component, can alter a variety of anabolic and catabolic pathways, contributing to the development of a variety of disease states [5]. Alterations in mitochondrial dynamics have been related to a number of neurodegenerative diseases, including Alzheimer's, Parkinson's, and Huntington's. Similarly, changes in mitochondrial redox potential are implicated in a variety of cardiovascular disorders, including cardiac hypertrophy, myocardial ischemia, reperfusion damage, and hypertension.

CONCLUSION

There is a limited amount of data available to correlate the direct role that coenzymes play in these diseases. However, their importance in the regulation of enzymes known to contribute to certain disease states allows researchers to conclude that coenzymes have an unavoidable impact on these health conditions. While there is still a dearth of understanding, some clinical studies have revealed that combining certain coenzyme treatments can boost the occurrence of favorable results in the treatment of various malignancies and other disorders. More research to better understanding of the molecular activities coenzymes play in certain disease states, researchers hope, may result in the discovery of novel therapeutic targets.

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