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Mini Review

Tricarboxylic Acid (TCA) Cycle in Mammals

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Abstract

The tricarboxylic acid (TCA) cycle, often known as the Krebs cycle, is a critical metabolic system that oxidizes foods to sustain cellular bioenergetics. Recently, it has become clear that TCA cycle activity is dynamic, and that TCA cycle products can be co-opted in cancer and other pathologic situations. We explore the TCA cycle in this overview, including its possible beginnings and the history of its discovery (Elmlinger et al., 2002). TCA (Tricarboxylic Acid) Cycle "TCA cycle is a series of chemical reactions used by all aerobic organisms to release stored energy through the oxidation of acetyl CoA derived from carbohydrates, fats, and proteins into ATP." The TCA cycle, also known as the Tricarboxylic Cycle, is also known as Kreb's Cycle or the Citric Acid Cycle (Soldin et al., 2005).

Keywords: Krebs cycle, Tricarboxylic acid cycle, Cellular immunity, Immunometabolism

INTRODUCTION

TCA cycle, also known as citric acid cycle, is the second stage of cellular respiration, a three-step process by which living cells break down organic fuel molecules in the presence of oxygen to capture the energy they require to grow and divide. Most plants, animals, fungi, and bacteria go through this metabolic process. Except for bacteria, the TCA cycle occurs in the matrix of intracellular structures known as mitochondria. The TCA cycle is important in the breakdown, or catabolism, of organic fuel molecules such as glucose and other sugars, fatty acids, and amino acids. Before these relatively big molecules may join the TCA cycle, they must be reduced into acetyl coenzyme A (acetyl CoA), a two-carbon chemical. Acetyl CoA is transformed into carbon dioxide and energy once it enters the TCA cycle (Owen et al., 2010).

The TCA cycle is made up of eight stages that are catalyzed by eight distinct enzymes. (1) The cycle begins when acetyl CoA interacts with oxaloacetate to create citrate and release coenzyme A (CoA-SH). Then, in a series of reactions, (2) citrate is rearranged to form isocitrate; (3) isocitrate loses a molecule of carbon dioxide and is oxidized to form alpha-ketoglutarate; (4) alpha-ketoglutarate loses a molecule of carbon dioxide and is oxidized to form succinate; (5) succinate is enzymatically converted to succinate; (6) succinate is oxidized to fumarate; (7) fumarate is hydrated to form malate, and (8) malate is oxidized to oxaloacetate. Each complete cycle turn results in oxaloacetate regeneration and the creation of two molecules of carbon dioxide (Konforte et al., 2013).

In this cycle of reactions, energy is created in a number of phases. Step 5 produces one molecule of adenosine triphosphate (ATP), the chemical that fuels most cellular processes. However, the majority of the energy gained from the TCA cycle is caught by the molecules nicotinamide adenine dinucleotide (NAD+) and flavin adenine dinucleotide (FAD) and later converted to ATP (Yang et al., 2005). Energy is transferred by relaying electrons from one material to another, which is accomplished by chemical processes known as oxidation and reduction, or redox reactions. (Oxidation is the removal of electrons from a material and the reduction of electron addition.) Three molecules of NAD+ are reduced to NADH for each TCA cycle turn, while one molecule of FAD is converted to FADH2. The energy from these molecules is subsequently transferred to the electron transport chain, which is part of the third stage of cellular respiration. The electron transport chain then releases energy, which is transformed to ATP via the oxidative phosphorylation process (Davis et al., 2006).

Cellular metabolism is a complicated network of biochemical events that turn nutrients into metabolic building blocks that drive living organisms' development and survival. Energy exchange is required for metabolic activities, which is accomplished by oxidation-reduction reactions that move high-energy electrons from one molecule to another (Carel et al., 2009). Energy, reducing equivalents, and macromolecular precursors are the three basic types of metabolic process outputs. All live cells require these outputs, but the proportional degree to which cells rely on each output is determined by the unique requirements of different cell types and cell states. As a result, a plethora of signaling channels and regulatory networks regulate the balance between catabolic pathways, which break down molecules to harness chemical energy, and anabolic pathways, which organize macromolecular synthesis (Zec et al., 2012).

The TCA cycle does not use molecular oxygen or generate significant amounts of ATP; rather, it takes electrons (reducing equivalents) from inputs (e.g., acetyl-CoA) and transfers them to electron carriers, which deposit their electrons into the electron transport chain (ETC). Electrons passing through the ETC complexes generate mitochondrial membrane potential, which is then used to power the production of the cellular currency (ATP) in a process known as oxidative phosphorylation (OXPHOS), as oxygen serves as the terminal acceptor for electrons passing through the ETC. The TCA cycle is therefore related to oxygen consumption since the ETC regenerates the oxidized electron carriers necessary to continue turning the cycle, and the combined activity of these two pathways allows for the synthesis of considerable amounts of ATP. Because the TCA cycle's primary role in this form is to convert fuel sources into energy, it is commonly referred to be a catabolic process. However, some TCA cycle chemical intermediates also serve as important precursors for biosynthetic events. The TCA cycle is classified as an amphibolic route since it acts in both catabolic and anabolic capacities (Chan et al., 2009).

Cells must carefully tune anabolic and catabolic pathways to maintain nutrient supply and demand balance. The importance of the TCA cycle in both supplying important anabolic substrates and sustaining energy generation, it is not unexpected that TCA cycle activity is tightly regulated physiologic. Multiple metabolic cues modulate both TCA cycle inputs and directionality, and growing evidence reveals the necessity of such TCA cycle flexibility for optimizing cellular fitness under healthy and pathological settings. The repercussions of altering TCA cycle function in animals may be observed in a series of illnesses known as inborn errors of metabolism, which are caused by inherited abnormalities in genes encoding metabolic enzymes. Human patients with TCA cycle-associated gene mutations exhibit neonatal symptoms, developmental abnormalities, and failure to thrive. These findings support the idea that the TCA cycle is important in maintaining mammalian tissue function. The purpose of this review is to go over the wiring of the TCA cycle in great detail, drawing on both historical and contemporary research to present an updated picture of the mammalian TCA cycle as a dynamic metabolic network at the centre of cell life (Elmlinger et al., 2005).

CONCLUSION

Despite the fact that the main biochemical processes of the TCA cycle were discovered over a half-century ago, research into the control and function of the TCA cycle in mammalian cells continues to produce fresh insights. Diverse cell culture model systems and in vivo isotope tracing techniques have combined to reveal significant variability in TCA cycle substrate choice and wiring in both normal and diseased situations. How this variety is accomplished, and to what degree cells may transition between metabolic states, are key unanswered topics. Functional screening advances, as well as efforts to studying metabolism in vivo with greater precision, will uncover cell type-specific metabolic preferences and dependencies that may be targeted to alter cell growth or homeostasis. Given the importance of the TCA cycle in all pathways in cell metabolism, it will be critical to continue to investigate how metabolic networks are coordinated across cellular compartments and how changes in TCA cycle activity signal to modulate key cellular functions like differentiation. A better knowledge of how unique signalling and environmental factors regulate TCA cycle activity may help future efforts to modify cell growth and survival for therapeutic purposes.

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