OPINION ARTICLE

Diabetes Management

The role of glycolysis in energy production: Regulation and its significance

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Description

Glycolysis, a fundamental metabolic pathway, serves as the Foundation of cellular energy production in living organisms. From simple single-celled organisms to complex multicellular beings, glycolysis stands as a universal process essential for sustaining life.

Glycolysis, derived from the greek words "glykys" (sweet) and "lysis" (splitting), is a series of biochemical reactions that convert glucose, a six-carbon sugar molecule, into two molecules of pyruvate, a three-carbon compound. This process occurs in the cytoplasm of cells and serves as the primary means of generating Adenosine Tri Phosphate (ATP), the universal currency of cellular energy.

■ The steps of glycolysis

Glycolysis consists of ten enzymatic reactions, each meticulously orchestrated to convert glucose into pyruvate while generating ATP and Nicotinamide Adenine Dinucleotide (NADH), a coenzyme involved in cellular respiration.

Glucose phosphorylation: Glucose is phosphorylated by the enzyme hexokinase, requiring the input of ATP to form glucose-6-phosphate.

Isomerization: Glucose-6-phosphate is converted into fructose-6-phosphate through the action of phosphoglucose isomerase.

Second phosphorylation: Fructose-6-phosphate is phosphorylated by phosphofructokinase-1, utilizing another ATP molecule to form fructose-1,6-bisphosphate.

Cleavage: Fructose-1,6-bisphosphate is cleaved into two three-carbon molecules, Di Hydroxy Acetone Phosphate (DHAP) and Glyceraldehyde-3-Phosphate (G3P).

Isomerization: DHAP is converted into G3P by the enzyme triose phosphate isomerase, ensuring continuity in subsequent reactions.

Oxidation and ATP generation: G3P is oxidized by glyceraldehyde-3-phosphate dehydrogenase, producing NADH and 1,3-bisphosphoglycerate. Subsequently, phosphoglycerate kinase catalyzes the transfer of a phosphate group from 1,3-bisphosphoglycerate to ADP, yielding ATP and 3-phosphoglycerate.

Phosphorylation: 3-phosphoglycerate is converted into 2-phosphoglycerate by phosphoglycerate mutase, followed by the transfer of a phosphate group to form Phospho Enol Pyruvate (PEP) by enolase.

ATP generation: The high-energy phosphate group of PEP is transferred to ADP by pyruvate kinase, yielding ATP and pyruvate, the final product of glycolysis.

■ Regulation of glycolysis

Glycolysis is tightly regulated to meet the energy demands of cells while adapting to varying physiological conditions. Key regulatory steps.

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Hexokinase and phosphofructokinase-1: These enzymes are subject to allosteric regulation by metabolites such as ATP, ADP, and fructose-2,6-bisphosphate, modulating the rate of glycolytic flux.

Phosphofructokinase-2/fructose-2,6-bisphosphatase: The enzyme phosphofructokinase-2 synthesizes fructose-2,6-bisphosphate, a potent activator of phosphofructokinase-1, promoting glycolysis. Conversely, fructose-2,6-bisphosphatase degrades fructose-2,6-bisphosphate, inhibiting glycolysis.

Pyruvate kinase: Pyruvate kinase is regulated by allosteric effectors such as ATP and alanine, as well as by phosphorylation/dephosphorylation events mediated by protein kinases and phosphatases.

Glycolysis plays a central role in cellular energy production, fueling vital processes such as muscle contraction, nerve impulse transmission, and biosynthesis of cellular components. Moreover, glycolysis serves as a metabolic hub, supplying intermediates for other biochemical pathways, including gluconeogenesis, the pentose phosphate pathway, and lipid biosynthesis.

Dysregulation of glycolysis is implicated in various pathological conditions, including metabolic disorders, cancer, and neurodegenerative diseases. In cancer cells, increased glycolytic activity, known as the Warburg effect, provides a metabolic advantage for rapid proliferation and survival. Targeting glycolytic enzymes or metabolic pathways associated with glycolysis represents a promising strategy for cancer therapy.

Glycolysis stands as a testament to the elegance and efficiency of cellular metabolism, providing a blueprint for energy generation and metabolic adaptation across diverse organisms. By unraveling the difficulty of glycolysis, researchers continue to deepen our understanding of cellular physiology and disease pathogenesis, preparing for innovative therapies and interventions to address metabolic disorders and beyond. As we peer into the molecular complex of glycolysis, we gain newfound appreciation for the remarkable complexity and resilience of life's metabolic system.