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COMPREHENSIVE BIOCHEMICAL ANALYSIS OF HUMAN METABOLISM: INTEGRATED PATHWAYS, REGULATORY MECHANISMS, AND CLINICAL CORRELATIONS

Prepared by: Sagdilloyeva Asila
Tashkent Medical Academy Department of Biological Chemistry
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Scientific Supervisor: Odilova Sh. X.
Faculty: Treatment (or Pediatrics/Dentistry)

Abstract

Biochemistry is the study of chemical processes within and relating to living organisms. At its core, metabolism is a highly coordinated cellular activity in which many multi-enzyme systems (metabolic pathways) cooperate to obtain chemical energy, convert nutrient molecules into the cell's own characteristic molecules, and polymerize monomeric precursors into macromolecules.

Introduction

1. Introduction: The Molecular Logic of Life

Biochemistry is the study of chemical processes within and relating to living organisms. At its core, metabolism is a highly coordinated cellular activity in which many multi-enzyme systems (metabolic pathways) cooperate to obtain chemical energy, convert nutrient molecules into the cell's own characteristic molecules, and polymerize monomeric precursors into macromolecules.

Metabolism is divided into two main parts:

Catabolism: The degradative phase, where complex organic molecules (carbohydrates, fats, proteins) are broken down into simpler end products (CO2, H2O, NH3), releasing energy in the form of ATP.

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Anabolism: The biosynthetic phase, where small precursors are assembled into proteins, nucleic acids, and lipids, requiring an input of energy.

2. Carbohydrate Metabolism: The Primary Energy Flux
The central pathway of carbohydrate metabolism is the oxidation of glucose.

2.1. Glycolysis (The Embden-Meyerhof Pathway)
Glycolysis occurs in the cytosol of all cells. It is a sequence of 10 reactions that converts one molecule of glucose into two molecules of pyruvate.
Key Regulatory Step: The conversion of Fructose-6-phosphate to Fructose-1,6-bisphosphate by Phosphofructokinase-1 (PFK-1). This is the "committed step" of glycolysis.
Energy Yield: A net gain of 2 ATP and 2 NADH per glucose molecule.

2.2. The Citric Acid Cycle (Krebs Cycle)
In aerobic conditions, pyruvate enters the mitochondria and is converted into Acetyl-CoA.
Function: The cycle is the final common pathway for the oxidation of fuel molecules.
Intermediates: Citrate, Isocitrate, \alpha-Ketoglutarate, Succinyl-CoA, Succinate, Fumarate, Malate, and Oxaloacetate.
Anaplerotic Reactions: These reactions replenish cycle intermediates, ensuring that the cycle continues even when intermediates are drawn off for biosynthesis.

3. Lipid Metabolism: Energy Storage and Membranes
Lipids are the most concentrated form of energy storage in the body.

3.1. Fatty Acid \beta-Oxidation
Fatty acids are broken down in the mitochondria to generate Acetyl-CoA, NADH, and FADH_2.
Carnitine Shuttle: This is the rate-limiting transport mechanism that moves long-chain fatty acids into the mitochondria.

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Ketogenesis: When Acetyl-CoA levels exceed the capacity of the Krebs cycle (e.g., during starvation or diabetes), the liver produces ketone bodies (Acetoacetate, \beta-hydroxybutyrate), which serve as an alternative fuel for the brain.

3.2. Lipid Biosynthesis

Cholesterol synthesis occurs primarily in the liver via the Mevalonate pathway. The enzyme HMG-CoA Reductase is the target of statin drugs, demonstrating the direct application of biochemistry in pharmacology.

4. Protein and Amino Acid Metabolism

Amino acids are not stored in the body like fats or carbohydrates; they must be constantly recycled.

4.1. Deamination and the Urea Cycle

The removal of the amino group (-NH_2) is the first step in amino acid catabolism. The resulting ammonia is highly toxic and must be converted to urea in the liver.

Enzymatic Defects: Deficiencies in urea cycle enzymes lead to hyperammonemia, causing severe neurological damage.

4.2. Glucogenic vs. Ketogenic Amino Acids

Amino acids are classified based on their breakdown products. Glucogenic amino acids can be converted into glucose via gluconeogenesis, while ketogenic amino acids are converted into ketone bodies.

5. Bioenergetics and Oxidative Phosphorylation

The Electron Transport Chain (ETC) is located in the inner mitochondrial membrane.

Chemiosmotic Theory: Proposed by Peter Mitchell, it explains that the energy from electron transfer is used to pump protons (H^+) across the membrane, creating a gradient.

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ATP Synthase: This enzyme acts as a molecular turbine, using the flow of protons back into the matrix to phosphorylate ADP into ATP.

6. Integration and Hormonal Control of Metabolism

Metabolism is not a collection of isolated pathways but an integrated system controlled by hormones.

6.1. The Role of Insulin and Glucagon

Insulin: Secreted by the pancreas in response to high blood glucose. It promotes glycolysis, glycogenesis, and lipogenesis ("the hormone of plenty").
Glucagon: Secreted during fasting. It stimulates gluconeogenesis and glycogenolysis in the liver to maintain blood glucose levels.

6.2. Signal Transduction (GPCRs and Tyrosine Kinases)

Hormones act through receptors. For example, epinephrine binds to G-protein coupled receptors (GPCRs), activating adenylate cyclase and increasing cAMP levels, which triggers a cascade of protein phosphorylation.

7. Clinical Biochemistry: When Metabolism Fails

Understanding biochemical pathways allows us to diagnose and treat diseases:
Diabetes Mellitus: A failure in insulin signaling leading to "starvation in the midst of plenty."
Inborn Errors of Metabolism: Genetic defects like Phenylketonuria (PKU), where the enzyme phenylalanine hydroxylase is missing.
Cancer Metabolism (The Warburg Effect): Cancer cells prioritize aerobic glycolysis over oxidative phosphorylation to produce building blocks for rapid cell division.

8. Conclusion

The complexity of biochemistry reveals the intricate balance required for life. From the rotation of ATP synthase to the hormonal regulation of blood sugar, every process is a marvel of molecular engineering. Ongoing research in

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"Omics" (Genomics, Proteomics, Metabolomics) continues to expand our understanding, paving the way for personalized medicine and gene therapy.

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