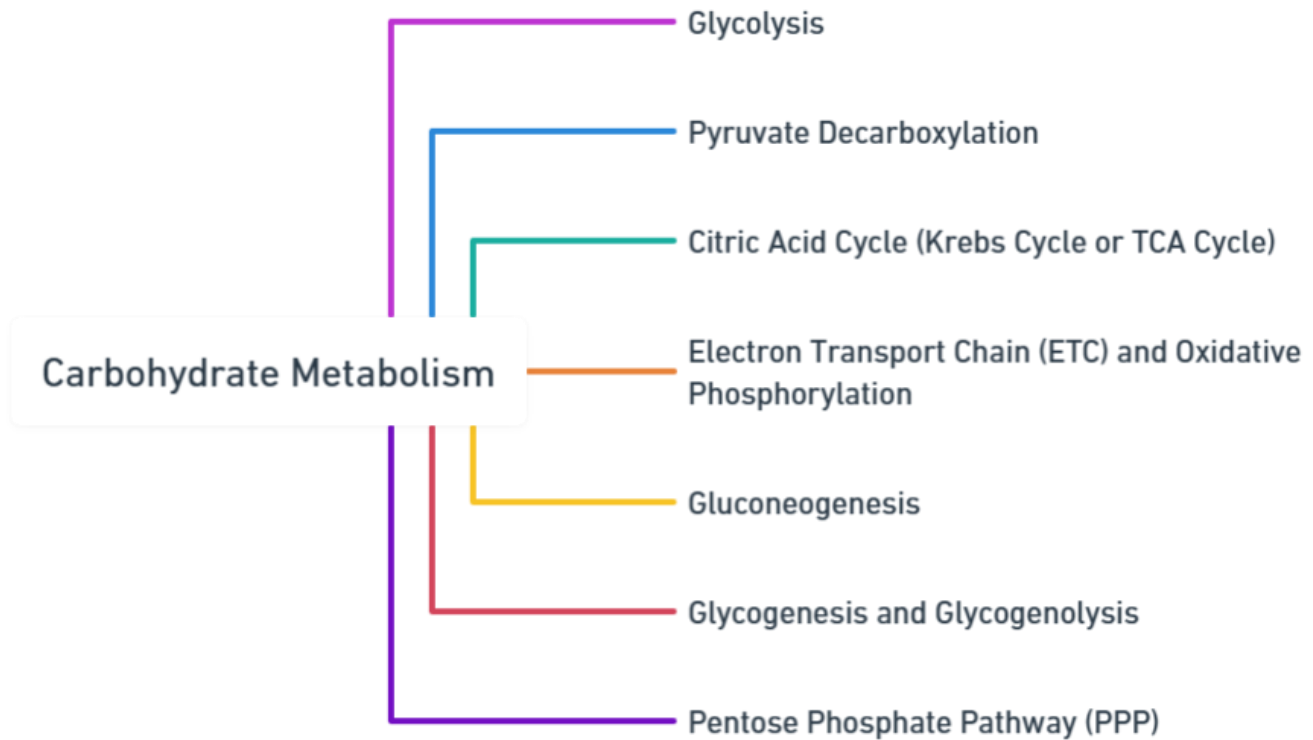


Carbohydrate metabolism

Carbohydrate Metabolism: Key Stages

- Carbohydrate metabolism involves the synthesis, breakdown, and transformation of carbohydrates, primarily for energy production.

Let's delve into the key stages of carbohydrate metabolism in a detailed and organized manner:



1. Glycolysis

- **Location:** Cytoplasm of the cells
- **Process:** The conversion of glucose (a six-carbon molecule) into two molecules of pyruvate (three carbons each).
- **Energy Yield:** 2 ATP (net gain) and 2 NADH per molecule of glucose.
- **Key Points:** Glycolysis is an anaerobic process (does not require oxygen) and is the initial step in the utilization of glucose, providing substrates for further metabolic pathways.

2. Pyruvate Decarboxylation

- **Location:** Mitochondria
- **Process:** Conversion of pyruvate into acetyl CoA via the pyruvate dehydrogenase complex.
- **Outcome:** Production of acetyl CoA, which is a critical intermediate that feeds into the citric acid cycle.
- **Significance:** This step links glycolysis to the citric acid cycle and is crucial for aerobic respiration.

3. Citric Acid Cycle (Krebs Cycle or TCA Cycle)

- **Location:** Mitochondrial matrix
- **Process:** Acetyl CoA enters the cycle, undergoing a series of enzyme-catalyzed reactions that produce NADH, FADH₂, and GTP/ATP.
- **Energy Yield:** Each acetyl CoA molecule results in 3 NADH, 1 FADH₂, and 1 GTP (or ATP), contributing to significant ATP production through oxidative phosphorylation.
- **Role:** Central metabolic pathway that generates high-energy electron carriers for the electron transport chain.

4. Electron Transport Chain (ETC) and Oxidative Phosphorylation

- **Location:** Inner mitochondrial membrane
- **Process:** Utilizes NADH and FADH₂ to generate a proton gradient across the membrane, driving the synthesis of ATP through ATP synthase.
- **Energy Yield:** The majority of ATP in cellular respiration is produced here, with approximately 34 ATP molecules generated per glucose molecule.
- **Mechanism:** Electrons from NADH and FADH₂ pass through a series of complexes, ultimately reducing oxygen to water.

5. Gluconeogenesis

- **Location:** Mainly in the liver and to some extent in the kidneys
- **Process:** Synthesis of glucose from non-carbohydrate sources, such as lactate, glycerol, and amino acids.
- **Importance:** Essential during fasting or prolonged exercise to maintain blood glucose levels.

6. Glycogenesis and Glycogenolysis

- **Glycogenesis:** The synthesis of glycogen from glucose, primarily occurring in the liver and muscle cells for energy storage.
- **Glycogenolysis:** The breakdown of glycogen back into glucose, providing a rapid source of glucose when needed by the body.
- **Regulation:** These processes are tightly regulated by hormones (e.g., insulin promotes glycogenesis, while glucagon stimulates glycogenolysis).

7. Pentose Phosphate Pathway (PPP)

- **Location:** Cytoplasm
- **Process:** An alternative glucose metabolic pathway that generates NADPH (for biosynthetic reactions and antioxidant defense) and ribose-5-phosphate (a precursor for nucleotide synthesis).
- **Significance:** Provides essential components for fatty acid synthesis, nucleotide biosynthesis, and maintenance of reduced glutathione levels.

Regulation and Hormonal Control

- **Insulin:** Promotes glucose uptake, glycogenesis, and fat synthesis.
- **Glucagon:** Stimulates glycogenolysis and gluconeogenesis to raise blood glucose levels.

Glycolysis – Pathway, energetics, and significance

Pathway of Glycolysis

- Glycolysis is the **first step of cellular respiration**, where **one molecule of glucose (6-carbon)** is broken down into **two molecules of pyruvate (3-carbon)**.
- It occurs in the **cytoplasm** of all cells and does not require oxygen (anaerobic).
- Glycolysis is divided into **two phases**:

Phase 1: Energy Investment Phase (Steps 1–5)

- This phase uses **2 ATP molecules** to activate glucose and convert it into **two molecules of glyceraldehyde-3-phosphate (G3P)**.

1. Hexokinase/Glucokinase:



(Phosphorylation of glucose, trapping it inside the cell)

2. Phosphoglucose Isomerase:



(Isomerization from aldose to ketose sugar)

3. Phosphofructokinase-1 (PFK-1):



(Key regulatory step; highly regulated, irreversible)

4. Aldolase:



(Cleavage of 6-carbon sugar into two 3-carbon sugars)

5. Triose Phosphate Isomerase:



(Only G3P continues in glycolysis, so DHAP is converted)

Phase 2: Energy Payoff Phase (Steps 6–10)

- Each G3P molecule is oxidized to form **pyruvate**, producing **ATP and NADH**.

1. Glyceraldehyde-3-phosphate dehydrogenase:



(Oxidation step; formation of high-energy intermediate)

2. Phosphoglycerate kinase:

- $1,3\text{BPG} + \text{ADP} \rightarrow 3\text{-Phosphoglycerate (3PG)} + \text{ATP}$

(First ATP-producing step: substrate-level phosphorylation)

3. Phosphoglycerate mutase:

- $3\text{PG} \leftrightarrow 2\text{-Phosphoglycerate (2PG)}$

(Isomerization)

4. Enolase:

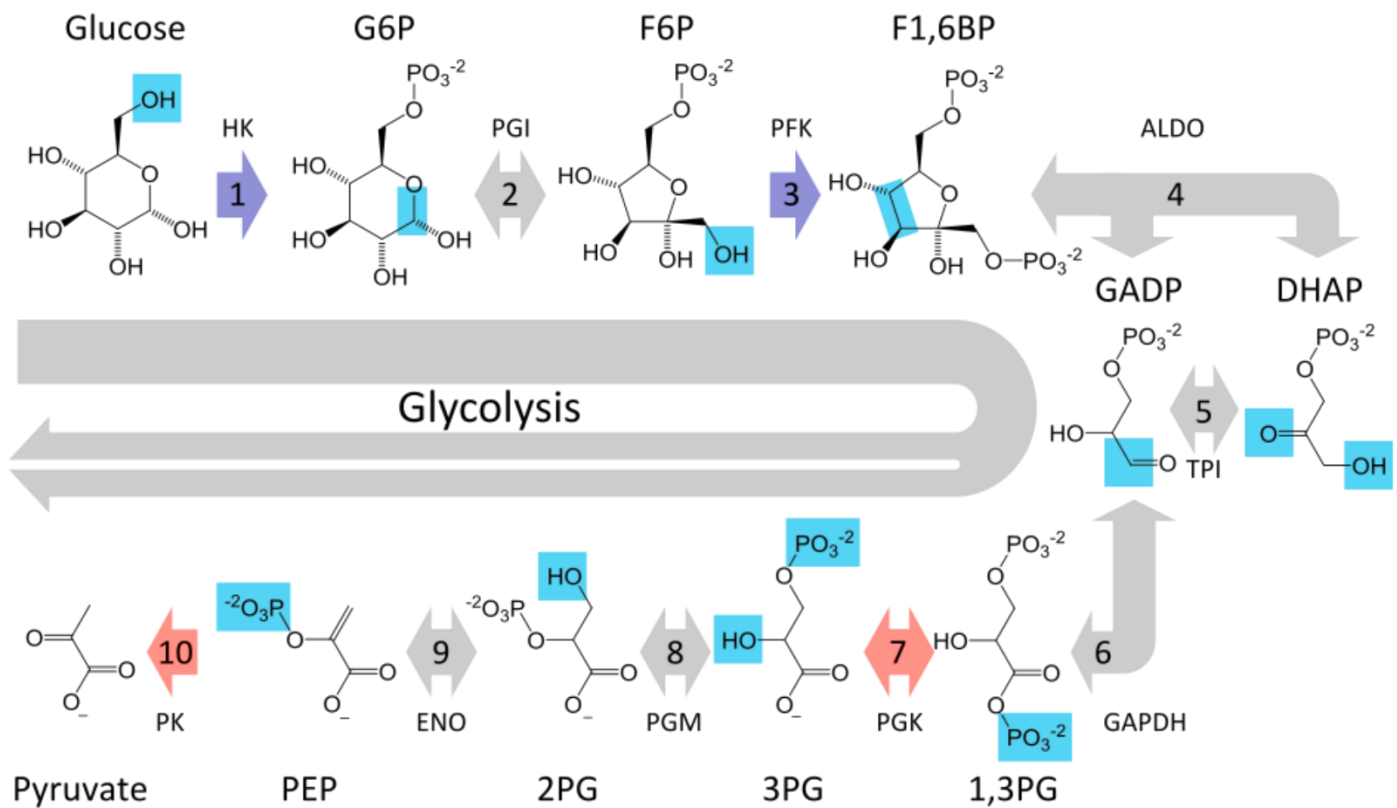
- $2\text{PG} \rightarrow \text{Phosphoenolpyruvate (PEP)} + \text{H}_2\text{O}$

(Dehydration reaction; formation of high-energy compound)

5. Pyruvate kinase:

- $\text{PEP} + \text{ADP} \rightarrow \text{Pyruvate} + \text{ATP}$

(Second substrate-level phosphorylation)



Energetics of Glycolysis

Molecule	Produced/Consumed per glucose
ATP used	2 (Steps 1 and 3)
ATP produced	4 (Steps 7 and 10, 2 per G3P)
Net ATP	2 ATP
NADH produced	2 NADH (Step 6, 1 per G3P)

- In **aerobic conditions**, NADH is shuttled into the mitochondria to generate ATP via oxidative phosphorylation (~3-5 ATP from 2 NADH).
- In **anaerobic conditions**, NADH is used to reduce pyruvate to **lactate** (in animals) or **ethanol** (in yeast), regenerating NAD^+ .

Significance of Glycolysis

1. **Energy Production:** Primary source of ATP in cells lacking mitochondria (e.g., RBCs) or under anaerobic conditions.
2. **Intermediate Metabolites:** Provides intermediates for other pathways (e.g., pentose phosphate pathway, amino acid synthesis).
3. **Survival Under Hypoxia:** Only source of ATP in hypoxic tissues like tumors.
4. **Universal Pathway:** Occurs in all organisms, highlighting evolutionary conservation.
5. **Precursor to Other Pathways:** Pyruvate enters the citric acid cycle under aerobic conditions.

Citric acid cycle- Pathway, energetics and significance

Introduction

- The **citric acid cycle (TCA cycle)** is a central metabolic pathway that oxidizes acetyl-CoA to CO_2 and generates NADH, FADH_2 , and GTP/ATP.
- It occurs in the mitochondrial matrix under aerobic conditions, as NADH and FADH_2 must be oxidized via the electron transport chain (ETC), which requires oxygen.

Pathway of the Citric Acid Cycle

Each turn of the cycle processes **one molecule of acetyl-CoA**.

1. Acetyl-CoA + Oxaloacetate → Citrate

- Enzyme: **Citrate synthase**
- Highly exergonic, irreversible.

2. Citrate ↔ Isocitrate

- Enzyme: **Aconitase**
- Isomerization via cis-aconitate intermediate.

3. Isocitrate → α -Ketoglutarate

- Enzyme: **Isocitrate dehydrogenase**
- Produces **CO_2 + NADH**
- First oxidative decarboxylation; key regulatory step.

4. α -Ketoglutarate → Succinyl-CoA

- Enzyme: **α -Ketoglutarate dehydrogenase**

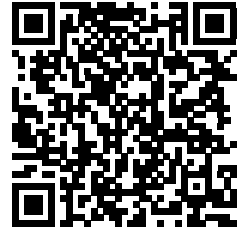


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