Carbohydrate Metabolism

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Carbohydrate metabolism includes the breakdown, synthesis, and transformation of carbohydrates to produce energy and maintain glucose levels.

Key Stages:

1. **Glycolysis**
   - **Location:** Cytoplasm
   - **Process:** Glucose → 2 Pyruvate
   - **Energy:** 2 ATP (net), 2 NADH
   - **Note:** Anaerobic; first step in glucose utilization
2. **Pyruvate Decarboxylation**
   - **Location:** Mitochondria
   - **Process:** Pyruvate → Acetyl CoA
   - **Link:** Connects glycolysis to TCA cycle
3. **Citric Acid Cycle (TCA/Krebs)**
   - **Location:** Mitochondrial matrix
   - **Process:** Acetyl CoA oxidation
   - **Energy:** 3 NADH, 1 $FADH_2$, 1 GTP per cycle
   - **Function:** Supplies electrons for ETC
4. **Electron Transport Chain (ETC) & Oxidative Phosphorylation**
   - **Location:** Inner mitochondrial membrane
   - **Process:** NADH/$FADH_2$ → ATP via proton gradient
   - **Energy:** ~34 ATP per glucose
   - **Final Product:** Water (O_2 reduced)
5. **Gluconeogenesis**
   - **Location:** Liver & kidney
   - **Process:** Non-carb precursors → Glucose
   - **Role:** Maintains glucose during fasting

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6. Glycogenesis & Glycogenolysis

- **Glycogenesis:** Glucose → Glycogen (storage)
- **Glycogenolysis:** Glycogen → Glucose (release)
- **Regulation:** Insulin (storage), Glucagon (release)

7. Pentose Phosphate Pathway (PPP)

- **Location:** Cytoplasm
- **Purpose:** Produces NADPH & Ribose-5-phosphate
- **Uses:** Fatty acid & nucleotide synthesis, antioxidant defense

Hormonal Control

- **Insulin:** Enhances glucose uptake, storage
- **Glucagon:** Increases glucose production

Glycolysis

Definition:

- Glycolysis is a fundamental metabolic pathway that converts one molecule of glucose into two molecules of pyruvate, generating energy in the form of **ATP** and **NADH**.
- It takes place in the **cytoplasm** of all cells and can proceed **anaerobically** (without oxygen).

Phases of Glycolysis

- Glycolysis consists of **two distinct phases**:
  1. **Energy Investment Phase (Preparatory Phase)**
  2. **Energy Generation Phase (Payoff Phase)**

Energy Investment Phase (Preparatory Phase)

- The energy investment phase of glycolysis involves the initial consumption of ATP to prepare glucose for further breakdown.

The steps are as follows:

1. Phosphorylation of Glucose

- Glucose is phosphorylated to glucose-6-phosphate (G6P).
- **Enzyme**: Hexokinase
- **ATP used**: 1

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2. Isomerization

- G6P is isomerized to fructose-6-phosphate (F6P).
- **Enzyme**: Phosphoglucose isomerase

3. Second Phosphorylation

- F6P is phosphorylated to fructose-1,6-bisphosphate (F1,6BP).
- **Enzyme**: Phosphofructokinase-1 (PFK-1)
- **ATP used**: 1

4. Cleavage

- F1,6BP is cleaved into two 3-carbon molecules: glyceraldehyde-3-phosphate (G3P) and dihydroxyacetone phosphate (DHAP).
- **Enzyme**: Aldolase

5. Isomerization of DHAP

- DHAP is converted into another G3P.
- **Enzyme**: Triose phosphate isomerase

Energy Generation Phase (Payoff Phase)

- This phase produces ATP and NADH by processing the two glyceraldehyde-3-phosphate molecules formed in the investment phase.

The steps are as follows:

1. Oxidation and Phosphorylation

- Each G3P is oxidized to 1,3-bisphosphoglycerate (1,3BPG).
- **Enzyme**: Glyceraldehyde-3-phosphate dehydrogenase (GAPDH)
- **NADH produced**: 1 per G3P (total 2 NADH)

2. ATP Formation

- 1,3BPG donates phosphate to ADP, forming ATP and 3-phosphoglycerate (3PG).
- **Enzyme**: Phosphoglycerate kinase
- **ATP produced**: 1 per G3P (total 2 ATP)

3. Conversion

- 3PG is converted to 2-phosphoglycerate (2PG).
- **Enzyme**: Phosphoglycerate mutase

4. Dehydration

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- 2PG is dehydrated to form phosphoenolpyruvate (PEP).
- **Enzyme**: Enolase

5. Final ATP Formation

- PEP donates phosphate to ADP, forming ATP and pyruvate.
- **Enzyme**: Pyruvate kinase
- **ATP produced**: 1 per G3P (total 2 ATP)

Energetics

- ATP used: 2
- ATP produced: 4
- Net ATP gain: 2
- NADH produced: 2

Tricarboxylic Acid (TCA) cycle or Citric acid cycle (TCA)

- The Citric Acid Cycle, also known as the Krebs cycle or the Tricarboxylic Acid (TCA) cycle, is a cornerstone of cellular metabolism, pivotal in the breakdown and conversion of carbohydrates, fats, and proteins into usable energy.
- This cycle takes place in the mitochondrial matrix of eukaryotic cells, where it serves the dual purpose of generating high-energy molecules (ATP, NADH, and FADH2) and facilitating carbon dioxide excretion as a byproduct.

Citric Acid Cycle or Krebs cycle Pathway

1. Formation of Citrate:

- **Enzyme**: Citrate synthase
- **Process**: Acetyl CoA (2 carbons) combines with oxaloacetate (4 carbons) to form citrate (6 carbons), releasing CoA.

2. Isomerization to Isocitrate:

- **Enzyme**: Aconitase
- **Process**: Citrate is rearranged into isocitrate via cis-aconitate as an intermediate.

3. Oxidation and Decarboxylation to α-Ketoglutarate:

- **Enzyme**: Isocitrate dehydrogenase
- **Process**: Isocitrate is oxidized to oxalosuccinate (6 carbons), then decarboxylated to α-ketoglutarate (5 carbons), producing NADH and releasing CO2.

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4. **Further Oxidation and Decarboxylation:**
   - **Enzyme**: α-Ketoglutarate dehydrogenase complex
   - **Process**: α-Ketoglutarate is further oxidized and decarboxylated to form succinyl CoA (4 carbons), generating another NADH and releasing a second CO2 molecule.
5. **Conversion to Succinate:**
   - **Enzyme**: Succinyl-CoA synthetase
   - **Process**: Succinyl CoA is converted into succinate, producing one molecule of GTP (or ATP).
6. **Oxidation of Succinate:**
   - **Enzyme**: Succinate dehydrogenase
   - **Process**: Succinate is oxidized to fumarate, reducing FAD to FADH2.
7. **Hydration to Malate:**
   - **Enzyme**: Fumarase
   - **Process**: Fumarate is hydrated to form malate.
8. **Oxidation to Oxaloacetate:**
   - **Enzyme**: Malate dehydrogenase
   - **Process**: Malate is oxidized back to oxaloacetate, reducing NAD+ to NADH and preparing the cycle to begin anew.

Products of the Krebs Cycle per Acetyl CoA

1. **3 NADH molecules**: For use in the electron transport chain.
2. **1 FADH2 molecule**: Also, for use in the electron transport chain.
3. **1 ATP (or GTP) molecule**: Directly usable energy.
4. **2 CO2 molecules**: Waste products released.

Energetics of the Citric Acid Cycle

- **3 NADH → ~7.5 ATP** (via oxidative phosphorylation)
- **1 FADH2 → ~1.5 ATP**
- **1 GTP (or ATP)** directly produced Each cycle generates around **10 ATP equivalents**.

Glycogen metabolism Pathways

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