Gluconeogenesis: The Body's Glucose Backup Plan

Gluconeogenesis is the process of making glucose from non-carbohydrate sources.

It maintains blood sugar during fasting and prevents dangerous hypoglycemia.

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The Gluconeogenic Pathway: An Overview

Main sites

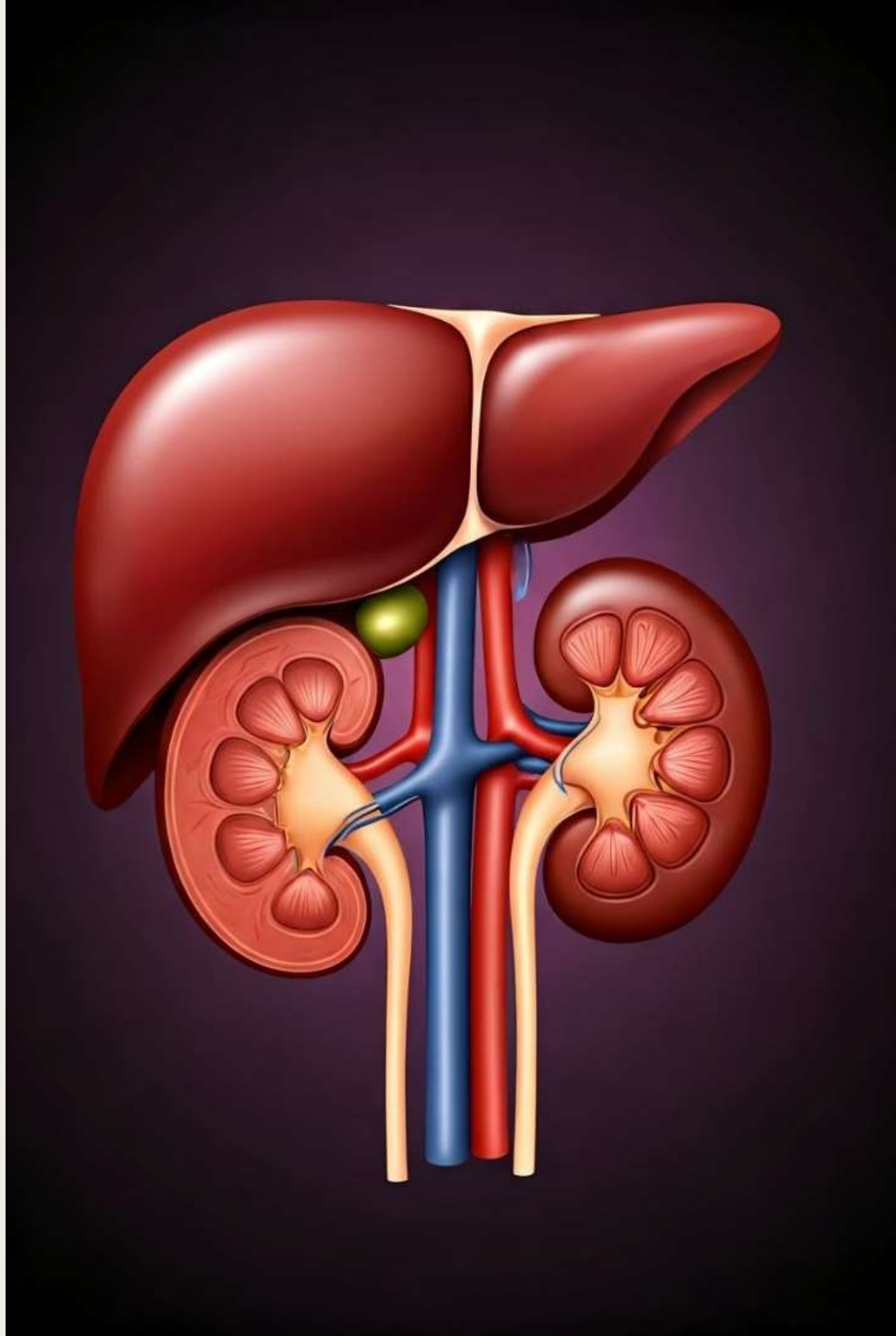
Liver performs 90% and kidneys 10% of gluconeogenesis.

Pathway specifics

Bypasses irreversible glycolysis steps for glucose synthesis.

Energy use

Consumes six ATP/GTP molecules per glucose made.



Key Precursors: Fueling the Pathway

Pyruvate

Derived from muscle lactate and alanine.

Lactate

Produced by anaerobic glycolysis in muscles and red blood cells.

Glycerol & Amino Acids

- Glycerol from fat breakdown in adipose tissue
- Amino acids from protein catabolism

The Bypasses: Overcoming Glycolysis' Hurdles

Pyruvate to PEP

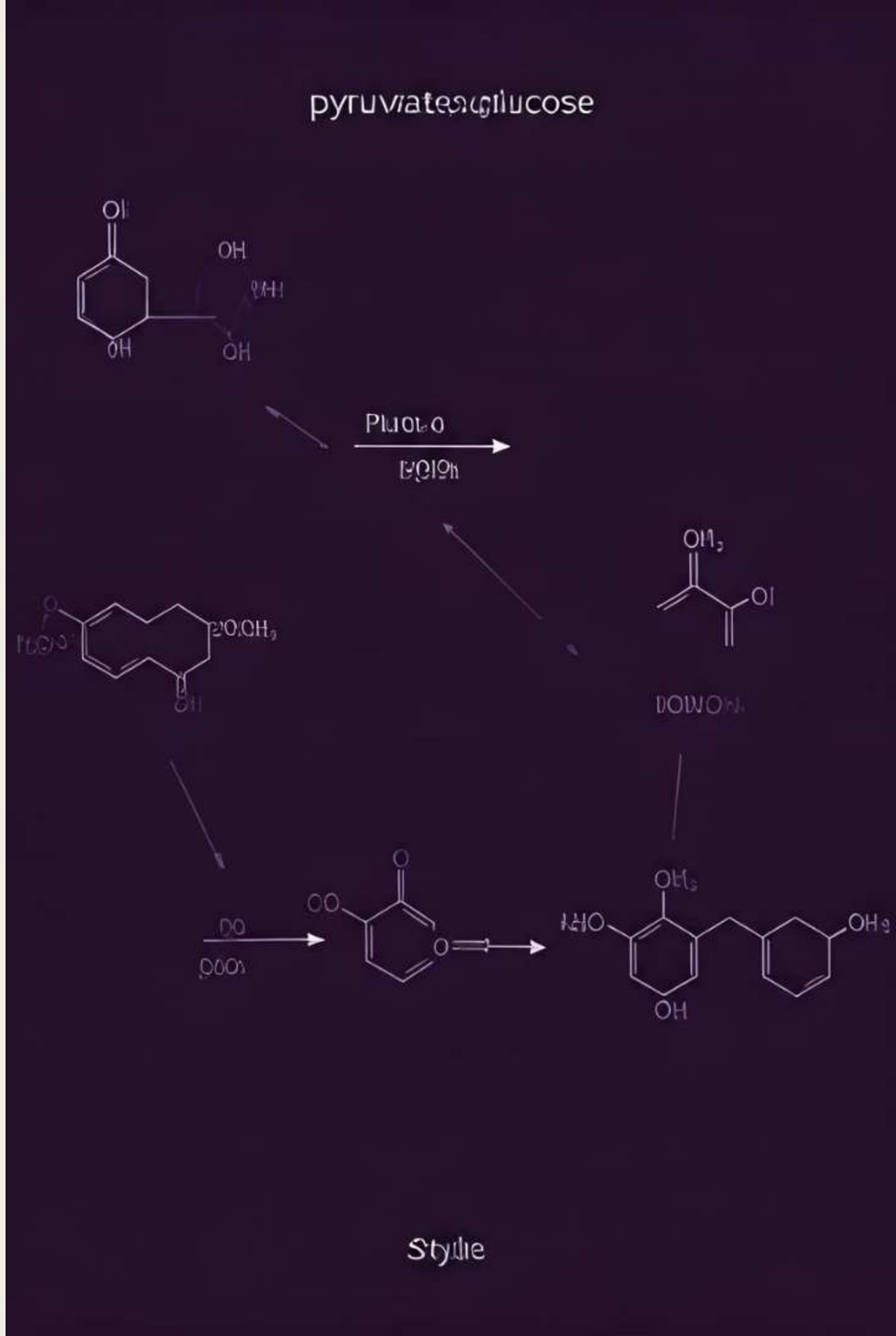
Two-step conversion via pyruvate carboxylase and PEP carboxykinase.

Fructose-1,6-bisphosphate to Fructose-6-phosphate

Facilitated by fructose-1,6-bisphosphatase (FBPase-1).

Glucose-6-phosphate to Glucose

Occurs in liver and kidneys using glucose-6-phosphatase (G6Pase).



Energy Requirements: The Cost of New Glucose

High energy consumption

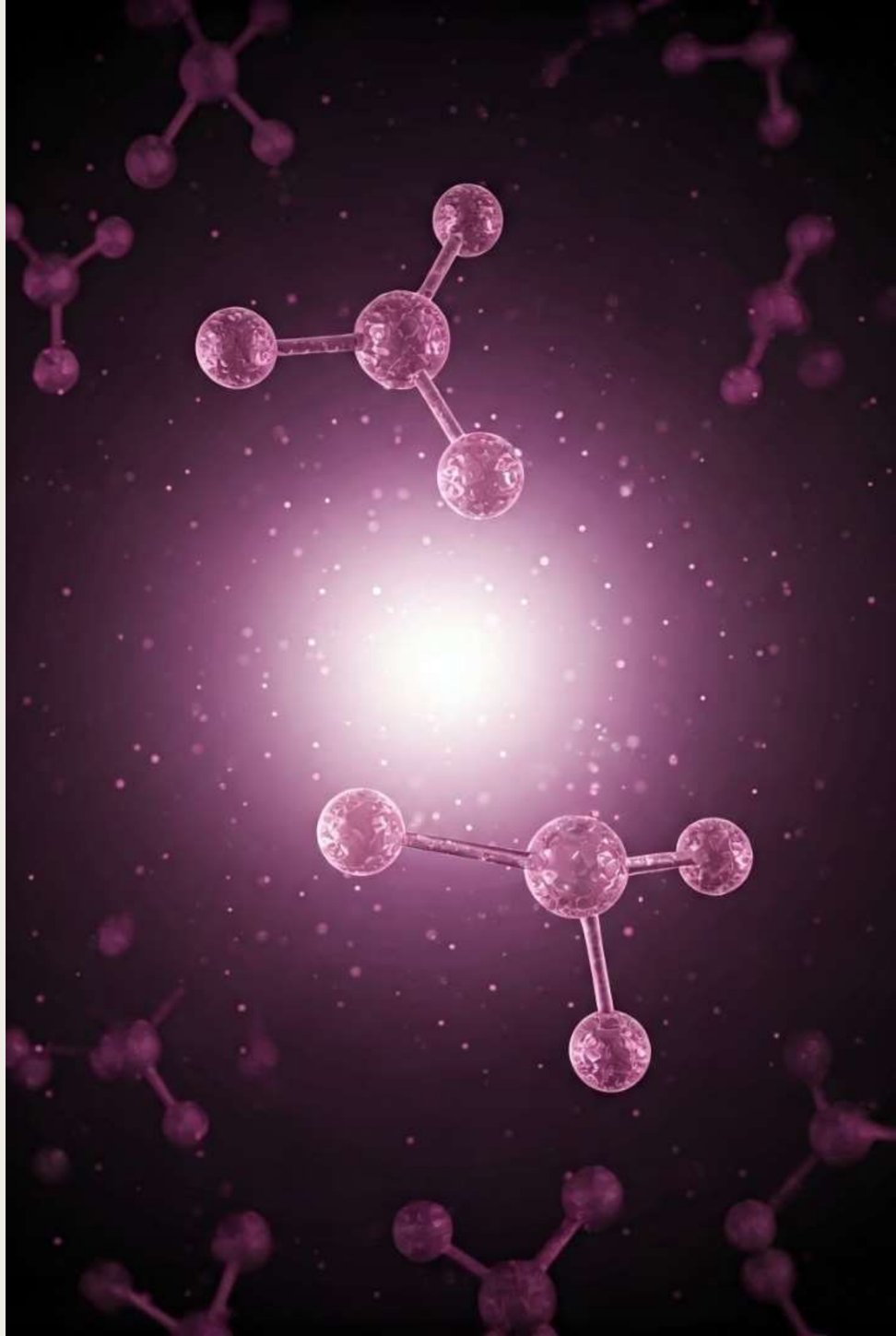
Gluconeogenesis uses 6 ATP/GTP, reflecting anabolic demands.

Energy source priority

Body prioritizes glucose synthesis in energy deficits.

Chemical equation

2 Pyruvate + energy → 1 Glucose + byproducts



Hormonal Regulation: Balancing Act

1. **Insulin**

   Inhibits gluconeogenesis to reduce glucose output.

2. **Glucagon & Cortisol**

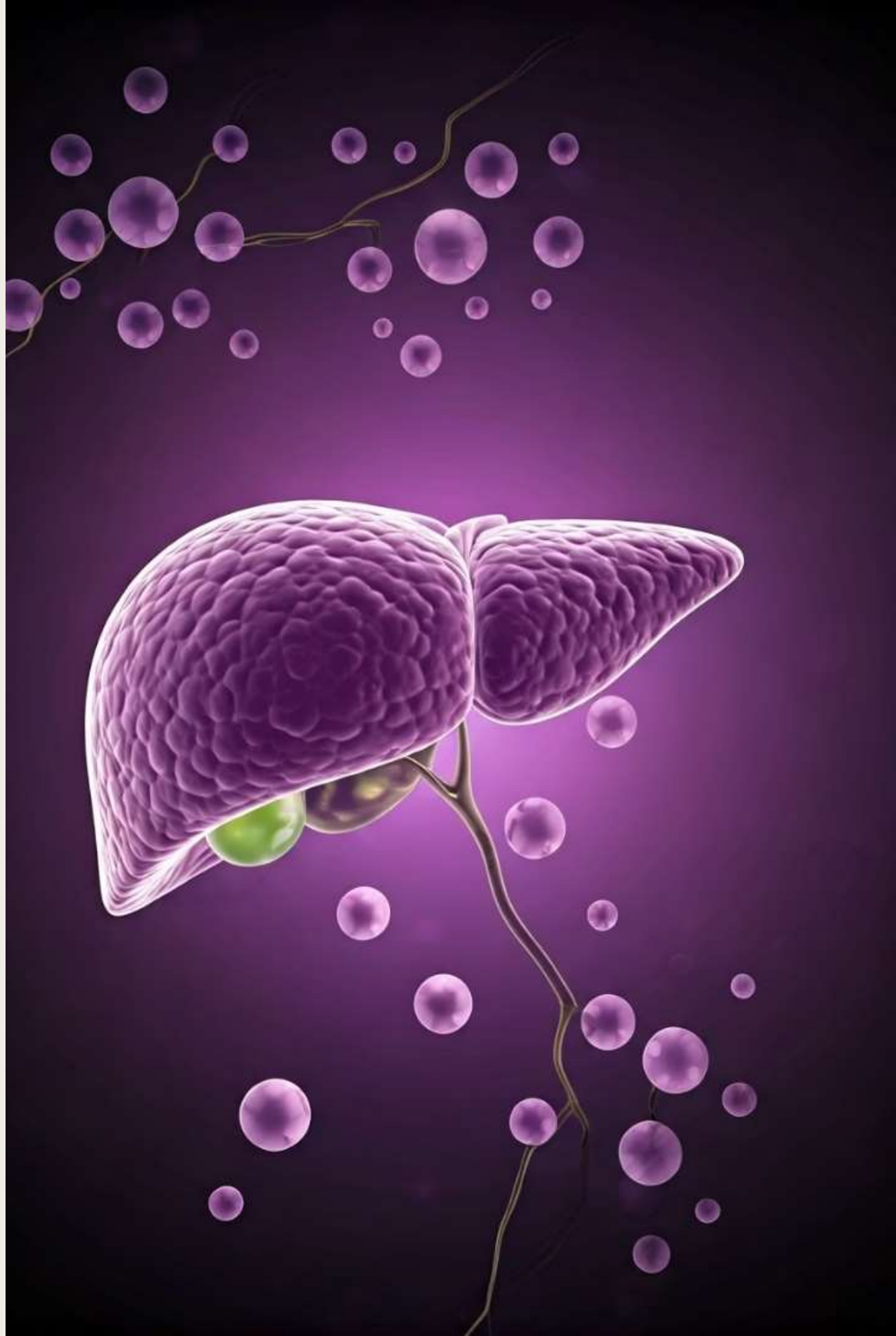
   Stimulate gluconeogenesis during energy need.

3. **Enzyme modulation**

   Key enzymes like FBPase-1 are activated or inhibited hormonally.

4. **Glycogen metabolism**

   Liver phosphorylase modulates glycogen breakdown and synthesis.



Clinical Significance: Health Implications

Type 2 diabetes

Uncontrolled gluconeogenesis contributes to high blood sugar.

Metabolic syndrome

Elevated hepatic glucose production worsens health risks.

Therapeutic targets

Gluconeogenic enzymes are potential drug targets.

Summary: Gluconeogenesis' Crucial Role

Glucose homeostasis

Gluconeogenesis keeps blood sugar stable during fasting.

Tight regulation

Hormones finely control pathway to meet energy needs.

Health impact

Dysfunction links to diabetes and metabolic disorders.