

Gluconeogenesis is the metabolic process by which the body synthesizes **glucose from non-carbohydrate precursors**. It is essential during **fasting, starvation, prolonged exercise, or low-carbohydrate intake** to maintain normal blood glucose levels.

Definition

Gluconeogenesis = **Formation of new glucose** from substances other than carbohydrates.

Site

- **Liver** (major site)
- **Kidney cortex** (especially during prolonged fasting)
- Small amount in the intestinal epithelium

Precursors

- **Lactate** (from anaerobic glycolysis; Cori cycle)
- **Alanine and other glucogenic amino acids**
- **Glycerol** (from fat breakdown)
- **Propionate** (mainly in ruminants; minor in humans)

Steps (Key Bypass Reactions)

Gluconeogenesis bypasses the three irreversible steps of glycolysis:

1. **Pyruvate → Oxaloacetate**
 - Enzyme: **Pyruvate carboxylase**
 - Requires: **ATP** and **biotin**
 - Occurs in mitochondria
2. **Oxaloacetate → Phosphoenolpyruvate (PEP)**
 - Enzyme: **PEP carboxykinase (PEPCK)**
 - Requires: **GTP**
3. **Fructose-1,6-bisphosphate → Fructose-6-phosphate**
 - Enzyme: **Fructose-1,6-bisphosphatase**
 - Major regulatory step
4. **Glucose-6-phosphate → Glucose**
 - Enzyme: **Glucose-6-phosphatase**
 - Present mainly in the liver and kidney

Energy Requirement

To produce **1 molecule of glucose** from **2 molecules of pyruvate**, the process requires:

- **4 ATP**
- **2 GTP**
- **2 NADH**

Regulation

Stimulated by:

- Glucagon
- Cortisol
- Epinephrine
- High ATP and acetyl-CoA levels

Inhibited by:

- Insulin
- AMP
- Fructose-2,6-bisphosphate

Importance

- Maintains blood glucose during fasting.
- Supplies glucose to glucose-dependent tissues such as the **brain** (especially early fasting), **red blood cells**, and the **renal medulla**.
- Helps recycle lactate and amino acids into glucose.

Easy Mnemonic

"GNG Makes Glucose During Going Hungry."

- Glycerol
- Non-carbohydrate sources
- Glucose production during fasting

In summary: Gluconeogenesis is the pathway that produces glucose from non-carbohydrate precursors, mainly in the liver, to maintain blood glucose levels when dietary glucose is unavailable.