Pentose Phosphate Pathway

Glucose-6-Phosphate

6-Phosphoglucono-δ-lactone

6-Phosphogluconate

Ribulose-5-Phosphate

Xylulose-5-Phosphate

Sedoheptulose-7-Phosphate

Fructose-6-Phosphate

Ribose-5-Phosphate

Glyceraldehyde-3-Phosphate

Erythrose-4-Phosphate
Pentose Phosphate Pathway
Pentose Phosphate Pathway

Oxidation

Isomerization

Carbon Rearrangement
Pentose Phosphate Pathway

G6P

NADP⁺

NADPH + H⁺

6-PG-δL

H₂O

H⁺

6-PG

NADP⁺

NADPH + H⁺

Ru-5-P

Glucose-6-phosphate Dehydrogenase

-6phosphogluconate Dehydrogenase
Pentose Phosphate Pathway

- Pathway Reactions

Isomerization

Ribulose-5-phosphate (Ru-5-P)

Ribose-5-phosphate (R-5P)

Ru-5-P Isomerase

Important Reaction for Nucleotide Metabolism
Pentose Phosphate Pathway

- Pathway Reactions

Ribulose-5-phosphate (Ru-5-P)

Xylulose-5-phosphate (Xu-5-P)

Ru-5-P Epimerase

An Alternate Pentose Source
Pentose Phosphate Pathway
• Pathway Reactions

Transketolase Requires Thiamine Pyrophosphate

Also Used in Calvin Cycle
Pentose Phosphate Pathway

- Pathway Reactions

S-7-P + GLYAL-3-P → F6P + E4-P

Deficiency Leads to Liver Cirrhosis

Autoimmunity Target in Multiple Sclerosis

Transaldolase
Pentose Phosphate Pathway

- Pathway Flexibility

Glycolysis/Gluconeogenesis

Nucleotide Synthesis

High Levels

High Levels
Pentose Phosphate Pathway

- Pathway Flexibility

High Levels

Nucleotide Breakdown

Aromatic Amino Acid Synthesis
Pentose Phosphate Pathway

- Pathway Flexibility

Very Little G6P

Not Easily Reversible

G6P → NADP⁺ → NADPH + H⁺

6-PG-δL → H₂O → H⁺

6-PG → NAD⁺ → NADPH + H⁺ + CO₂

Glycolysis/Gluconeogenesis

Nucleotide Breakdown

Ru-5-P → R-5-P → S-7-P → GLYAL-3-P → E4-P

Xu-5-P → GLYAL-3-P → F6P

F6P → GLYAL-3-P → E4-P
Glycogen Metabolism
• Regulation

- Polymer of Glucose in Animals
- Stored in Liver and Muscles
- Similar to Amylopectin of Plants
- Helps Modulate Blood Glucose and Respond to Needs

Glycogenin Protein
Up to 20,000 Glucose Units
Glycogen Breakdown
• Glycogen Phosphorylase

\[
\text{Glycogen Phosphorylase} \quad \xrightleftharpoons{\text{HPO}_4^{2-}} \quad \text{Glycogen} \quad \text{(With X Glucoses)}
\]

\[
\text{Glucose-1-Phosphate} \quad \text{Glycogen} \quad \text{(With X-1 Glucoses)}
\]
Glycogen Breakdown
• Glycogen Phosphorylase

\[
\text{Glucose-1-Phosphate (G1P)} \quad \xrightarrow{\text{Phosphoglucomutase}} \quad \text{Glucose-6-Phosphate (G6P)}
\]
Glycogen Breakdown

- Glycogen Phosphorylase & Debranching Enzyme

Glycogen Phosphorylase Action

Debranching Enzyme Action

Move

Free Glucose
Glycogen Breakdown
Glycogen Synthesis

- Making the Substrate

\[
\text{UDP-Glucose Pyrophosphorylase}
\]

\[
\text{Glucose 1-phosphate} + \text{UTP} \rightleftharpoons \text{UDP-glucose} + \text{PPi}
\]
Glycogen Synthesis

- Growing the Glycogen Chain
Glycogen Synthesis

- Adding Branches
Glycogen Phosphorylase Regulation
Glycogen Phosphorylase (GPa) Regulation
Glycogen Phosphorylase (GPb) Regulation

Figure 6.40 - Allosteric regulation of GPb

Image by Aleia Kim
**Glycogen Metabolism**

- Regulation

System to Put Phosphate on Glycogen Enzymes is Activated by Epinephrine or Glucagon
Glycogen Metabolism

- Regulation

1. Hormone Stimulation (epinephrine/glucagon)
2. Causes Phosphorylation
3. Gets Phosphorylated (Phosphates Removed by Phosphatase)
4. Must Be Broken Down
5. Turns Self Off

Glycogen Synthase
- b (inactive)

Glycogen Synthase
- a

Phosphorylase Kinase
- a

Phosphorylase Kinase
- b

Glycogen
- $x_{-1}$
- $x$

Glucose 1-phosphate
Phosphorylase Kinase Regulation
Glycogen Metabolism

• Regulation

When Glucose Levels are Low

Epinephrine or Glucagon Increases Glucose Concentration by

1. Favoring Glycogen Breakdown (Activates Glycogen Phosphorylase)

and

2. Inhibiting Glycogen Synthesis (Inhibits Glycogen Synthase)

Epinephrine

Glucagon

http://www.ebi.ac.uk/
Glycogen Metabolism
• Insulin Signaling

Countering the Epinephrine/Glucagon System is the Insulin System

Insulin Stimulates Phosphoprotein Phosphatase to Remove Phosphates From Glycogen Enzymes

• Favoring Glycogen Synthesis (Activates Glycogen Synthase)

and

• Inhibiting Glycogen Breakdown (Inhibits Glycogen Phosphorylase)

Insulin Also Stimulates Uptake of Glucose by Cells, Reducing Blood Glucose Levels
When Glucose Needed

Epinephrine/Glucagon Stimulates Phosphorylation and Release of Glucose from Glycogen

When Glucose Abundant

Insulin Stimulates Dephosphorylation and Incorporation of Glucose into Glycogen
Glycogen Metabolism

Odd observation

Start with GPa (active) and GSa (inactive)
Add only glucose, get GPb (inactive) and GSb (active)
Why?
Phosphoprotein Phosphatase Regulation