Pentose Phosphate Pathway

Chapter 26, Stryer Short Course

Glucose Metabolism Overview

- Gluconeogenesis
- Glycogen metabolism
- Pentose Phosphate Pathway

Pentose Phosphate Pathway

- Dual Purpose
  - Synthesis of "reducing potential"
  - Synthesis of 5-carbon sugars
- At cost of one carbon worth of carbohydrate
- Net reaction:

\[
\text{Glucose 6-phosphate} + 2 \text{ NADP}^+ + \text{H}_2\text{O} \rightarrow \text{Ribulose 5-phosphate} + 2 \text{ NADPH} + \text{CO}_2 + 2 \text{ H}^+ 
\]
2-Stage Process

- Oxidative Stage
  - Generates reducing power and ribose
- Non-oxidative stage
  - Regenerates 3- and 6-carbon sugars from 5 carbon sugars

Oxidative Stage

Oxidative Stage Step 1:

- G-6-P DH
- Lactone formation
Oxidative Stage Step 2:

- Also a spontaneous hydrolysis
- Recognize hydrolysis
- Predict carbohydrate orientation

Oxidative Stage Step 3:

- Oxidative decarboxylation
- We will see this process again

Biosynthesis of Ribose
Non-oxidative Stage

- To understand purpose, realize that we generally need to make much more NADPH than ribose
- Problem: stuck with C5, but need C6 and C3
- Solution: “Shunt” C5 back to C6 through near-equilibrium reactions

PPP Reactions

- Epimerase
- Isomerase
- Transketolase
- Transaldolase

Epimerase

\[
\text{Ribulose 5-phosphate} \xrightarrow{\text{Phosphopentose epimerase}} \text{Xylulose 5-phosphate}
\]
Transketalase, Transaldolase

- Transketalase
  - Transfer of an acyl anion
  - Requires TPP to stabilize unstable anion
- Transaldolase
  - Transfer of somewhat stable enolate ion
  - Schiff base helps
- Be able to recognize need for TK vs. TA

Transketalase or transaldolase?

Mechanism (just FYI...)

[Diagrams and mechanisms for transketalase, transaldolase, and their mechanisms]

Different Modes for Different Purposes

Physiological Purposes

Table 26.3 Tissues with active pentose phosphate pathways

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenal gland</td>
<td>Steroid synthesis</td>
</tr>
<tr>
<td>Liver</td>
<td>Fatty acid and cholesterol synthesis</td>
</tr>
<tr>
<td>Testes</td>
<td>Steroid synthesis</td>
</tr>
<tr>
<td>Adipose tissue</td>
<td>Fatty acid synthesis</td>
</tr>
<tr>
<td>Ovary</td>
<td>Steroid synthesis</td>
</tr>
<tr>
<td>Mammary gland</td>
<td>Fatty acid synthesis</td>
</tr>
<tr>
<td>Red blood cells</td>
<td>Maintenance of reduced glutathione</td>
</tr>
</tbody>
</table>

Glutathione: Protection from Oxidation

- Glutathione is the redox buffer of the cell
- Regenerated by NADPH
- PPP especially important in RBC because it is only means to generate reducing power (no mitochondria)
Summary of glucose metabolism