**Glucose Metabolism**

**13.1 Glycolysis**

* Describe the substrates, products, and chemical reaction for each step of glycolysis.
  + Compare the energy-consuming and energy-generating phases of glycolysis.
  + List the flux-control points for the pathway.
  + Describe the metabolic uses of pyruvate.

**1. Hexokinase**

* Electrostatic catalysis facilitates transfer of phosphoryl group
* Metabolically irreversible reaction = commitment step

**2. Phosphoglucose Isomerase**

* ;
* Near-equilibrium = freely reversible; mass action effects drive direction of reaction

**3. Phosphofructokinase**

* Second ATP consumed in phosphorylation of fructose-6-phosphate
* Metabolically irreversible reaction

**4. Aldolase**

* Lys residue: forms a Schiff base via nucleophilic attack
* Asp residue: base catalyst
* Schiff base facilitates split between C3 and C4
* Hydrolysis of Schiff base releases second product
* *ΔG*°’ =+22.8 kJ/mol; *ΔG* <0 *in vivo* because products are reactants for subsequent reaction

**5. Triose Phosphate Isomerase**

* TPI is catalytically perfect: limited only by rate of diffusion
* Catalytic mechanism involves low barrier H-bonds
* Active site protein loop stabilizes transition state
* Reversible reaction; pulls aldolase reaction forward by consuming DHAP

**6. Glyceraldehyde-3-Phosphate Dehydrogenase**

* Oxidation and phosphorylation
* Pi added to aldehyde group
* Aldehyde is oxidized and NAD+ is reduced
* Covalent catalysis by Cys residue
* Attack by phosphate forms product and regenerates enzyme
* Reversible reaction; pulls aldolase reaction forward by consuming G-3-P

**7. Phosphoglycerate Kinase**

* Removal of phosphate from acyl phosphate: large free energy release
* Drives formation of ATP
* *ΔG*°’ = -18.8 kJ/mol; pulls GAPDH (*ΔG*°’ =+6.7 kJ/mol) reaction forward
* Pairing results in net decrease in free energy

**8. Phosphoglycerate Mutase**

* Sequential transfer of phosphoryl groups via active site His residue
* Freely reversible reaction

**9. Enolase**

* Dehydration reaction
* Mg2+ ion coordinates with C3 OH facilitating exit

**10. Pyruvate Kinase**

* Second ATP generated
* Metabolically irreversible

**Post-Glycolysis/Fates of Pyruvate**

Lactate Dehydrogenase (lactate)

Pyruvate Decarboxylase + Alcohol Dehydrogenase (ethanol)

Pyruvate Dehydrogenase (acetyl CoA)

Pyruvate Carboxylase (oxaloacetate)

**13.2 Gluconeogenesis**

* Describe the substrates, products, and reactions of gluconeogenesis.
  + List the enzymes that are unique to gluconeogenesis or are shared with glycolysis.
  + Explain how the rates of gluconeogenesis and glycolysis are related.

**1, 2. Pyruvate Carboxylase + Phosphoenolpyruvate Carboxykinase**

* Sequential carboxylation and decarboxylation
* ATP and GTP consumed
* Amino acids are gluconeogenic precursors

**9. Fructose Bisphosphatase**

* Unique to gluconeogenesis
* Hydrolysis of the phosphoryl group from C1 yields fructose-6-phosphate

**11. Glucose-6-Phosphatase**

* Hydrolyzes the phosphoryl group on C6 to yield glucose and Pi

**13.3 Glycogen Synthesis and Degradation**

* Compare the processes of glycogen synthesis and degradation.
  + Identify the substrates and products for each process.
  + Compare the free energy needs of each pathway.
  + List the metabolic fates of glucose-6-phosphate.

**Phosphoglucomutase**

* G-6-P to G-1-P

**UDP-glucose Phosphorylase + Inorganic Pyrophosphatase**

* Activation of G-1-P with UTP

**Glycogen Synthase**

* Transfer to C4 OH

**Glycogen Phosphorylase**

* Glycogen to G-1-P

**Phosphoglucomutase**

* G-1-P to G-6-P

**Glucose-6-Phosphatase**

* G-6-P to glucose (not muscle)

**13.4 Pentose Phosphate Pathway**

* Describe the substrates, products, and reactions of the pentose phosphate pathway.
  + Identify the oxidation-reduction reactions of the pentose phosphate pathway.
  + Explain how the pathway responds to the cell’s need for ribose groups.

**Glucose-6-Phosphate Dehydrogenase**

* Hydride ion transferred from G6P to NADP+

**6-Phospho-Glucono-Lactonase**

* Ring-opening

**6-Phosphogluconate Dehydrogenase**

* Oxidative decarboxylation
* Second NADPH generated

**Ribulose-5-Phosphate Isomerase**

* Isomerization

**Ribonucleotide Reductase**

* Uses NADPH (reduction) from PPP

**13.5: Clinical Connection: Disorders of Carbohydrate Metabolism**

* Relate enzyme deficiencies to defects in carbohydrate metabolism.
  + Explain why red blood cells are so susceptible to defects in glucose metabolic pathways.
  + Describe the symptoms of glycogen storage diseases affecting liver and muscle.