CHAPTER 8 CELLULAR RESPIRATION

Chapter Outline

8.1 Cellular Respiration

A. How Cells Acquire ATP

1. Cellular respiration involves various metabolic pathways that break down carbohydrates and other metabolites and build up ATP.
2. Cellular respiration requires oxygen and gives off CO_2.
3. Cellular respiration usually breaks down glucose into CO_2 and H_2O.
4. Overall equation for complete breakdown of glucose requires oxygen (is aerobic): $C_6H_{12}O_6 + 6\ O_2 \rightarrow 6\ CO_2 + 6\ H_2O$ + energy
5. Glucose is high-energy molecule; CO_2 and H_2O are low-energy molecules; process is exergonic and releases energy.
6. Electrons are removed from substrates and received by oxygen which combines with H^+ to become water.
7. Glucose is oxidized and O_2 is reduced.
8. The buildup of ATP is an endergonic reaction that requires energy.
9. The pathways of cellular respiration allow energy in glucose to be released slowly; therefore ATP is produced gradually.
10. In contrast, rapid breakdown of glucose would lose most energy as non-usable heat.
11. Breakdown of glucose yields synthesis of 36 or 38 ATP; this preserves 39% of the energy available in glucose.
12. This is relatively efficient compared to the 25% efficiency of a car burning gasoline.

B. NAD^+ and FAD

1. Each metabolic reaction in cellular respiration is catalyzed by its own enzyme.
2. As a metabolite is oxidized, NAD^+ accepts two electrons and a hydrogen ion (H^+); this results in NADH + H^+.
3. Electrons received by NAD^+ and FAD are high-energy electrons and are usually carried to the electron transport system.
4. NAD^+ is a coenzyme of oxidation-reduction since it both accepts and gives up electrons.
5. Only a small amount of NAD^+ is needed in cells because each NAD^+ molecule is used over and over.
6. FAD coenzyme of oxidation-reduction can replace NAD^+; FAD accepts two electrons and becomes $FADH_2$.

C. Phases of Complete Glucose Breakdown

1. Cellular respiration includes four phases:
    a. Glycolysis is the breakdown of glucose in the cytoplasm into two molecules of pyruvate.
        1) Enough energy is released for immediate buildup of two ATP.
        2) Glycolysis takes place outside the mitochondria and does not utilize oxygen.
    b. In the transition reaction, pyruvate is oxidized to an acetyl group and CO_2 is removed; this reaction occurs twice per glucose molecule.
    c. The citric acid cycle:
        1) occurs in the matrix of the mitochondrion and results in NADH and $FADH_2$.
        2) is a series of reactions gives off CO_2 and produces ATP.
        3) turns twice because two acetyl-CoA molecules enter the cycle per glucose molecule.
        4) produces two immediate ATP molecules per glucose molecule.
    d. The electron transport system:
        1) is a series of carriers accepts electrons from glucose; electrons are passed from carrier to carrier until received by oxygen.
        2) passes electrons from higher to lower energy states, allowing energy to be released and stored for ATP production.
        3) accounts for 32 or 34 ATP depending on the cell conditions.
2. Pyruvate is a pivotal metabolite in cellular respiration.
    a. If O_2 is not available to the cell, fermentation, an anaerobic process, occurs in the cytoplasm.

b. During fermentation, glucose is incompletely metabolized to lactate or CO_2 and alcohol.
c. Fermentation results in a net gain of only two ATP per glucose molecule.

8.2 Outside the Mitochondria: Glycolysis

A. Glycolysis**:**
1. occurs in the cytoplasm outside the mitochondria.
2. is the breakdown of glucose into two pyruvate molecules.
3. is universal in organisms; therefore, most likely evolved before the citric acid cycle and electron transport system.

B. Energy-Investment Steps
1. Glycolysis begins with two ATP activating glucose to split into two C_3 molecules known as PGAL.
2. PGAL carries a phosphate group.

C. Energy-Harvesting Steps
1. Oxidation of PGAL occurs by removal of electrons and hydrogen ions.
2. Two electrons and one hydrogen ion are accepted by NAD^+ and result in two NADH.
3. Enough energy is released from breakdown of glucose to generate four ATP molecules; this is substrate-level phosphorylation.
4. Two of four ATP molecules produced are required to replace two ATP molecules used in the phosphorylation of glucose; therefore there is a net gain of two ATP from glycolysis.
5. Pyruvate enters mitochondria if oxygen is available and cellular respiration follows.
6. If oxygen is not available, glycolysis becomes a part of fermentation.

8.3 Inside the Mitochondria

A. Glucose Breakdown
1. This involves the transition reaction, the citric acid cycle, and the electron transport system.
2. It is a process in which pyruvate from glycolysis is broken down completely to CO_2 and H_2O.
3. CO_2 and ATP are transported out of the mitochondria into the cytoplasm.
4. The H_2O can remain in the mitochondria or cell, or it can enter the blood and be excreted by the kidneys.

B. Mitochondria
1. A mitochondrion has a double membrane with an intermembrane space between the outer and inner membrane.
2. The **cristae** are the inner folds of membrane that jut into the matrix.
3. The **matrix** is the innermost compartment of a mitochondrion and is filled with a gel-like fluid.
4. The transition reaction and citric acid cycle enzymes are in matrix; the electron transport system is in cristae.
5. Most of the ATP produced in cellular respiration is produced in mitochondria.

C. Transition Reaction
1. The transition reaction connects glycolysis to the citric acid cycle.
2. In this reaction, pyruvate is converted to a two-carbon acetyl group attached to **coenzyme A.**
3. This redox reaction removes electrons from pyruvate by dehydrogenase using NAD^+ as coenzyme.
4. This reaction occurs twice for each original glucose molecule.

D. The Citric Acid Cycle
1. The citric acid cycle metabolic pathway is located in the matrix of mitochondria.
2. The cycle is named for Sir Hans Krebs, who received Nobel Prize for identifying these reactions.
3. This cycle begins by adding a C_2 acetyl group to a C_4 molecule, forming a 6-carbon citrate molecule.
4. The acetyl group is then oxidized to two molecules of CO_2.
5. During the oxidation process, in three cases, two electrons (e) and one hydrogen ion are accepted by NAD^+ and NADH is formed.
6. During this oxidation process, in one case, two electrons and one hydrogen ion are taken by FAD, forming $FADH_2$.
7. NADH and $FADH_2$ carry these electrons to electron transport system.
8. Some energy released is used to synthesize ATP by substrate-level phosphorylation, as in glycolysis.
9. One high-energy metabolite accepts a phosphate group and passes it on to convert ADP to ATP.
10. The citric acid cycle turns twice for each original glucose molecule.
11. Products of the citric acid cycle per glucose molecule include 4 CO_2, 2 ATP, 6 NADH and 2 $FADH_2$.
12. The six carbon atoms in the glucose molecule have now become part of six CO_2, two from the transition reaction and four from the citric acid cycle.

E. The Electron Transport System
   1. The electron transport system is located in cristae of mitochondria and consists of carriers that pass electrons.
   2. Some of the protein carriers are cytochrome molecules.
   3. Electrons that enter the electron transport system are carried by NADH and $FADH_2$.
   4. NADH gives up its electrons and becomes NAD^+; the next carrier then gains electrons and is reduced.
   5. At each sequential oxidation-reduction reaction, energy is released to form ATP molecules.
   6. Because O_2 must be present for system to work, it is also called oxidative phosphorylation.
   7. Oxygen serves as terminal electron acceptor and combines with hydrogen ions to form water.
   8. NADH delivers electrons to system; by the time electrons are received by O_2, three ATP are formed.
   9. If $FADH_2$ delivers electrons to system, by the time electrons are received by O_2, two ATP are formed.
   10. Coenzymes and ATP Recycle
      a. Cell needs a limited supply of coenzymes NAD^+ and FAD because they constantly recycle.
      b. Once NADH delivers electrons to electron transport system, it is free to pick up more hydrogen atoms.
      c. Components of ATP also recycle.
      d. Efficiency of recycling NAD^+, FAD, and ADP eliminates the need to synthesize them anew.

F. The Cristae of a Mitochondrion
   1. Electron transport system consists of three protein complexes and two protein mobile carriers that transport electrons between complexes.
   2. NADH dehydrogenase complex, cytochrome *b-c* complex, and cytochrome oxidase complex all pump H^+ ions into the intermembrane space.
   3. Energy released from flow of electrons down electron transport chain is used to pump H^+ ions, carried by NADH and $FADH_2$, into intermembrane space.
   4. Accumulation of H^+ ions in this intermembrane space creates a strong electrochemical gradient.
   5. **ATP synthase complexes** are channel proteins that also serve as enzymes for ATP synthesis.
   6. As H^+ ions flow from high to low concentration, ATP synthase synthesizes ATP.
   7. Chemiosmosis is the term used for this ATP production tied to an electrochemical (H^+) gradient across a membrane.
   8. Respiratory poisons confirm the chemiosmotic nature of ATP synthesis (i.e., a poison that inhibits ATP synthesis increases the H^+ gradient).
   9. Once formed, ATP molecules diffuse out of the mitochondrial matrix through channel proteins.

G. Energy Yield From Glucose Breakdown
   1. Substrate-Level Phosphorylation
      a. Per glucose molecule, there is a net gain of two ATP from glycolysis in cytoplasm.
      b. The citric acid cycle in the matrix of the mitochondria produces two ATP per glucose.
      c. Total of four ATP are formed by substrate-level phosphorylation outside of the electron transport system.
   2. Electron Transport System and Chemiosmosis
      a. Most ATP is produced by the electron transport system and chemiosmosis.
      b. Per glucose, 10 NADH and two $FADH_2$ molecules provide electrons and H^+ ions to the electron transport system.
      c. For each NADH formed within the mitochondrion, three ATP are produced.
      d. For each $FADH_2$ formed by the citric acid cycle, two ATP result since $FADH_2$ delivers electrons after NADH.
      e. For each NADH formed outside mitochondria by glycolysis, two ATP are produced as electrons are shuttled across the mitochondrial membrane by an organic molecule and delivered to FAD.
   3. Efficiency of Cellular Respiration
      a. The energy difference between total reactants (glucose and O_2) and products (CO_2 and H_2O) is 686 kcal.
      b. An ATP phosphate bond has an energy of 7.3 kcal; 36 to 38 ATP are produced during glucose breakdown for total of at least 263 kcal.
      c. This efficiency is 263/686, or 39% of the available energy in glucose is transferred to ATP.

8.4 Fermentation

A. Cellular Respiration Includes Fermentation
   1. Fermentation consists of glycolysis plus reduction of pyruvate to either lactate or alcohol and CO_2.

2. NADH passes its electrons to pyruvate instead of to an electron transport system; NAD^+ is then free to return and pick up more electrons during earlier reactions of glycolysis.
3. Examples
    a. Anaerobic bacteria produce lactic acid when we manufacture some cheeses.
    b. Anaerobic bacteria produce industrial chemicals: isopropanol, butyric acid, propionic acid, and acetic acid.
    c. Yeasts use CO_2 to make bread rise and produce ethyl alcohol in wine-making.
    d. Animals reduce pyruvate to lactate when it is produced faster than it can be oxidized by Krebs cycle.

B. Advantages and Disadvantages of Fermentation
1. Despite a low yield of two ATP molecules, fermentation provides a quick burst of ATP energy for muscular activity.
2. The disadvantage is that lactate is toxic to cells.
    a. When blood cannot remove all lactate from muscles, lactate changes pH and causes muscles to fatigue.
    b. Individual is in **oxygen debt** because oxygen is needed to restore ATP levels and rid the body of lactate.
    c. Recovery occurs after lactate is sent to liver where it is converted into pyruvate; some pyruvate is then respired or converted back into glucose.

C. Efficiency of Fermentation
1. Two ATP produced per glucose molecule during fermentation is equivalent to 14.6 kcal.
2. Complete glucose breakdown to CO_2 and H_2O during cellular respiration represents a possible yield of 686 kcal. of energy.
3. Efficiency for fermentation is 14.6/686 or about 2.1%, much less efficient than complete breakdown of glucose.

8.5 Metabolic Pool

A. Degradative and Synthetic Reactions
1. Degradative reactions participate in catabolism and break down molecules; they tend to be exergonic.
2. Synthetic reactions participate in anabolism and build molecules; they tend to be endergonic.

B. **Catabolism**
1. Just as glucose was broken down in cellular respiration, other molecules undergo catabolism.
2. Fat breaks down into glycerol and three fatty acids.
    a. Glycerol is converted to PGAL, a metabolite in glycolysis.
    b. An 18-carbon fatty acid is converted to nine acetyl-CoA molecules that enter the citric acid cycle.
    c. Respiration of fat products can produce 108 kcal in ATP molecules; fats are an efficient form of stored energy.
3. Amino acids break down into carbon chains and amino groups.
    a. Hydrolysis of proteins results in amino acids.
    b. *R*-group size determines whether carbon chain is oxidized in glycolysis or the citric acid cycle.
    c. A carbon skeleton is produced in liver by removal of the amino group, a process of deamination.
    d. The amino group becomes ammonia (NH_3), which enters urea cycle and becomes part of excreted urea.
    e. Length of *R*-group determines number of carbons left after deamination.

C. Anabolism
1. ATP produced during catabolism drives anabolism.
2. Substrates making up pathways can be used as starting materials for synthetic reactions.
3. The molecules used for biosynthesis constitute **metabolic pool.**
4. Carbohydrates can result in fat synthesis: PGAL converts to glycerol, acetyl groups join to form fatty acids.
5. Some metabolites can be converted to amino acids by transamination, transfer of an amino acid group to an organic acid.
6. Plants synthesize all amino acids they need; animals lack some enzymes needed to make some amino acids.
7. Humans synthesize 11 of 20 amino acids; remaining 9 **essential amino acids** must be provided by diet.