4.2 Aerobic Respiration: The Details

The process of aerobic respiration extracts the energy that your body needs from simple food molecules. Of the many thousands of chemical reactions that take place in living cells, the reactions that make up aerobic respiration are among the most essential. They take place in every oxygen-breathing organism on Earth. In fact, aerobic respiration made the evolution of large animals possible because it allowed them to meet their very high energy demands.

As you read this section, remember that every one of your billions of active cells requires access to more than one million ATPs per second! Those ATPs are generated within each cell by aerobic cellular respiration. In this section, you will learn about the four stages of aerobic cellular respiration: glycolysis, pyruvate oxidation, the citric acid cycle, and the electron transport chain. You will learn how the energy that is released during the final stage drives most ATP synthesis.

Glycolysis

Glycolysis is the first set of reactions for extracting energy from sugar molecules. It is considered to be the most fundamental and probably most ancient of all metabolic pathways. This is supported by the following facts. First, glycolysis is nearly universal, being found in almost all organisms, both prokaryotes and eukaryotes, from all branches of the tree of life. Second, it does not require O_2. Oxygen became abundant in Earth's atmosphere only about 2.5 billion years ago—about 1.5 billion years after scientists think that life began. Third, glycolysis occurs in the cytosol of all cells and involves soluble enzymes. Therefore, it does not require more sophisticated cellular organelles in order to operate.

Glycolysis is one of the first metabolic pathways that was studied and is one of the best understood, in terms of the enzymes involved, their mechanisms of action, and the regulation of the pathway to meet the energy needs of the organism. The first experiments investigating glycolysis took place over 100 years ago. Using extracts from yeast cells, researchers showed that they could study biological reactions in an isolated system. These experiments became the foundation of modern biochemistry.

The Reactions of Glycolysis

Glycolysis consists of 10 sequential enzyme-catalyzed reactions that lead to the oxidation of the 6-carbon sugar glucose, producing two molecules of the 3-carbon compound pyruvate. The potential energy and electrons released in the oxidation leads to the overall synthesis of both ATP and NADH. Glycolysis has two phases: an initial energy investment phase followed by an energy payoff phase (**Figure 1**). Both the initial energy investment phase and the energy payoff phase have five steps (**Figure 2**, next page).

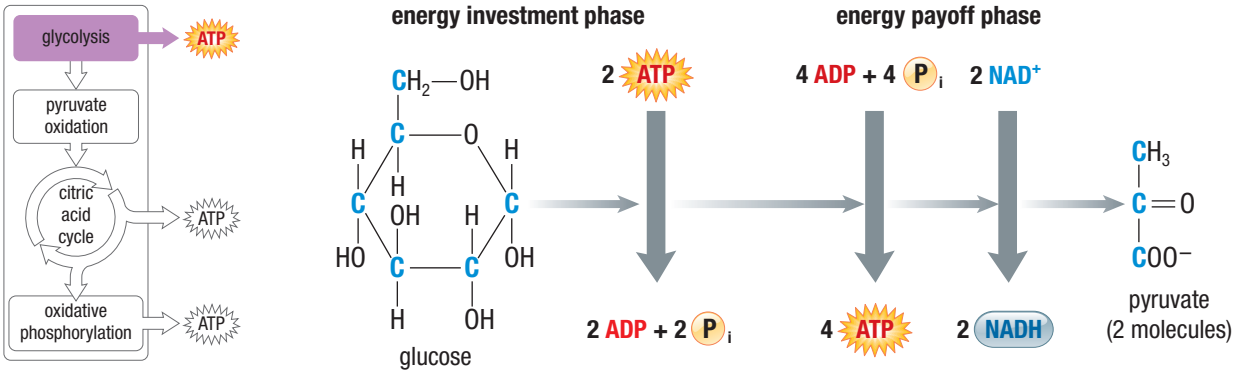

Figure 1 Summary of glycolysis showing the energy inputs and outputs

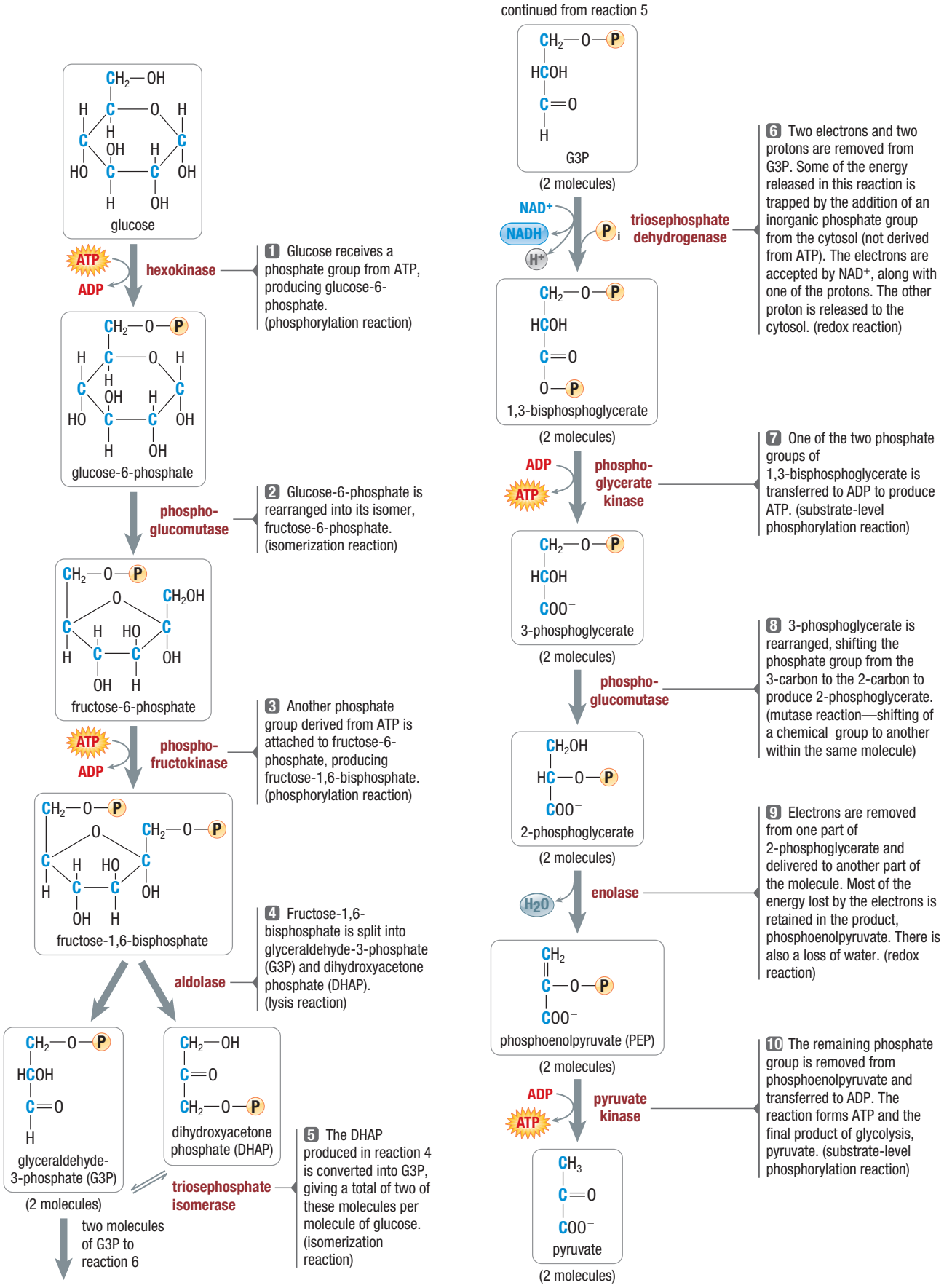

Figure 2 The reactions of glycolysis, including the initial five-step energy investment phase followed by the five-step energy payoff phase. Because two molecules of G3P are produced in reaction 5, all the reactions from 6 to 10 are doubled (not shown). The names of the enzymes that catalyze each reaction are in red.

As you look at Figures 1 and 2, there are three key points to keep in mind:

1. Initially, 2 ATP are consumed as glucose and fructose-6-phosphate become phosphorylated. In the energy investment phase, 2 ATP increase the free energy of the chemicals in the glycolytic pathway. However, even more free energy is released in the payoff phase, as 4 ATP and 2 NADH molecules are synthesized.
2. Besides yielding a net of 2 ATP and 2 NADH for each molecule of glucose that is oxidized, no carbon is lost. All six carbons in glucose are accounted for in the two molecules of pyruvate. However, since glucose has been partially oxidized, the potential energy in two molecules of pyruvate is less than the potential energy in one molecule of glucose. Although two water molecules were produced in Step 9, they are not usually included in the overall equation for glycolysis because they are later consumed in the hydrolysis of the 2 ATP molecules and the reforming of 2 ADP and 2 P_i.
3. During glycolysis, ATP is produced using substrate-level phosphorylation (**Figure 3**). In this mode of ATP synthesis, an enzyme transfers a phosphate group from a high-energy substrate molecule to adenosine diphosphate (ADP), producing ATP. Substrate-level phosphorylation is also the mode of ATP synthesis that is used during the citric acid cycle.

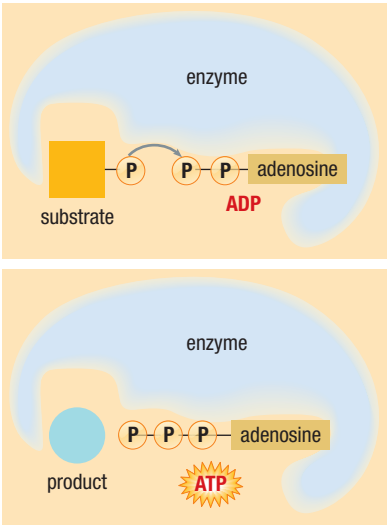

Figure 3 During substrate-level phosphorylation, a phosphate group is transferred from a high-energy donor directly to ADP, forming ATP.

The net equation for glycolysis is given below:

$$\text{glucose} + 2\ \text{ADP} + 2\ P_i + 2\ NAD^+ \rightarrow 2\ \text{pyruvate} + 2\ \text{ATP} + 2\ \text{NADH} + 2H^+$$

The energy that is stored by the synthesis of two moles of ATP is 62 kJ. The energy that could be released by the complete oxidation of one mole of glucose is 2870 kJ. The glycolysis energy conversion efficiency (per mole of glucose processed) can be represented as follows:

$$\text{energy conversion efficiency} = \frac{62\ \text{kJ}}{2870\ \text{kJ}} \times 100\ \% = 2.2\ \%$$

For every one mole of glucose, only about 2.2 % of the available free energy is converted to ATP in glycolysis. Some of the energy is lost as thermal energy, but most is still stored in two pyruvate molecules and two NADH molecules, which will continue through the subsequent stages of aerobic respiration. Different organisms use a variety of methods to transfer the NADH (or the electrons it carries) into the mitochondria and to the electron transport chain. These methods vary in their energy cost, so the amount of ATP generated for each NADH formed in glycolysis can vary. Though the percentage return for glycolysis is low, some organisms use glycolysis as their primary source of energy. For aerobic organisms, however, this is just the beginning process.

Pyruvate Oxidation and the Citric Acid Cycle

The two molecules of pyruvate that are synthesized by glycolysis still contain approximately 75 % of the energy found in one molecule of glucose. The extraction of the remaining free energy in pyruvate continues via pyruvate oxidation and the citric acid cycle (**Figure 4**, next page). In these reactions, more ATP and more of the electron carriers NADH and $FADH_2$ are formed, while the remaining glucose is completely oxidized. Carbon is released in the form of waste CO_2.

Pyruvate Oxidation

The reactions of the citric acid cycle occur in the mitochondrial matrix, so the pyruvates that are produced in glycolysis must pass through both the outer and inner mitochondrial membranes. Large pores in the outer membrane allow pyruvate to diffuse through. For pyruvate to cross the inner membrane, however, a pyruvate-specific membrane carrier is required. Once pyruvate enters the matrix, it is converted into an acetyl group, which is then temporarily bonded to a sulfur atom on the end of a large molecule called coenzyme A, or CoA. The result is an acetyl-CoA complex. This multistep process is referred to as pyruvate oxidation (or pyruvic acid oxidation).

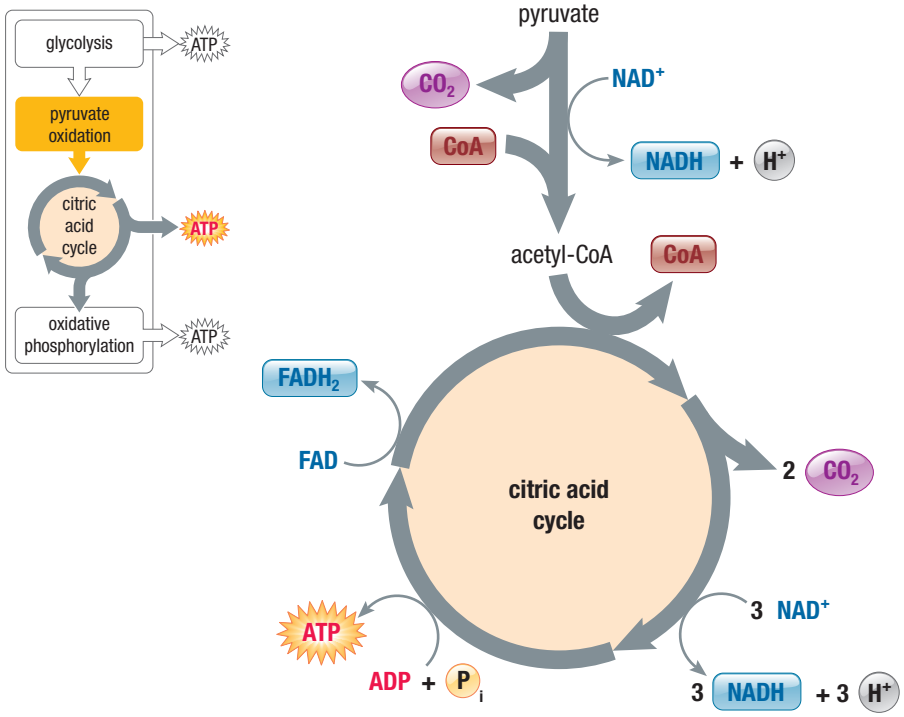

Figure 4 The overall reactions of pyruvate oxidation and the citric acid cycle

The conversion of pyruvate to acetyl-CoA starts with a **decarboxylation reaction** in which the carboxyl ($-COO^-$) group of pyruvate is removed and forms a CO_2 as a waste product (**Figure 5**). In fact, this reaction produces one-third of the CO_2 that we exhale! Decarboxylation is followed by oxidation of the remaining two carbon molecules, producing an acetyl group. This **dehydrogenation** reaction transfers two electrons and a proton to NAD^+, forming NADH, and releases an H^+ ion into solution. Lastly, the acetyl group reacts with the sulfur atom of coenzyme A, forming the high-energy intermediate acetyl-CoA. The net reaction for pyruvate oxidation can be represented as follows:

$$2 \text{ pyruvate} + 2 \text{ NAD}^+ + 2 \text{ CoA} \rightarrow 2 \text{ acetyl-CoA} + 2 \text{ NADH} + 2 \text{ H}^+ + 2 \text{ CO}_2$$

decarboxylation reaction a chemical reaction that removes a carboxyl group to form CO_2

dehydrogenation the removal of a hydrogen atom from a molecule

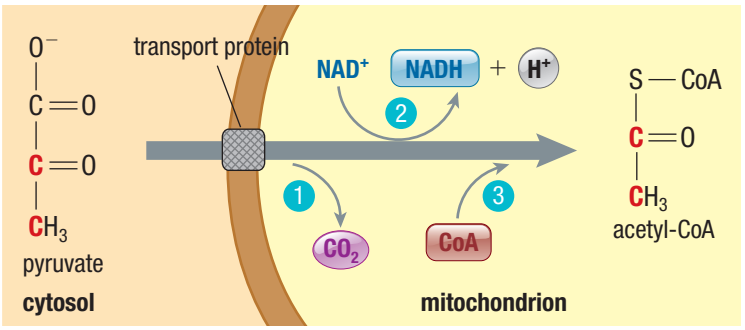

Figure 5 In the mitochondrion, pyruvate is oxidized to an acetyl group, which is carried to the citric acid cycle by CoA. The reactions that are catalyzed by the pyruvate dehydrogenase complex include (1) decarboxylation, followed by (2) a dehydrogenation, and finally (3) a reaction with coenzyme A (CoA) that produces acetyl-CoA. Note that the sulfur atom (S) is part of coenzyme A.

The Citric Acid Cycle

In 1937, Sir Hans Krebs (1900–1981), a biochemist at the University of Sheffield in England, discovered the metabolic reactions that became known as the Krebs cycle (now called the citric acid cycle). The citric acid cycle consists of eight enzyme-catalyzed reactions. Seven of these reactions take place in the mitochondrial

matrix, and one binds to the matrix side of the inner mitochondrial membrane. Combined, these reactions result in the oxidization of acetyl groups to CO_2, accompanied by the synthesis of ATP, NADH, and another nucleotide-based molecule, flavin adenine dinucleotide (FAD; the reduced form is $FADH_2$) (**Figure 6**). For each acetyl-CoA that enters the citric acid cycle, three NADH and one $FADH_2$ are produced, along with one ATP that is synthesized by substrate-level phosphorylation. In a complete turn of the cycle, one 2-carbon acetyl unit is consumed and two CO_2 molecules are released, thereby completing the conversion of all the carbon atoms that were originally in glucose into CO_2. The CoA molecule that carried the acetyl group to the cycle is released and again participates in pyruvate oxidation to pick up another acetyl group. The net reactants and products of one turn of the citric acid cycle are given below:

$$\text{acetyl-CoA} + 3\,NAD^+ + FAD + ADP + P_i \rightarrow 2\,CO_2 + 3\,NADH + 3\,H^+ + FADH_2 + ATP + CoA$$

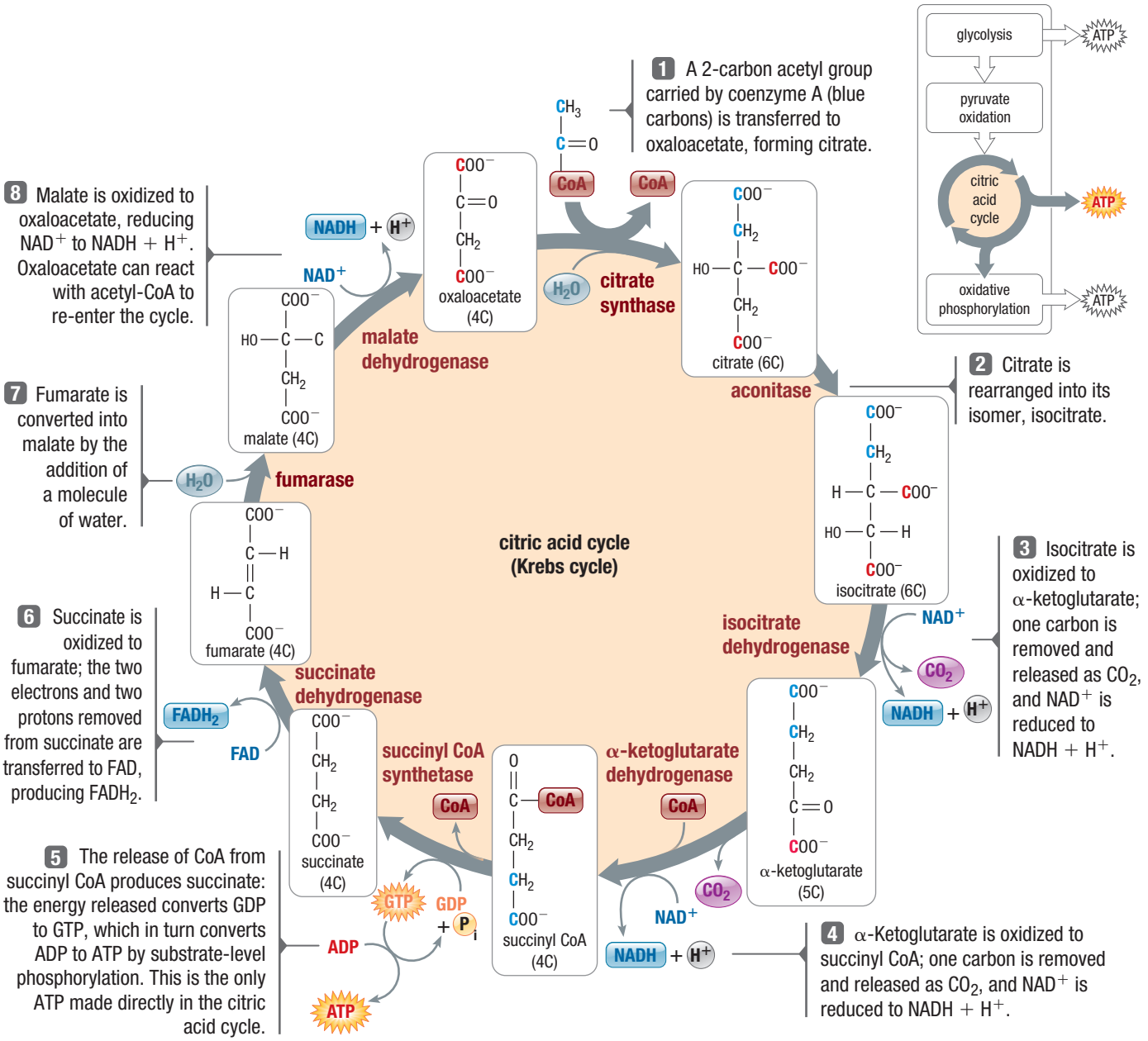

Figure 6 The reactions in the citric acid cycle: Enzyme names are in red. The CoA that is released in reaction 1 can cycle back for another turn of pyruvate oxidation.

During glycolysis, one molecule of glucose is converted into two molecules of pyruvate. Then, during pyruvate oxidation, each molecule of pyruvate is converted into one acetyl group. Therefore, all of the reactants and products are doubled when the citric acid cycle is considered as a continuation of glycolysis and pyruvate oxidation. Review Figure 6 as you consider the citric acid cycle:

- Two acetyl-CoA molecules enter the citric acid cycle from glycolysis and the pyruvate oxidation of one glucose molecule.
- In Step 1, the acetyl group enters the cycle as it reacts with oxaloacetate to form one molecule of citrate. This is why the process is called the citric acid cycle.
- In Steps 3, 4, 5, 6, and 8, some of the released energy is captured and used to form NADH, ATP, and $FADH_2$.
- In Steps 3, 4, and 8, NAD^+ is reduced to form NADH.
- Step 5 produces ATP from ADP and P_i by substrate-level phosphorylation.
- Step 6 reduces FAD to form $FADH_2$.
- Because one glucose molecule yields two pyruvate molecules, each glucose molecule generates two turns of the citric acid cycle.

By the end of the citric acid cycle, the original glucose molecule has been completely dismantled. The original carbon and oxygen atoms are in the form of CO_2 and are released as waste. All that remains of the original glucose molecule are the hydrogens, which are now carried by NADH and $FADH_2$. The electrons associated with these hydrogens retain a large amount of chemical potential energy.

Investigation 4.2.1

Observing the Products of Cellular Respiration (p. 199)
In this investigation, you will design an experiment that compares the rate of energy consumption before, during, and after exercise.

Mini Investigation

Observing Evidence of Respiration

Skills: Performing, Observing, Analyzing

SKILLS HANDBOOK A1, A2.1

In this investigation, you will analyze the results of exhaling CO_2 to make a direct connection between pyruvate oxidation and the citric acid cycle—the source of all exhaled carbon dioxide. Keep in mind that CO_2 forms carbonic acid when it reacts with water. The following chemical equation represents the formation of carbonic acid, H_2CO_3, from CO_2 and water:

$$CO_2(g) + H_2O(l) \leftrightarrow H^+(aq) + H_2CO_3^-(aq)$$

Equipment and Materials: drinking straw; limewater; slightly basic solution (0.01 mol/L NaOH); phenolphthalein indicator

Do not inhale through the straw. Do not share straws.

Sodium hydroxide solution is corrosive. Avoid skin and eye contact. If sodium hydroxide comes in contact with your skin or eyes, wash the affected area for 15 min with cool water and notify your teacher.

Phenolphthalein indicator is flammable. Keep it away from open flames.

1. Take a deep breath, and then slowly exhale the entire breath out the drinking straw into a small flask with limewater.
2. Repeat Step 1 until you observe a marked change in the limewater solution.
3. Observe the change in the limewater solution over time. Record how many breaths it took to observe a change in the limewater solution.
4. Repeat Steps 1 to 3, but now exhale into a slightly basic solution containing phenolphthalein indicator.

A. What happened to the limewater as you exhaled through the straw? Why? T/I

B. What happened to the phenolphthalein indicator as you exhaled CO_2 into the slightly basic solution? Why? T/I

The Electron Transport Chain and Chemiosmosis

In the citric acid cycle, all the carbon that was present in glucose was oxidized and released as CO_2. In addition, while some ATP was formed by substrate-level phosphorylation, most of the potential energy that was originally present in glucose was captured during the formation of NADH and $FADH_2$. The electron transport chain extracts the potential energy in these molecules and makes it available for the synthesis of additional ATP.

The Electron Transport Chain

The electron transport chain comprises a system of components that, in eukaryotes, occurs on the inner mitochondrial membrane (**Figure 7(a)**). This chain facilitates the transfer of electrons from NADH and $FADH_2$ to O_2. It consists of four protein complexes: complex I, NADH dehydrogenase; complex II, succinate dehydrogenase; complex III, cytochrome complex; and complex IV, cytochrome oxidase. Complex II is a single peripheral membrane protein, whereas the other three complexes are composed of multiple proteins.

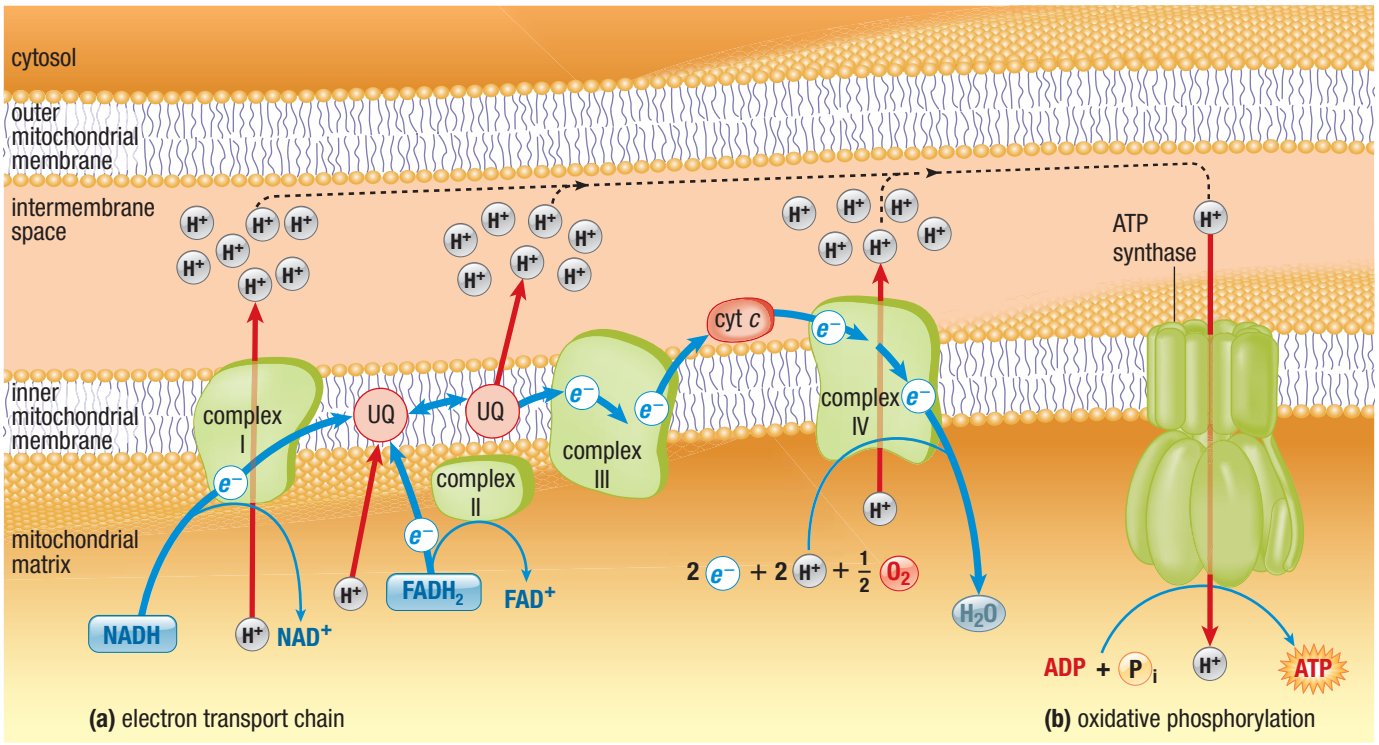

Figure 7 (a) During the electron transport chain, electrons flow through a series of proton (H^+) pumps. The energy released builds an H^+ gradient across the inner mitochondrial membrane. (b) During oxidative phosphorylation, ATP synthase catalyzes ATP synthesis using energy from the H^+ gradient across the membrane (chemiosmosis).

The flow of electrons from one complex to another is facilitated by two mobile electron shuttles. Ubiquinone (UQ), which is a hydrophobic molecule found in the core of the membrane, shuttles electrons from complexes I and II to complex III. A second shuttle, cytochrome *c* (cyt *c*), is located on the intermembrane space side of the membrane and transfers electrons from complex III to complex IV.

THE DRIVING FORCE BEHIND ELECTRON TRANSPORT

Complexes I, III, and IV are protein complexes with increasing electronegativity along the chain. These complexes have cofactors that alternate between reduced and oxidized states as they pull electrons from upstream molecules and subsequently donate electrons to more electronegative downstream molecules. Thus, it is not the proteins themselves that transfer electrons, but rather non-protein groups bound to the proteins of each complex. The electron transport chain is the final destination of all the oxygen we breathe, which is transported around the body. Oxygen goes to the mitochondria to perform the single vital task of pulling electrons away from complex IV.

Before oxygen removes electrons from complex IV, all the carriers and NADH are fully reduced, with stable, full electron shells. Nothing can happen due to their stable state. For example, NADH cannot have its electrons removed by complex I because complex I already has a full complement of electrons. However, oxygen is highly electronegative. When oxygen interacts with complex IV, it removes a pair of electrons.

As an oxygen atom removes two electrons from complex IV, it also reacts with two protons (2 H^+) from the matrix to form a single molecule of water. In total, then, for every O_2 gas molecule we breathe in, four electrons are pulled through the electron transport chain and two water molecules are produced. This triggers a chain reaction. Complex IV cannot get the electrons back from oxygen (which has a stronger pull), but it is in contact with the slightly weaker (less electronegative) complex III. It takes two electrons away from complex III, which, in turn, takes electrons away from complex I. This cascade of events continues along the chain and is very fast—almost instantaneous.

The electrons are being pulled by forces of attraction through the chain, beginning with O_2, which has the highest electronegativity. The electronegative nature of O_2 drives the entire process of the electron transport chain. The individual electron carriers of the chain are, in fact, organized in a very specific way, from high to low free energy (**Figure 8**). Each component is more electronegative than the preceding carrier in the chain. Oxygen has the strongest pull on electrons, and NADH has the weakest pull. Overall, molecules such as NADH contain an abundance of free energy and can be readily oxidized, whereas O_2, the terminal electron acceptor of the chain, is strongly electronegative. The electrons in NADH have the most free energy. This energy is released as they form stronger and stronger bonds, moving through the electron transport chain (bond formation releases energy).

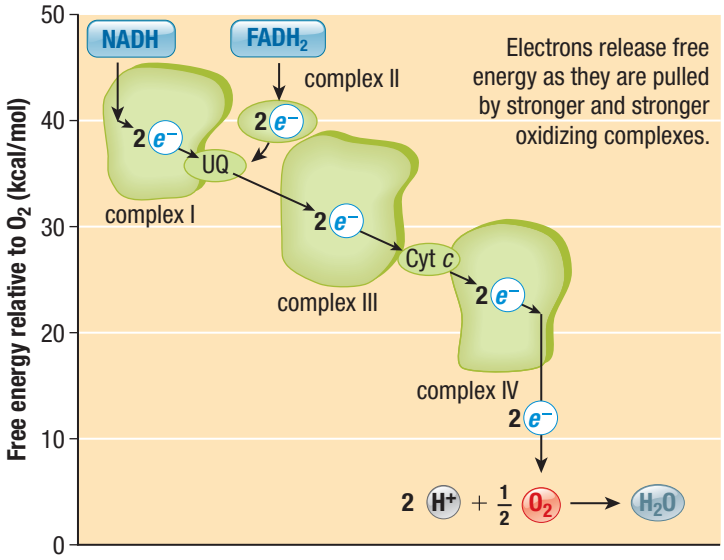

Figure 8 Redox components of the electron transport chain are organized from high to low energy. Without the driving force of oxygen, the entire chain would stop.

Mini **Investigation**

Modelling the Oxidation Shuffle

Skills: Questioning, Performing, Observing, Analyzing, Evaluating, Communicating

SKILLS HANDBOOK A2.1

This investigation will help you understand how and why the electron transport chain (ETC) works and what conditions can stop it from moving forward.

Equipment and Materials: 10 balls (representing electrons); 7 team members (1 helper and 6 "chemicals" representing 1 NADH, 4 electron transport chain complexes, and 1 oxygen atom); 6 oxidation strength cards

1. Six students stand in a straight line, facing forward, with the NADH student on the left end and the oxygen student on the right end. The four students in the middle represent ETC complexes.
2. The helper hands the NADH and ETC students two electrons (balls) each. They place one electron in each hand. The oxygen student is not given any electrons.
3. Then the helper passes out the oxidation strength cards. The higher the number on the card, the greater is the ability of the complex to replace any missing electrons (the greater its electronegativity). NADH is always given card number 1 (the weakest oxidizer). Oxygen is always given card number 6 (the strongest oxidizer). The other four cards are shuffled and given to the four remaining students at random. Record the order of the cards; for example, 1, 3, 4, 2, 5, 6.

4. In this simulation, any student who is missing two electrons or has just lost two electrons can take two electrons from a student standing immediately next to them, but ONLY if the oxidation strength of the next student is less than theirs.
5. The simulation will always begin when the oxygen student takes two electrons from the student standing next to them.
6. As long as any student without electrons has a greater oxidation strength than an adjacent student, electron transfer can happen.
7. Continue acting out the electron transport reactions until a student cannot replace their lost electrons. When this happens, the trial ends.
8. Record the position of the student with the missing electrons. Was it the NADH student?
9. Repeat Steps 1 to 8, being sure to reshuffle the cards for the four middle students.
10. Continue to conduct new trials of the simulation until a trial ends with the removal of electrons from NADH.

A. Explain what order(s) of cards allowed the complete electron transport from NADH to oxygen. T/I
B. How does this investigation model the protein complexes in the electron transport chain? T/I
C. In glycolysis and the citric acid cycle, which molecules obtain electrons? Where did these electrons originally come from? T/I
D. Can the electrons ever move along the chain without oxygen? T/I
E. What might happen to the chain if there were no source of NADH? T/I
F. What happens to NADH after it loses electrons? T/I
G. In a modified version of this simulation, oxygen atoms continuously arrive at the end of the transport chain, while NADH molecules continuously lose electrons at the other end but get "replacements" from a large container. In aerobic cellular respiration pathways, what would this large container represent? T/I

Chemiosmosis

Although the end result of aerobic cellular respiration is the synthesis of ATP, electron transport from NADH or $FADH_2$ to O_2 does not, in itself, produce any ATP. To understand how ATP is formed from electron transport, go back to Figure 7. Recall that NADH has more free energy than O_2. During electron transport, the free energy that is released is used to do work, specifically the work of transporting protons (H^+ ions) across the inner mitochondrial membrane, from the matrix into the intermembrane space. As a result of proton pumping across the inner membrane, the H^+ concentration in the intermembrane space becomes much higher than the H^+ concentration in the matrix. This difference in H^+ concentration is called a **proton gradient**, and it is a form of potential energy.

proton gradient a difference in proton (H^+ ion) concentration across a membrane

Electron flow through the electron transport chain drives a series of proton pumps in the inner mitochondrial membrane. Within complexes I and IV, specific protein components use the energy that is released from electron transport for proton pumping. In addition, as ubiquinone molecules (UQ) accept electrons from complexes I and II, they pick up protons from the matrix. After migrating through the membrane and donating electrons to complex III, ubiquinone retains a neutral charge by releasing protons into the intermembrane space.

When one side of the inner mitochondrial membrane has more protons than the other side, the difference represents a source of energy that can be harnessed to do work. The potential energy that is possessed by a proton gradient is derived from two factors. First, a chemical gradient exists across the membrane because the concentration of protons on both sides is not equal. Second, because the protons are charged, they repel each other and are attracted to the more negative interior of the matrix. The combination of a concentration gradient and an electrical potential (charge) gradient across the membrane produces a force known as the **proton-motive force.**

proton-motive force a force that moves protons because of a chemical gradient (often referred to as an electrochemical gradient) of protons across a membrane

The ability of cells to use the proton-motive force to do work is called **chemiosmosis**. It was first proposed as a mechanism to generate ATP by the British biochemist Peter Mitchell, who received a Nobel Prize in Chemistry in 1978. In mitochondria, the energy for chemiosmosis comes from the oxidation of energy-rich molecules, such as NADH, by the electron transport chain. Chemiosmosis also accounts for the generation of ATP in chloroplasts, where electron transport is driven by light energy. Chemiosmosis, however, does not only refer to the synthesis of ATP.

chemiosmosis a process in which ATP is synthesized using the energy of an electrochemical gradient and the ATP synthase enzyme

The proton-motive force is also used to pump substances across membranes and to drive the rotation of flagella in prokaryotes.

This mode of ATP synthesis, which is linked to the oxidation of energy-rich molecules by an electron transport chain, is called oxidative phosphorylation. Unlike substrate-level phosphorylation, which occurs during glycolysis and the citric acid cycle, oxidative phosphorylation relies on the action of a large multi-protein complex called ATP synthase.

ATP SYNTHASE: A MOLECULAR MOTOR

ATP synthase is a structure that spans the inner mitochondrial membrane. It consists of a basal unit that is embedded in the inner mitochondrial membrane and connected to a headpiece by a stalk (**Figure 7(b)**, page 178). The headpiece extends into the mitochondrial matrix. The basal unit forms a channel through which H^+ ions can pass freely. The proton-motive force moves protons in the intermembrane space through the channel in the enzyme's basal unit, down their concentration gradient, and into the matrix. The flow of protons powers ATP synthesis by the headpiece. Evidence indicates that the binding of three protons to sites in the headpiece causes the headpiece to rotate in a way that catalyzes the formation of one ATP molecule from ADP and P_i. The rotating of the headpiece of ATP synthase represents the smallest molecular rotary motor known in nature.

In Chapter 2, you learned about active transport pumps that use the energy created by the hydrolysis of ATP to ADP and P_i to transport ions across membranes against their concentration gradients. An active transport pump is, in fact, an ATP synthase that is operating in reverse. It does not synthesize ATP but rather uses the free energy from the hydrolysis of ATP to provide the energy needed to pump ions (such as protons) across a membrane. The ability to harness the potential energy that is present in a proton gradient to synthesize ATP is fundamental to almost all forms of life and is developed early in the evolution of life. This is shown, in part, by the fact that the structure and function of the ATP synthase complex in mitochondria are essentially identical to those in the thylakoid membrane of the chloroplast and the plasma membrane of prokaryotic cells.

Uncoupling Electron Transport and Chemiosmosis

During oxidative phosphorylation, the potential energy that is released by the oxidation of NADH is used to pump protons into the intermembrane space and build up the proton-motive force. When electron transport and ATP synthesis are uncoupled, the energy that is released during electron transport is not converted to ATP energy. Instead, it is released as thermal energy when protons rush back across the inner membrane without passing through ATP synthase. One way that the uncoupling is achieved is through regulating the expression of a number of uncoupling proteins. Uncoupling proteins, when present, are in the inner mitochondrial membrane and give protons an alternative pathway to re-enter the matrix—a pathway that does not produce ATP and instead releases thermal energy. Certain tissues, such as brown adipose fat, contain mitochondria in which the expression of uncoupling proteins is particularly high. The thermal energy that is generated by these tissues is important for the maintenance of body temperature in hibernating mammals (**Figure 9**), birds that need excess thermal energy in very cold environments, and very young offspring, including human infants. Uncoupling electron transport causes free energy that would be used to generate ATP to be released as thermal energy and maintain body temperature instead.

Figure 9 Bears are able to hibernate because cells in some of their tissues can uncouple the electron transport chain and chemiosmosis to produce thermal energy.

Several chemical compounds, called ionophores, can also act as uncouplers because they form channels across membranes through which ions, including protons, can leak. Because these compounds allow for high rates of electron transport but reduce ATP synthesis, they are potentially toxic. One such chemical, 2,4-dinitrophenol (DNP), was used in diet pills in the 1930s. Ingesting DNP reduces the rate of production of ATP, and cells respond by consuming stored fat more rapidly. Although DNP was effective for losing weight, it had many harmful side effects, including overheating, and its use was discontinued after only a few years. Any chemical may have serious effects if it is capable of influencing aerobic respiration and ATP production.

4.2 Review

Summary

- Glycolysis extracts energy from sugar molecules and produces ATP.
- Pyruvate oxidation converts two pyruvate molecules into two acetyl-CoA molecules, NADH, H^+, and CO_2 waste.
- The citric acid cycle consists of eight enzyme-catalyzed reactions. It uses acetyl-CoA to produce energy, in the form of NADH, $FADH_2$, and ATP, and release CO_2.
- The electron transport chain extracts the potential energy from NADH and $FADH_2$ and converts it to ATP.
- Chemiosmosis is the process of pumping protons across the inner mitochondrial membrane, creating a proton-motive force that provides the energy used to produce ATP.
- Harnessing the potential energy that is present in a proton gradient to synthesize ATP is fundamental to almost all forms of life and is developed early in the evolution of life.
- Uncoupling electron transport and the synthesis of ATP can be caused by making the inner mitochondrial membrane permeable to protons. The energy that is released during electron transport is then converted to thermal energy.

Questions

1. Why is glycolysis considered to be the most fundamental and probably the most ancient of all metabolic pathways? K/U
2. How efficient is glycolysis at converting glucose to ATP? Are there other high-energy products of glycolysis? K/U
3. Glycolysis, pyruvate oxidation, and the citric acid cycle produce only a small amount of ATP from the energy in a glucose molecule. In what form(s) is (are) the rest of the harvestable energy that is converted to ATP in the electron transport chain and chemiosmosis? K/U T/I
4. How does the electron transport chain produce ATP? What is the driving force? K/U
5. (a) Do the electrons in NADH have the most or the least free energy in the electron transport chain?
   (b) The electrons in NADH form bonds as they move through the electron transport chain. Do these bond formations use or release energy? K/U T/I
6. Which stages of aerobic cellular respiration occur in the mitochondria, and which stages do not? K/U
7. Write the overall chemical equation for each process. K/U
   (a) glycolysis
   (b) pyruvate oxidation
   (c) citric acid cycle
8. What important molecule is needed for oxidative phosphorylation but not needed for substrate-level phosphorylation? K/U
9. What is the primary function of the proton-motive force? K/U
10. Give an example of how uncoupling is used by organisms to increase survival. K/U
11. Research the applications of ionophores. How and why are they used in the cattle industry? T/I
12. The oxygen gas that animals breathe in is necessary to drive the electron transport chain and generate ATP, but it also undergoes a chemical reaction to produce a particular product. K/U T/I
    (a) What is the product?
    (b) For every mole of oxygen molecules you breathe in, how many moles of this product are formed?
    (c) How might this be of benefit to desert animals?

WEB LINK