**Cellular Respiration**

**Introduction**

Oxygen and food. They are both required for living organisms. Why must living organisms consume these resources in order to sustain life? To answer this question, we must first define what a living organism is. Two characteristics of living organisms are their ability to respire and their ability to acquire nutrition. Respiration can be defined as, “the release of energy from food substances in all living cells.”[[1]](#footnote-1) Nutrition can be defined as, “the process by which organisms obtain energy and raw materials from nutrients such as proteins, carbohydrates and fats”.[[2]](#footnote-2) Animals, just like humans, obtain oxygen through the physiological process of breathing and their nutrition through the food they consume. Now that we have working definitions of living organisms, respiration, and nutrition, we know partly what the purpose of consuming these resources is for. But, what about energy? What are the roles of these resources in the production and consumption of energy? Whether it be a human riding a bicycle or an Alaskan sled dog running a 1,000-mile Iditarod race, energy is required to successfully complete these activities. In order to make the energy needed for these activities, oxygen and food must work together as a team to convert the biochemical energy found in food into the “energy currency” molecule, adenosine triphosphate (ATP), by a process called cellular respiration. An important molecule extracted from food and used as a fuel for the cellular respiration process is the sugar called glucose.

**What is ATP?**

The ATP molecule is known as currency in the energy world because it is capable of carrying and storing the energy that an organism requires for any type of activity in the bonds of its phosphate groups. Organisms require ATP to carry out every day activities, so having this required energy stored allows organisms to operate much more quickly and efficiently when they need to.

**The Three Parts of Cellular Respiration**

Cellular respiration can be divided into three different stages: glycolysis, the Krebs cycle, and the electron transport chain. Each one of these stages plays a different role in producing the ATP an organism requires for life. From start to finish in cellular respiration, an efficient cell will produce thirty-eight ATP molecules from a single molecule of glucose. Glycolysis takes place within the cytosol of the cell while the Krebs cycle and the electron transport chain operate within the mitochondrial membranes, an organelle within the cell. It is within these mitochondrial membranes where the majority of ATP is produced. Therefore, it is sometimes referred to as “the powerhouse of the cell” and can be compared to a power plant responsible for producing all the electricity required to power an entire city. Let’s look at each stage of cellular respiration in more detail.

**Glycolysis**

Glycolysis is the first stop on the journey to producing ATP energy stocks for an organism. In order to initiate the production of ATP, energy must initially be consumed so that a single glucose molecule (C6H12O6) can be broken down into a less stable form known as fructose. Once the molecule is converted to fructose, several different enzymes will enter the picture and begin working on the molecule to convert it into different forms, as well as split it into two different compounds. An investment of two ATP molecules will be required to convert and split the glucose molecule we started with. From this point forward, every transformation and production will be done in duplicate. The splitting action is where the metabolic process gets its name, glyco- denoting a relationship to sugar and -lysis meaning to split a cell.[[3]](#footnote-3) The final product of the split compounds is known as pyruvic acid. The ATP molecules that are invested into the system to aid in molecule conversion and molecule splitting will donate a phosphate group to the cause and, as a result, be released as adenosine diphosphate (ADP), having just lost a phosphate group. At some point these ADP will need to be re-energized and transformed back to their original state of ATP. As you can expect, this is going to require some energy. This requirement is completed with the help of a coenzyme known as NAD+. NAD+ plays the role of electron transporter within the system, picking up and dropping off electrons to molecules whenever necessary. When a molecule of NAD+ gains an electron, it is reduced to NADH. When NADH loses an electron and returns to its original state, it has been oxidized. Along with the two pyruvic acid molecules that were produced from one glucose molecule, four new molecules of ATP were also produced, but because an investment of two ATPs was required to get the process moving, we have a net production of two ATPs. The NAD+ that were needed to transport electrons will also contribute two NADH molecules to the overall product sum of the glycolysis process. Now that the end of the line for this stage has been reached, we are now ready to move on to the second stage of cellular respiration – the Krebs cycle.

**The Kreb’s Cycle (Citric Acid Cycle)**

The Krebs cycle, also known as the citric acid cycle, is the second stop in the production of ATP. This process takes place inside the inner membrane compartment of the mitochondria. At the end of glycolysis, we were left with two pyruvic acid (pyruvate) molecules. These two pyruvate molecules are required to begin the Krebs cycle. Remember that the glucose molecule we began with was composed of six carbon atoms. Following a series of enzymatic reactions, the glucose molecule was split in two. This means that the two pyruvate molecules we are investing into the Krebs cycle are composed of three carbon atoms. A single pyruvate molecule will be turned into a two carbon molecule called acetyl-CoA. Make note that it is now a two-carbon molecule instead of three. Getting to this step will require some energy and to do that the molecule must be “oxidized”. Once oxidized, a single molecule of CO2 will be lost to the environment and a single molecule of NAD+ will enter the system and be reduced to NADH. With the help of the enzyme citrate synthase, acetyl-CoA is then combined to the four-carbon molecule oxaloacetic acid to become a six-carbon molecule called citric acid. This is where the Krebs cycle gets its alternate name from. The citric acid molecule is then oxidized through several different steps with the help of various enzymes that will cleave off a single carbon atom until it eventually makes its way back to the four-carbon molecule oxaloacetate. Each time a carbon atom is removed from the molecule it is released from the system as CO2 waste, which is removed from the entire organism through exhalation. At various stages through these conversions, NAD+ will be needed to move energy around. Three more NAD+ molecules will be reduced to NADH. FAD, another coenzyme responsible for electron transport, will be turned into FADH2. This process will take place twice for each pyruvate molecule invested, which will end up yielding a total of six NADH molecules, two ATP molecules, and two FADH2 molecules. Adding up what has been produced from glycolysis and the Krebs cycle, we now have 4 ATPs, 10 NADH, and 2 FADH2. As mentioned at the beginning of this chapter, the end goal and function for use of a single glucose molecule is to be able to produce 38 ATP. Where are the other ATP molecules going to come from and what is the use for these NADH and FADH2 molecules? This is where the electron transport chain comes into the picture.

**Electron Transport Chain**

Welcome to the final stage of cellular respiration! Also known as oxidative phosphorylation, this final process within the inner membrane of the mitochondria is where the majority of the ATP will be produced. At the end of the Krebs cycle we were left with 4 ATP molecules, 10 NADH molecules, and 2 FADH2 molecules. For every one molecule of NADH, three molecules of ATP can be formed and for every one FADH2 molecule, two molecules of ATP can be formed. Completion of these transformations will give us a total of 38 ATP molecules, but how exactly are these leftover molecules transformed into energy? In order to produce more ATP, NADH and FADH2 molecules will need to be oxidized. Remember that oxidation happens whenever a molecule loses electrons. There are 4 protein complexes along the electron transport chain. As NADH travels through the first complex it will donate an electron and a hydrogen proton will be pumped through this complex to the outer portion of the inner mitochondrial membrane. FADH2 will be fed into the second complex. The process of oxidation, reduction, and movement of electrons through the four different complexes will continue to take place until all of the leftover components from the Krebs cycle have been used and there is a concentration gradient of hydrogen protons in the outer area of the inner mitochondrial membrane. Because there is a concentration of hydrogens within this area, they will begin to move down this gradient to an area of less concentration. At the end of this gradient is the last complex, ATP synthase. This is where the magic happens. The hydrogen protons will begin flowing back down into the inner portion of the inner membrane through ATP synthase. This flow will spin the ATP synthase pump and power the complex to convert ADP into the ATP we are interested in harvesting. This is where the rest of the ATP molecules will come from and thus the process of cellular respiration is complete.

**Conclusion**

ATP is essential to life. Producing this life sustaining molecule requires oxygen and is the reason we breath. Without oxygen we cannot produce energy and without energy all systems would grind to a halt. Glucose isn’t the only source of nutrition that can be used to power cellular respiration. As it has been defined, nutrients can be obtained from things other than carbohydrates, such as proteins and fats. These sources of nutrients enter the system a little differently than sugars do, meaning they are not required to go through glycolysis, but the results are essentially the same – production of energy. So, whether it’s a human riding a bicycle or an Alaskan sled dog running a 1,000-mile Iditarod race, ATP is the ultimate requirement for completing these activities.

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