Cellular Respiration: An Overview

Original study notes prepared for demonstration and App Review purposes.

1. What Cellular Respiration Is

Cellular respiration is the process by which a cell converts the chemical energy stored in glucose into a form the cell can actually use, a molecule called adenosine triphosphate, or ATP. Nearly every activity a cell performs, from building proteins to pumping ions across a membrane, is paid for in ATP. Respiration is therefore not one reaction but a coordinated sequence of three stages: glycolysis, the citric acid cycle, and the electron transport chain. Each stage hands off partially oxidized carbon and captured electrons to the next, so that the energy in one glucose molecule is released gradually rather than all at once.

2. Glycolysis

Glycolysis takes place in the cytoplasm and does not require oxygen. A six-carbon glucose molecule is split and rearranged through ten enzyme-catalyzed steps into two three-carbon molecules of pyruvate. Along the way the cell invests two molecules of ATP early in the pathway and recovers four later, for a net gain of two ATP per glucose. Two molecules of the electron carrier NAD^+ are also reduced to NADH, capturing high-energy electrons that will be used further down the line. Because glycolysis needs no oxygen, it is the one stage of respiration available to a cell even under anaerobic conditions.

3. Pyruvate Oxidation

Before the citric acid cycle can begin, each three-carbon pyruvate produced by glycolysis is transported into the mitochondrial matrix and converted into a two-carbon acetyl group attached to coenzyme A, forming acetyl-CoA. This conversion releases one carbon dioxide molecule per pyruvate and reduces one more NAD^+ to NADH. Because glycolysis produces two pyruvate molecules per glucose, this step happens twice for every glucose molecule respired.

4. The Citric Acid Cycle

The citric acid cycle, also called the Krebs cycle, occurs in the mitochondrial matrix. Acetyl-CoA combines with a four-carbon molecule called oxaloacetate to form citrate, a six-carbon compound. Over eight subsequent steps, citrate is progressively oxidized and rearranged, releasing two carbon dioxide molecules and regenerating oxaloacetate so the cycle can run again. Each turn of the cycle yields one ATP (or an equivalent GTP), three NADH, and one molecule of a second electron carrier, $FADH_2$. Because the cycle turns once per acetyl-CoA, and two acetyl-CoA are produced per glucose, the cycle runs twice for each original glucose molecule.

5. The Electron Transport Chain and Oxidative Phosphorylation

The NADH and $FADH_2$ produced by the earlier stages carry their electrons to a series of protein complexes embedded in the inner mitochondrial membrane, collectively called the electron transport chain. As electrons pass from complex to complex, energy released in the process is used to pump protons from the matrix into the intermembrane space, building a steep concentration gradient. At the end of the chain, oxygen accepts the electrons and combines with protons to form water; this is the reason cellular respiration requires oxygen. The proton gradient built by the chain is then used by an enzyme called ATP synthase, which allows protons to flow back down the gradient through a channel that spins a molecular rotor, driving the synthesis of ATP from ADP and inorganic phosphate. This mechanism is called chemiosmosis.

6. Total ATP Yield

Textbooks vary slightly in their bookkeeping because the shuttle systems that move electrons into the mitochondrion have different costs, but a commonly cited estimate is about 30 to 32 ATP molecules per glucose when all three stages are combined, counting the small direct yields from glycolysis and the citric acid cycle together with the much larger yield from oxidative phosphorylation. The electron transport chain and chemiosmosis account for the great majority of that total, which is why the presence of oxygen dramatically increases the energy a cell can extract from a single glucose molecule compared to anaerobic pathways alone.

7. Fermentation as an Alternative

When oxygen is scarce, the electron transport chain stalls because there is no final acceptor for its electrons, and NADH accumulates instead of being recycled back to NAD+. Because glycolysis needs a steady supply of NAD+ to keep running, cells fall back on fermentation to regenerate it without oxygen. Animal cells convert pyruvate into lactate, a process familiar from the burning sensation in hard-working muscle, while yeast and some other organisms convert pyruvate into ethanol and carbon dioxide. Fermentation keeps glycolysis running and therefore keeps a small trickle of ATP flowing, but it does not touch the citric acid cycle or the electron transport chain, so its energy yield is far smaller than full aerobic respiration.

8. Comparing Aerobic and Anaerobic Yields

The contrast in ATP yield between aerobic respiration and fermentation is one of the clearest illustrations of why oxygen matters so much to energy metabolism. Fermentation nets only the two ATP produced directly by glycolysis, because its only job is to keep that pathway supplied with NAD+. Full aerobic respiration, by contrast, keeps glycolysis running and also extracts the energy in NADH and $FADH_2$ through the electron transport chain, raising the total to roughly fifteen times as much ATP per glucose molecule. This is why organisms and tissues capable of aerobic respiration can sustain far more energy-intensive activity than those relying on fermentation alone, and why an oxygen debt built up during intense exercise has to be repaid afterward.

9. Regulation of the Pathway

Respiration is not a pathway that simply runs at full speed at all times; it is regulated at several key enzymes so that ATP is produced roughly in step with how much the cell needs. A recurring theme is feedback inhibition: when ATP is already abundant, it tends to slow down the enzymes that commit glucose to being broken down, while a buildup of ADP, signaling that the cell has spent its energy, speeds those same enzymes back up. The enzyme that commits a molecule to the citric acid cycle is similarly sensitive to the ratio of NADH to NAD+, slowing the cycle when NADH is already plentiful and there is little point producing more. This regulation lets a cell match energy production to demand rather than wastefully burning through fuel at a constant rate.

10. Common Misconceptions

A frequent misconception is that glycolysis, the citric acid cycle, and the electron transport chain each produce roughly equal amounts of ATP; in reality the electron transport chain accounts for the large majority of the total, while glycolysis and the citric acid cycle contribute only a handful of ATP directly. Another common error is treating the citric acid cycle as the step that "produces energy," when its main contribution is capturing electrons in NADH and FADH2 for the electron transport chain to use; the cycle itself yields only one ATP-equivalent molecule per turn. Finally, it is easy to describe fermentation as an entirely separate pathway from respiration, but it is more accurate to think of it as glycolysis plus a short regeneration step, reusing the same first stage that aerobic respiration also depends on.

11. Why This Matters

Respiration links the food an organism eats to the energy every one of its cells depends on. Understanding the three-stage structure, where each stage happens, what it requires, and what it produces, gives a framework for predicting how a cell responds when oxygen, glucose, or a particular enzyme is limited. It also explains why mitochondria are often described as the site where most of a cell's usable energy is generated, and why tissues with high energy demands, such as cardiac muscle, are especially rich in mitochondria.