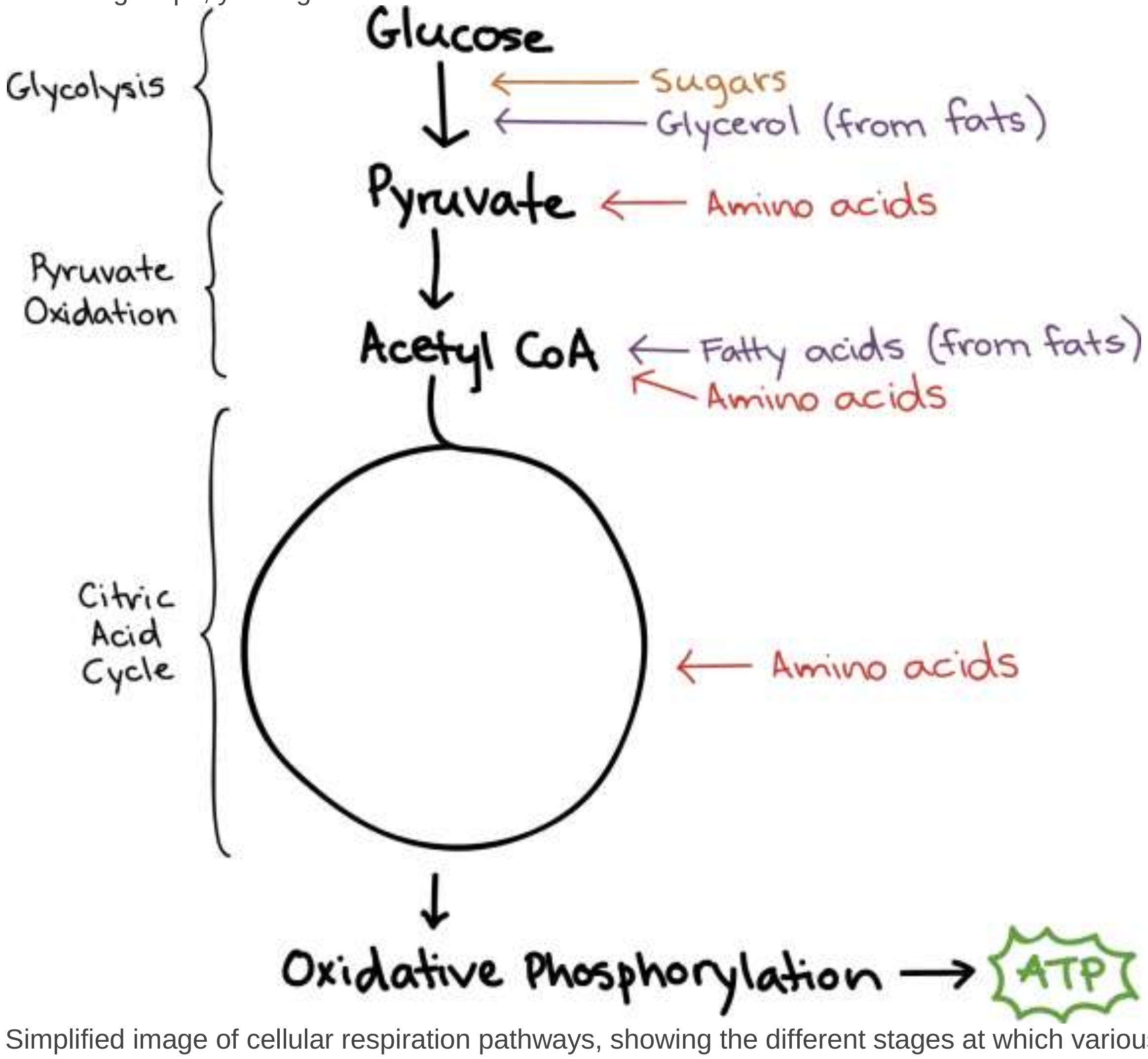
Connections between cellular respiration and other pathways

How molecules other than glucose enter cellular respiration. Use of cellular respiration intermediates for biosynthesis.

Introduction

So far, we've spent a lot of time describing the pathways used to break down glucose. When you sit down for lunch, you might have a turkey sandwich, a veggie burger, or a salad, but you're probably not going to dig in to a bowl of pure glucose. How, then, are the other components of food – such as proteins, lipids, and non-glucose carbohydrates – broken down to generate ATP? As it turns out, the cellular respiration pathways we've already seen are central to the extraction of energy from all these different molecules. Amino acids, lipids, and other carbohydrates can be converted to various intermediates of glycolysis and the citric acid cycle, allowing them to slip into the cellular respiration pathway through a multitude of side doors. Once these molecules enter the pathway, it makes no difference where they came from: they'll simply go through the remaining steps, yielding NADH and ATP.



Simplified image of cellular respiration pathways, showing the different stages at which various types of molecules can enter.

Glycolysis: Sugars, glycerol from fats, and some types of amino acids can enter cellular respiration during glycolysis.

Pyruvate oxidation: Some types of amino acids can enter as pyruvate.

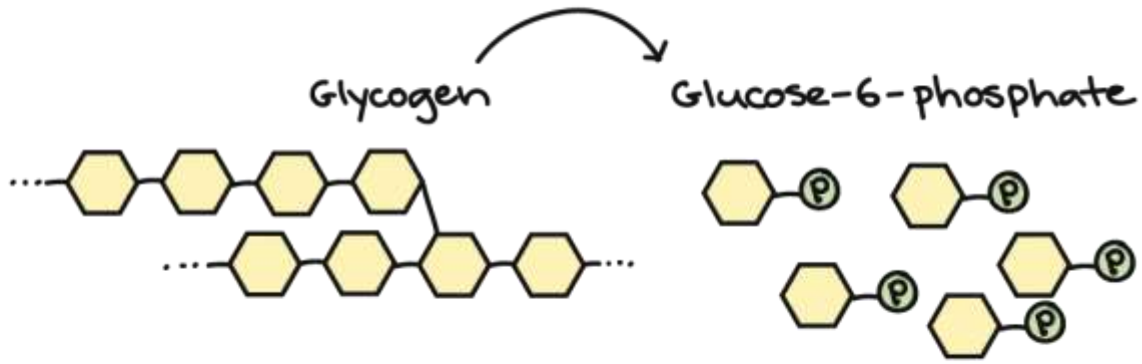
Citric acid cycle: Fatty acids from fats and certain types of amino acids can enter as acetyl CoA, and other types of amino acids can enter as citric acid cycle intermediates.

In addition, not every molecule that enters cellular respiration will complete the entire pathway. Just as various types of molecules can feed into cellular respiration through different intermediates, so intermediates of glycolysis and the citric acid cycle may be removed at various stages and used to make other molecules. For instance, many intermediates of glycolysis and the citric acid cycle are used in the pathways that build amino acids[1].

In the sections below, we'll look at a few examples of how different non-glucose molecules can enter cellular respiration.

How carbohydrates enter the pathway

Most carbohydrates enter cellular respiration during glycolysis. In some cases, entering the pathway simply involves breaking a glucose polymer down into individual glucose molecules. For instance, the glucose polymer glycogen is made and stored in both liver and muscle cells in our bodies. If blood sugar levels drop, the glycogen will be broken down into phosphate-bearing glucose molecules, which can easily enter glycolysis.



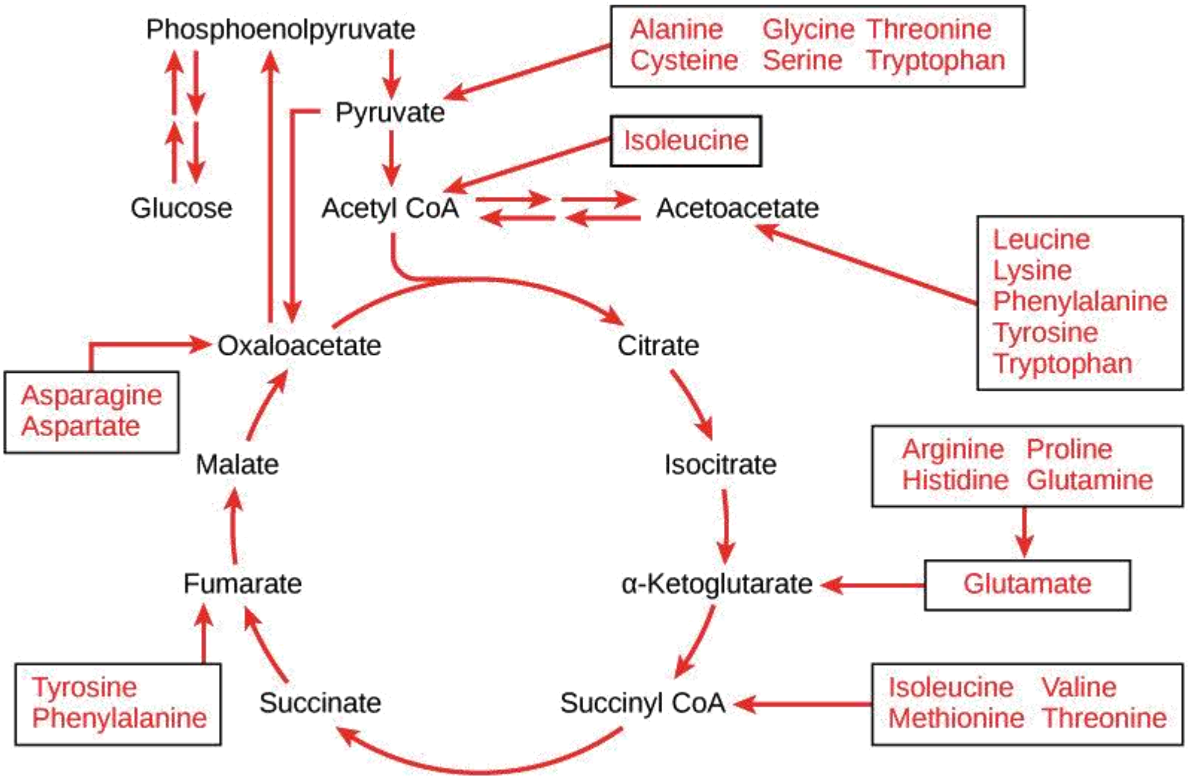
Non-glucose monosaccharide's can also enter glycolysis. For instance, sucrose (table sugar) is made up of glucose and fructose. When this sugar is broken down, the fructose can easily enter glycolysis: addition of a phosphate group turns it into fructose-6-phosphate, the third molecule in the glycolysis pathway. Because it enters so close to the top of the pathway, fructose yields the same number of ATP as glucose during cellular respiration.

How proteins enter the pathway

When you eat proteins in food, your body has to break them down into amino acids before they can be used by your cells. Most of the time, amino acids are recycled and used to make new proteins, not oxidized for fuel.

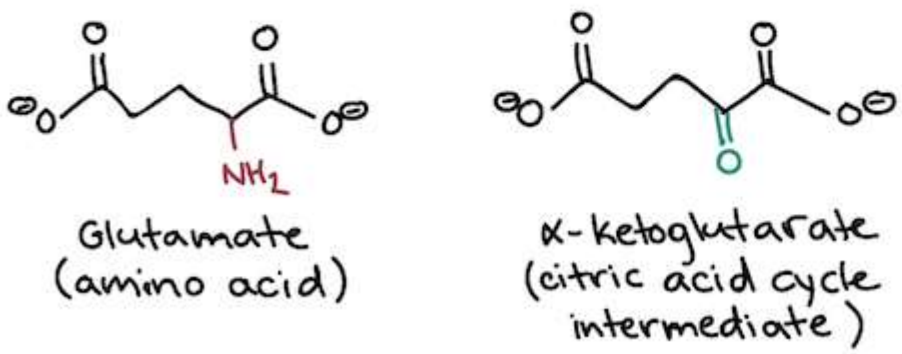
However, if there are more amino acids than the body needs, or if cells are starving, some amino acids will broken down for energy via cellular respiration. In order to enter cellular respiration, amino acids must first have their amino group removed. This step makes ammonia (NH_3 as a waste product, and in humans and other mammals, the ammonia is converted to urea and removed from the body in urine.

Once they've been de-aminated, different amino acids enter the cellular respiration pathways at different stages. The chemical properties of each amino acid determine what intermediate it can be most easily converted into.



This illustration shows that the amino acids alanine, glycine, threonine, cysteine, and serine can be converted into pyruvate. Leucine, lysine, phenylalanine, tyrosine, tryptophan, and isoleucine can be converted into acetyl CoA. Arginine, proline, histidine, glutamine, and glutamate can be converted into α-ketoglutarate. Isoleucine, valine, methionine, and threonine can be converted into succinyl CoA. Tyrosine and phenylalanine can be converted into fumarate, and aspartate and asparagine can be converted into oxaloacetate.

For example, the amino acid glutamate, which has a carboxylic acid side chain, gets converted into the citric acid cycle intermediate α-ketoglutarate. This point of entry for glutamate makes sense because both molecules have a similar structure with two carboxyl groups, as shown below.

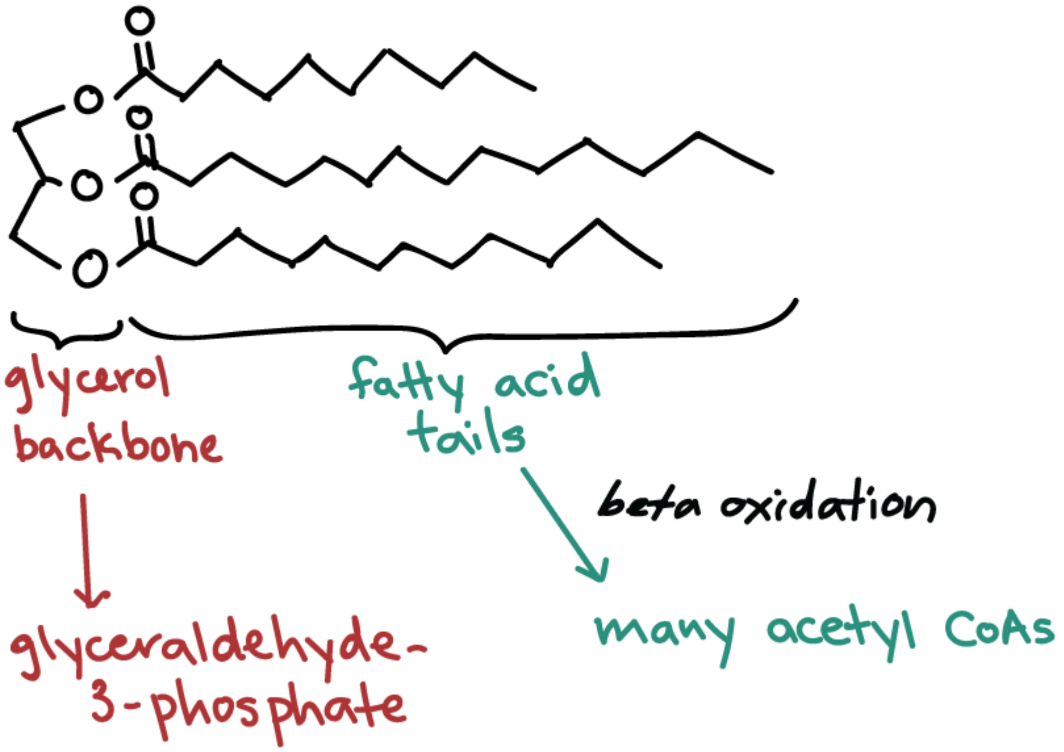


Glutamate (amino acid) and alpha-ketoglutarate (citric acid cycle intermediate) have similar structures. The only difference is that glutamate has an amino group where alpha-ketoglutarate has a carbonyl group.

How lipids enter the pathway

Fats, known more formally as triglycerides, can be broken down into two components that enter the cellular respiration pathways at different stages. A triglyceride is made up of a three-carbon molecule called glycerol, and of three fatty acid tails attached to the glycerol. Glycerol can be converted to glyceraldehyde-3-phosphate, an intermediate of glycolysis, and continue through the remainder of the cellular respiration breakdown pathway.

Fatty acids, on the other hand, must be broken down in a process called **beta-oxidation**, which takes place in the matrix of the mitochondria. In beta-oxidation, the fatty acid tails are broken down into a series of two-carbon units that combine with coenzyme A, forming acetyl CoA. This acetyl CoA feeds smoothly into the citric acid cycle.



Cellular respiration: It's a two-way street

We've thought a lot about how molecules can enter cellular respiration, but it's also important to consider how they can exit. Molecules in the cellular respiration pathway can be pulled out at many stages and used to build other molecules, including amino acids, nucleotides, lipids, and carbohydrates.

To give just one example, acetyl CoA (mentioned above) that's produced in cellular respiration can be diverted from the citric acid cycle and used to build the lipid cholesterol. Cholesterol forms the backbone of the steroid hormones in our bodies, such as testosterone and oestrogens. Whether it's better to "burn" molecules for fuel via cellular respiration or use them to build other molecules depends on the needs of the cell—and so does which specific molecules they're used to build!