Pyruvate oxidation

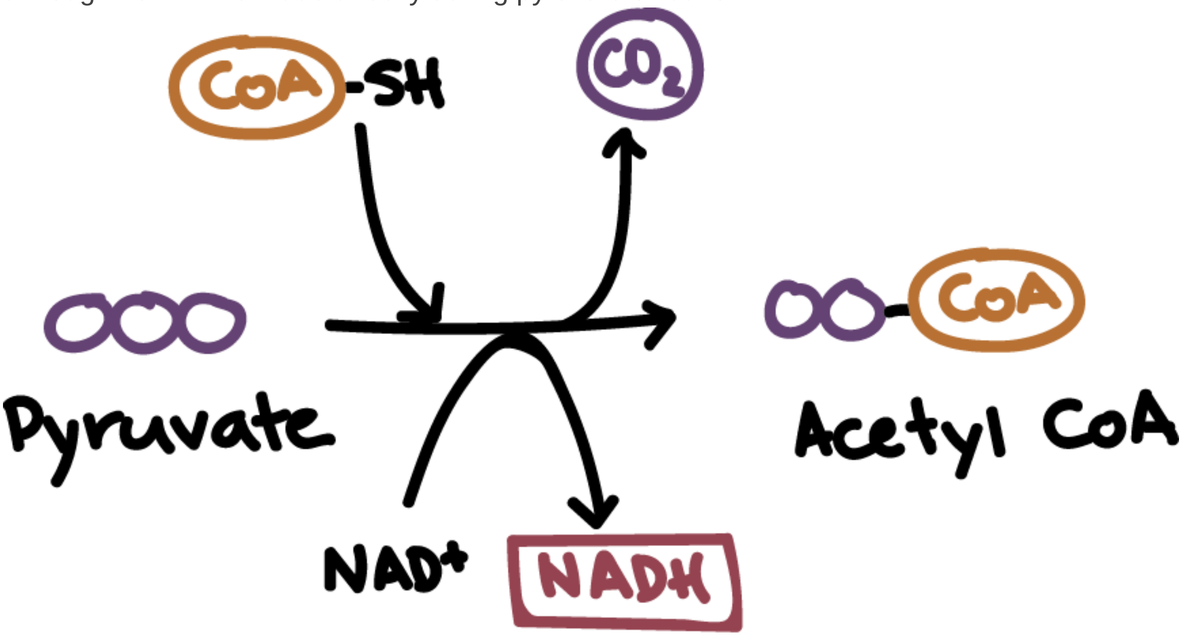
How pyruvate from glycolysis is converted to acetyl CoA so it can enter the citric acid cycle. Pyruvate is modified by removal of a carboxyl group followed by oxidation, and then attached to Coenzyme A.

Introduction

Among the four stages of cellular respiration, pyruvate oxidation is kind of the odd one out; it's relatively short in comparison to the extensive pathways of glycolysis or the citric acid cycle. But that doesn't make it unimportant! On the contrary, pyruvate oxidation is a key connector that links glycolysis to the rest of cellular respiration.

Overview of pyruvate oxidation

At the end of glycolysis, we have two pyruvate molecules that still contain lots of extractable energy. Pyruvate oxidation is the next step in capturing the remaining energy in the form of ATP although no ATP is made directly during pyruvate oxidation.

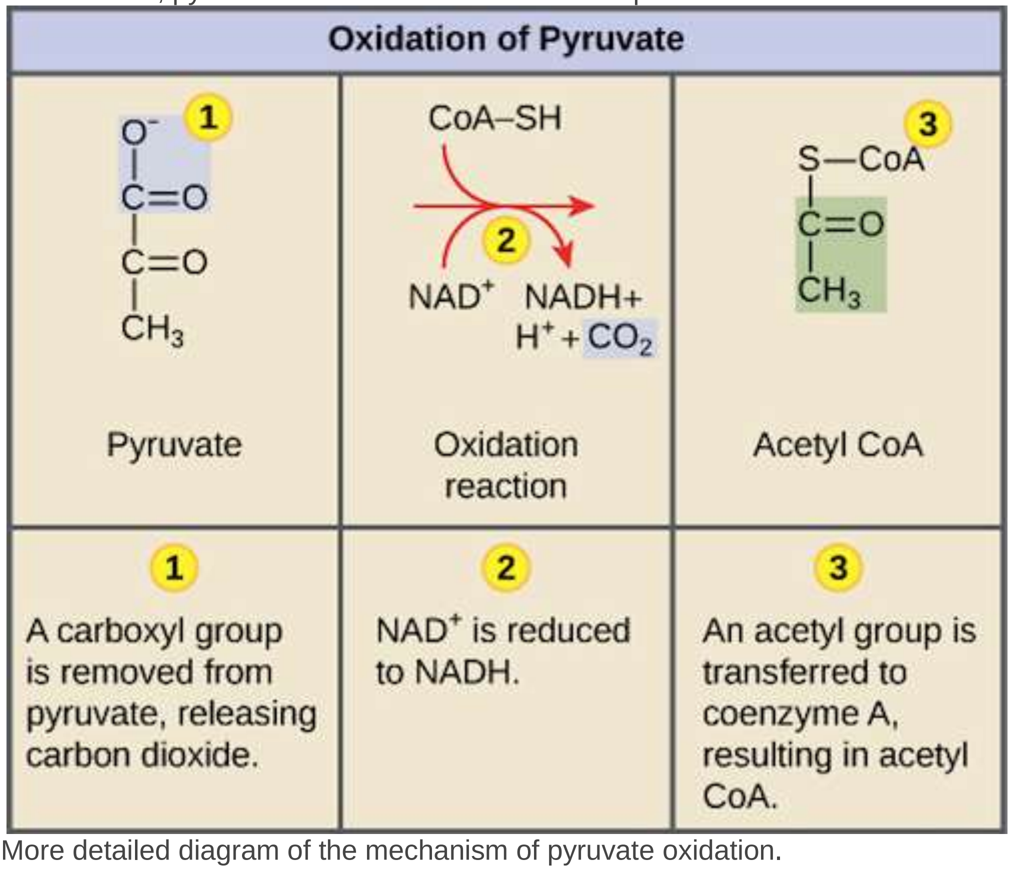


Simplified diagram of pyruvate oxidation. Pyruvate—three carbons—is converted to acetyl CoA, a two-carbon molecule attached to coenzyme A. A molecule of coenzyme A is a necessary reactant for this reaction, which releases a molecule of carbon dioxide and reduces a NAD^+ to NADH.

In eukaryotes, this step takes place in the matrix, the innermost compartment of mitochondria. In prokaryotes, it happens in the cytoplasm. Overall, pyruvate oxidation converts pyruvate—a three-carbon molecule—into acetyl CoA—a two-carbon molecule attached to Coenzyme A—producing an NADH and releasing one carbon dioxide molecule in the process. Acetyl CoA acts as fuel for the citric acid cycle in the next stage of cellular respiration.

Pyruvate oxidation steps

Pyruvate is produced by glycolysis in the cytoplasm, but pyruvate oxidation takes place in the mitochondrial matrix (in eukaryotes). So, before the chemical reactions can begin, pyruvate must enter the mitochondrion, crossing its inner membrane and arriving at the matrix.
In the matrix, pyruvate is modified in a series of steps:



More detailed diagram of the mechanism of pyruvate oxidation.

1. A carboxyl group is removed from pyruvate and released as carbon dioxide.
2. The two-carbon molecule from the first step is oxidized, and NAD^+ accepts the electrons to form NADH.
3. The oxidized two-carbon molecule, an acetyl group, is attached to Coenzyme A to form acetyl CoA.

Step 1. A carboxyl group is snipped off of pyruvate and released as a molecule of carbon dioxide, leaving behind a two-carbon molecule.
Step 2. The two-carbon molecule from step 1 is oxidized, and the electrons lost in the oxidation are picked up by NAD^+ to form NADH.
Step 3. The oxidized two-carbon molecule—an acetyl group, highlighted in green—is attached to Coenzyme A (CoA), an organic molecule derived from vitamin B5, to form acetyl CoA. Acetyl CoA, is sometimes called a carrier molecule, and its job here is to carry the acetyl group to the citric acid cycle.

The steps above are carried out by a large enzyme complex called **pyruvate dehydrogenase**, which consists of three interconnected enzymes and includes over 60 subunits. At a couple of stages, the reaction intermediates actually form covalent bonds to the enzyme complex—or, more specifically, to its cofactors. Pyruvate dehydrogenase is an important target for regulation, as it controls the amount of acetyl CoA fed into the citric acid cycle[1,2,3].

If we consider the two pyruvates that enter from glycolysis (for each glucose molecule), we can summarize pyruvate oxidation as follows:

- Two molecules of pyruvate are converted into two molecules of acetyl CoA.
- Two carbons are released as carbon dioxide—out of the six originally present in glucose.
- 2 NADH are generated from NAD^+.

Why make acetyl CoA. Acetyl CoA serves as fuel for the citric acid cycle in the next stage of cellular respiration. The addition of CoA helps activate the acetyl group, preparing it to undergo the necessary reactions to enter the citric acid cycle.