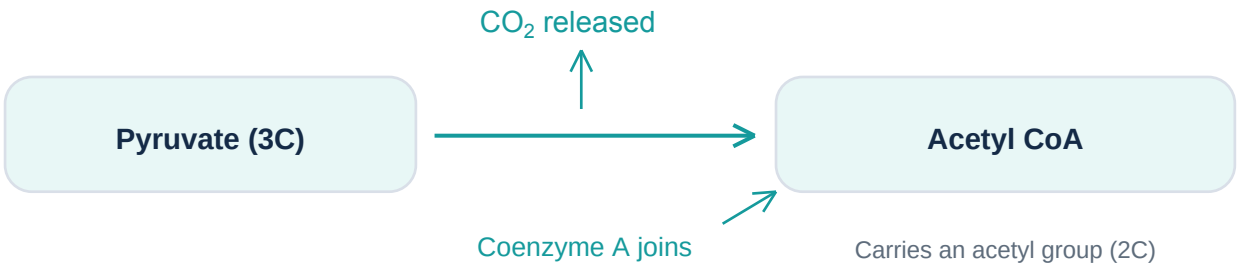
Prepare the acetyl group

In aerobic eukaryotic cells, pyruvate from glycolysis is transported into mitochondria. The link reaction occurs in the mitochondrial matrix.

1. FROM THREE CARBONS TO TWO



NAD is reduced to reduced NAD (NADH). No ATP is produced directly in the link reaction.

The 2C label refers to the acetyl group, not to the entire acetyl CoA molecule.

2. OXIDATIVE DECARBOXYLATION

Decarboxylation removes carbon dioxide. Dehydrogenation removes hydrogen and electrons, which reduce NAD. The remaining two-carbon acetyl group attaches to coenzyme A. These changes are coordinated by an enzyme complex.

3. COENZYME A IS A CARRIER

Coenzyme A transfers the acetyl group into the Krebs cycle. It is released when the acetyl group combines with oxaloacetate, so it can be reused. CoA carries acetyl groups; NAD carries reducing equivalents. They are not interchangeable.

Per glucose: two pyruvates undergo the link reaction, producing two acetyl CoA.

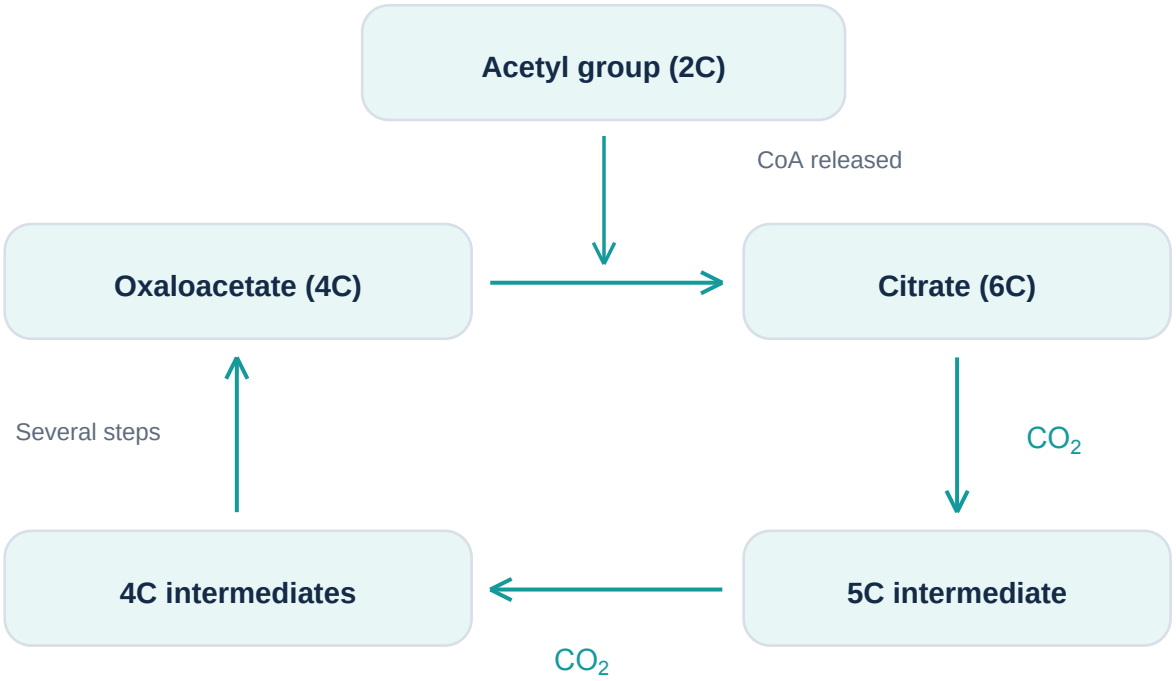
Pyruvate oxidation and acetyl transfer: OpenStax, Biology 2e 7.3.
Coenzyme roles: Cooper, The Cell, Metabolic Energy.

Scope: Cambridge Biology 9700, section 12.2, outcomes 1, 3-7, p. 33.

Regenerate the four-carbon acceptor

The Krebs cycle, also called the citric acid cycle, is an enzyme-controlled series of reactions in the mitochondrial matrix. Its acceptor is regenerated, not used up.

1. FOLLOW THE CARBON COUNTS



Simplified cycle: each turn accepts 2C and releases two CO_2. Intermediate reactions are grouped; oxaloacetate is restored.

2. CONSERVE ENERGY IN REDUCED COENZYMES

Dehydrogenation transfers hydrogen and electrons to NAD and FAD. One turn produces three reduced NAD and one reduced FAD. A small amount of ATP is also formed by substrate-linked phosphorylation.

3. A CYCLE, NOT A DEAD END

Regenerated oxaloacetate can accept another acetyl group. The two carbon atoms released in a turn are not necessarily the same two that have just entered. Carbon counts describe the pathway, not the immediate fate of each labelled atom.

Cycle, carbon release and coenzyme reduction: OpenStax, Biology 2e 7.3.
Oxaloacetate regeneration and energy transfer: Alberts et al., Energy from Food.

Scope: Cambridge Biology 9700, section 12.2, outcomes 1, 3-7, p. 33.

Count yields at the right scale

One glucose gives two pyruvates. Therefore, the link reaction happens twice and the Krebs cycle makes two turns for each glucose fully processed through these stages.

1. PRODUCT TOTALS

Stage / basis	CO_2	Reduced NAD	Reduced FAD	ATP*
Link / 1 pyruvate	1	1	0	0
Krebs / 1 acetyl group	2	3	1	1
Link + Krebs / 1 glucose	**6**	**8**	**2**	**2**

*Direct ATP equivalents; GTP can be formed at the substrate-linked step. This table excludes glycolysis and oxidative phosphorylation.

2. WHY MOST ATP COMES LATER

Reduced NAD and reduced FAD supply electrons to the electron transport system in the inner mitochondrial membrane. Their oxidation supports oxidative phosphorylation. Do not count reduced coenzymes as ATP molecules or assign the whole respiratory ATP yield to the Krebs cycle.

3. OXYGEN IS NEEDED INDIRECTLY

Neither the link reaction nor the Krebs cycle directly consumes molecular oxygen. In aerobic respiration, oxygen accepts electrons at the end of the electron transport chain. Without this route to regenerate oxidised coenzymes, these pathways cannot be sustained.

Location check: glycolysis - cytoplasm; link and Krebs - matrix; electron transport - inner membrane.

Yields and subsequent ATP production: Cooper, The Cell, Metabolic Energy.
Reduced carriers and aerobic respiration: Alberts et al., Energy from Food.

Scope: Cambridge Biology 9700, section 12.2, outcomes 1, 3-7, p. 33.