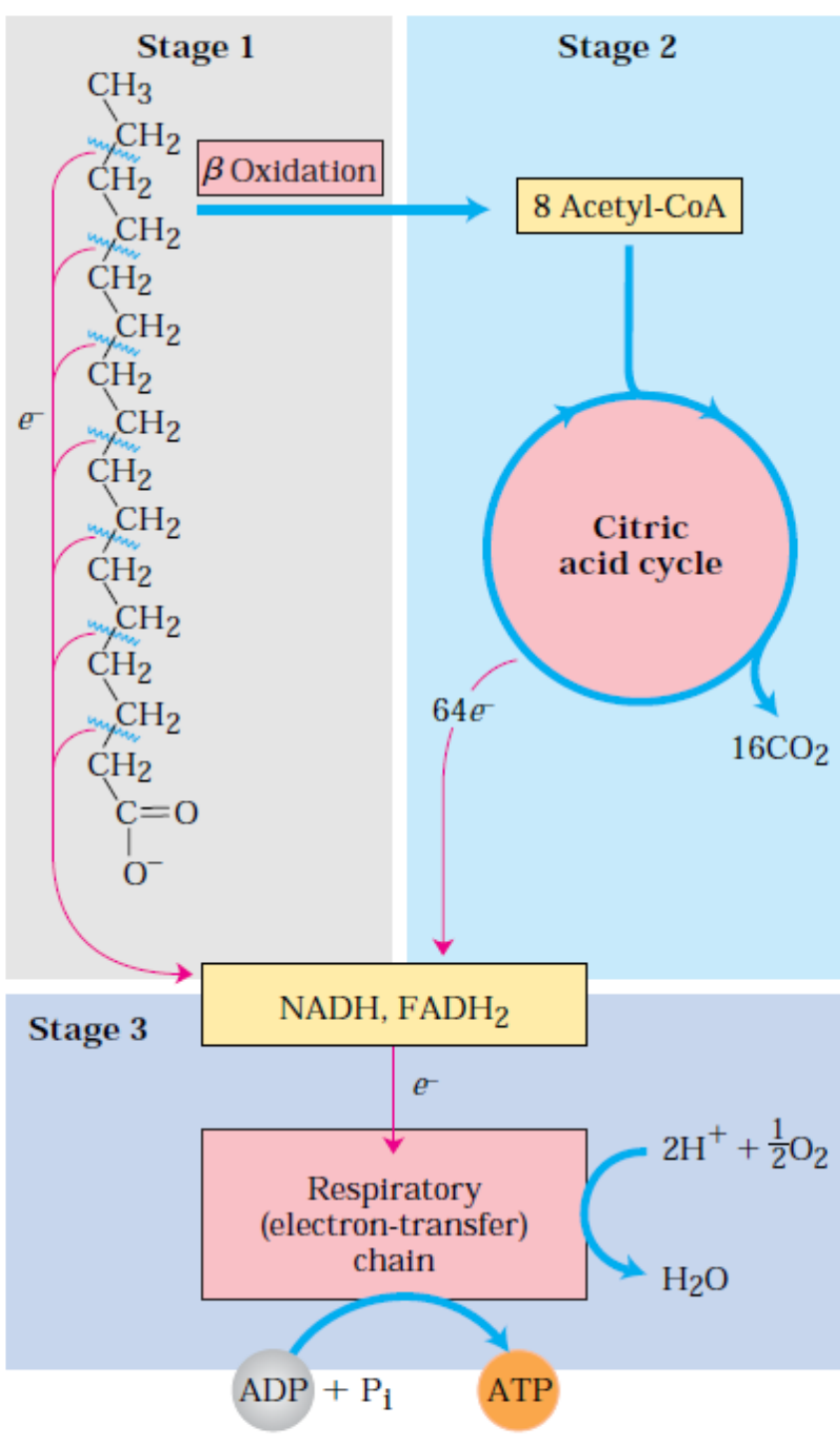# Disciplina: SLC0673

Ciclos energéticos vitais

Prof. Dr. Andrei Leitão

Fatty acid metabolism

Oxidation of Fatty Acids

Stage 1: A long-chain fatty acid is oxidized to yield acetyl residues in the form of acetyl-CoA. This process is called oxidation.
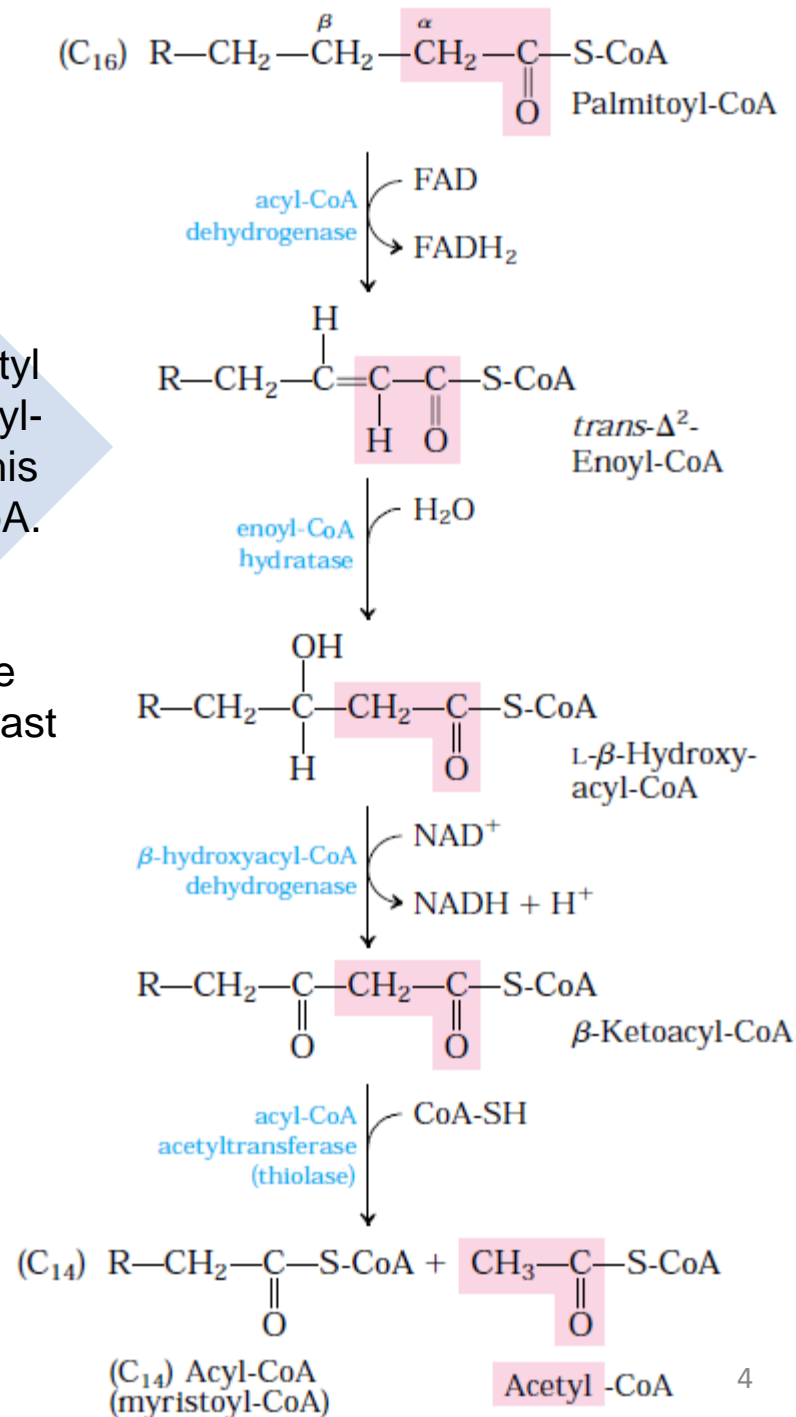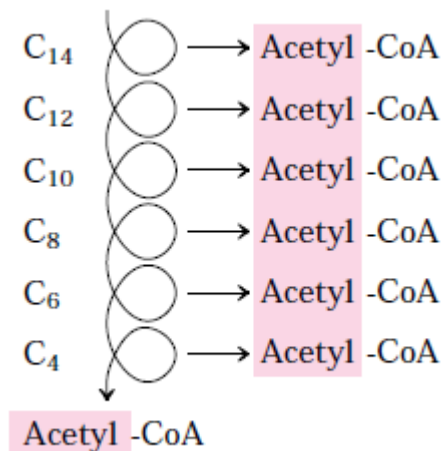
Stage 2: The acetyl groups are oxidized to CO_2 via the citric acid cycle.

Stage 3: Electrons derived from the oxidations of stages 1 and 2 pass to O2 via the mitochondrial respiratory chain, providing the energy for ATP synthesis by oxidative phosphorylation.
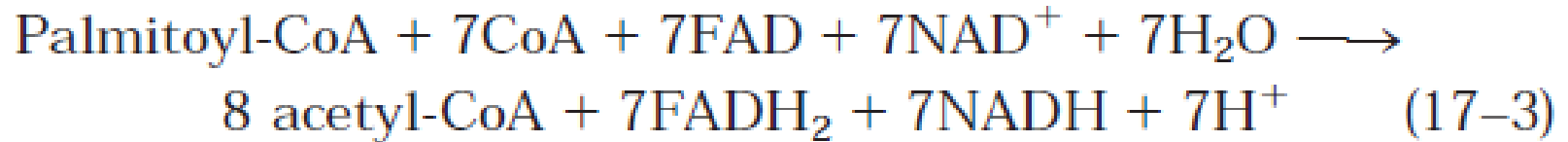
3

The β-oxidation pathway

In each pass through this four-step sequence, one acetyl residue (shaded in pink) is removed in the form of acetyl-CoA from the carboxyl end of the fatty acyl chain—in this example palmitate (C16), which enters as palmitoyl-CoA.

Six more passes through the pathway yield seven more molecules of acetyl-CoA, the seventh arising from the last two carbon atoms of the 16-carbon chain.

(C_{16}) R—CH$_2$—$\overset{\beta}{C}$H$_2$—$\overset{\alpha}{C}$H$_2$—C—S-CoA   Palmitoyl-CoA

acyl-CoA dehydrogenase — FAD → FADH$_2$

R—CH$_2$—C=C—C—S-CoA   trans-Δ^2-Enoyl-CoA

enoyl-CoA hydratase — H$_2$O

R—CH$_2$—C—CH$_2$—C—S-CoA   L-β-Hydroxy-acyl-CoA

β-hydroxyacyl-CoA dehydrogenase — NAD$^+$ → NADH + H$^+$

R—CH$_2$—C—CH$_2$—C—S-CoA β-Ketoacyl-CoA

acyl-CoA acetyltransferase (thiolase) — CoA-SH

(C_{14}) R—CH$_2$—C—S-CoA + CH$_3$—C—S-CoA

(C_{14}) Acyl-CoA (myristoyl-CoA)   Acetyl-CoA

C$_{14}$ → Acetyl-CoA
C$_{12}$ → Acetyl-CoA
C$_{10}$ → Acetyl-CoA
C$_8$ → Acetyl-CoA
C$_6$ → Acetyl-CoA
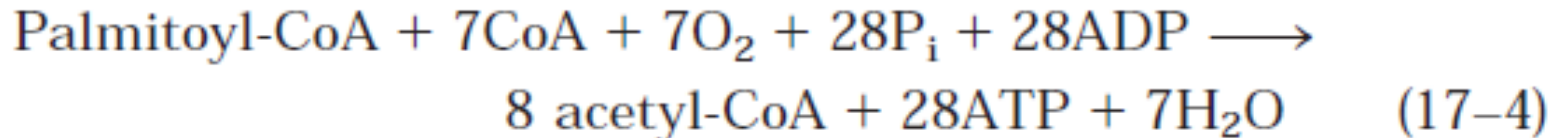C$_4$ → Acetyl-CoA
Acetyl-CoA

4

Production of ATP

Seven passes through the oxidation sequence are required to oxidize one molecule of palmitoyl-CoA to eight molecules of acetyl-CoA. The overall equation is:

$$\text{Palmitoyl-CoA} + 7\text{CoA} + 7\text{FAD} + 7\text{NAD}^+ + 7\text{H}_2\text{O} \longrightarrow$$
$$8 \text{ acetyl-CoA} + 7\text{FADH}_2 + 7\text{NADH} + 7\text{H}^+ \qquad (17\text{--}3)$$

The overall equation for the oxidation of palmitoyl-CoA to eight molecules of acetyl-CoA, including the electron transfers and oxidative phosphorylations, is:

$$\text{Palmitoyl-CoA} + 7\text{CoA} + 7\text{O}_2 + 28\text{P}_i + 28\text{ADP} \longrightarrow$$
$$8 \text{ acetyl-CoA} + 28\text{ATP} + 7\text{H}_2\text{O} \qquad (17\text{--}4)$$

Acetyl-CoA can also produce ATP from citric acid cycle.

Oxidation of Fatty Acids

TABLE 17–1 Yield of ATP during Oxidation of One Molecule of Palmitoyl-CoA to CO_2 and H_2O

Enzyme catalyzing the oxidation step	Number of NADH or $FADH_2$ formed	Number of ATP ultimately formed*
Acyl-CoA dehydrogenase	7 $FADH_2$	10.5
β-Hydroxyacyl-CoA dehydrogenase	7 NADH	17.5
Isocitrate dehydrogenase	8 NADH	20
α-Ketoglutarate dehydrogenase	8 NADH	20
Succinyl-CoA synthetase		8[†]
Succinate dehydrogenase	8 $FADH_2$	12
Malate dehydrogenase	8 NADH	20
Total		108

*These calculations assume that mitochondrial oxidative phosphorylation produces 1.5 ATP per $FADH_2$ oxidized and 2.5 ATP per NADH oxidized.

[†]GTP produced directly in this step yields ATP in the reaction catalyzed by nucleoside diphosphate kinase (p. XXX).