Why break glycogen down for energy rather than fats?

Fatty Acid Catabolism: β-oxidation

Chapter 23

Fatty acids

- Obtained from diet

phospholipids

triacylglycerols

Major source of fatty acids

Major stored energy reserve

Stored as large aggregated globules in adipocytes

Dietary fatty acid degradation

- Triacylglycerols from diet

↓

- Stomach **Lipases in low pH environment**

↓

- Duodenum **Alkaline pancreatic lipases hydrolyse TAGs at C1 and C3**
  Esterases hydrolyse ester linkages

↓

- Epithelial cells **FAs + glycerol → new TAGs + lipoproteins → chylomicrons**

↓

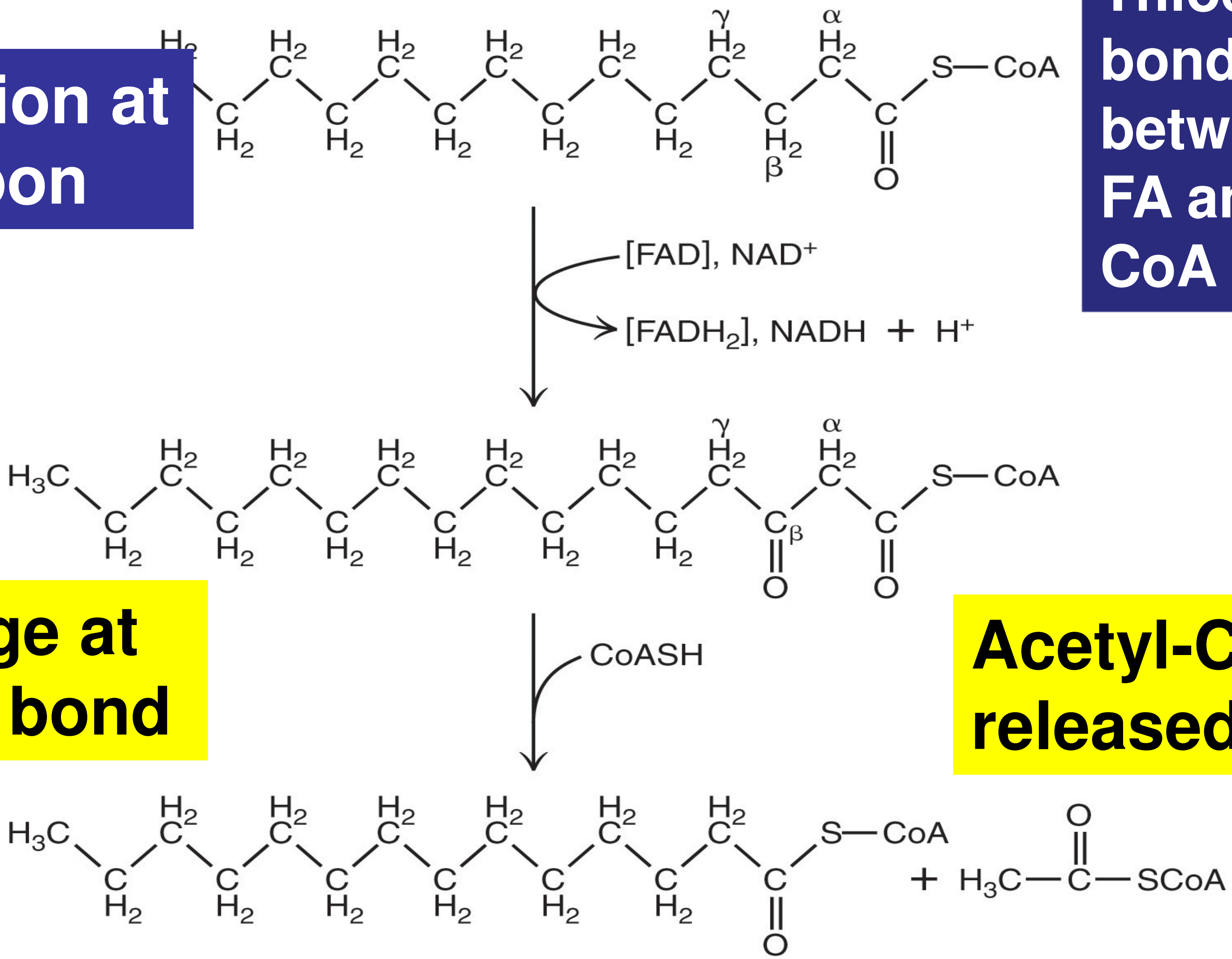
- Lymphatic system → bloodstream → organs

Hydrolysis to FAs → β oxidation

β-oxidation: catabolism of fatty acids

1. Thioester bond between FA and CoA

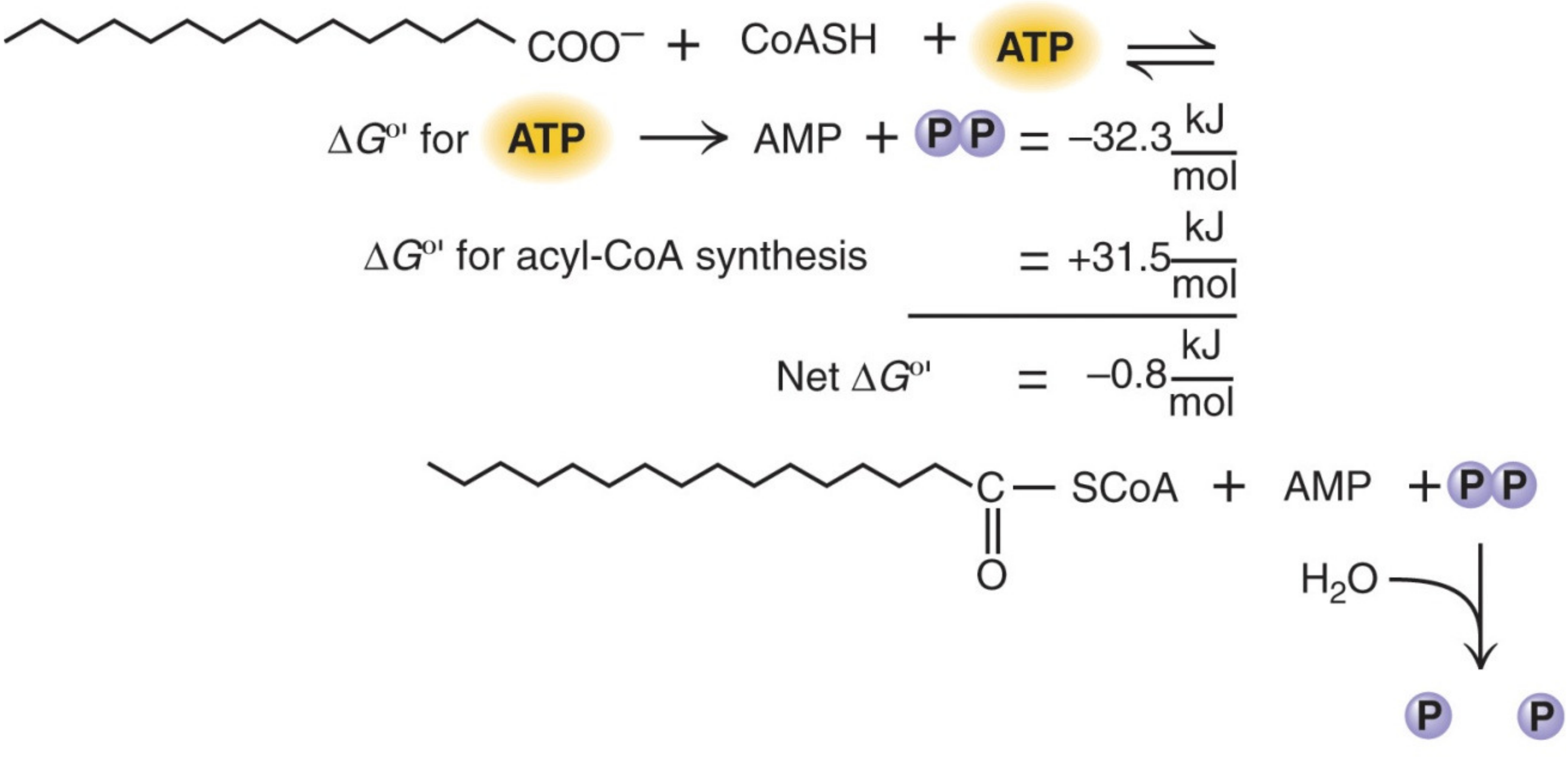
2. Oxidation at beta carbon



Cleavage at $C_{\alpha} – C_{\beta}$ bond

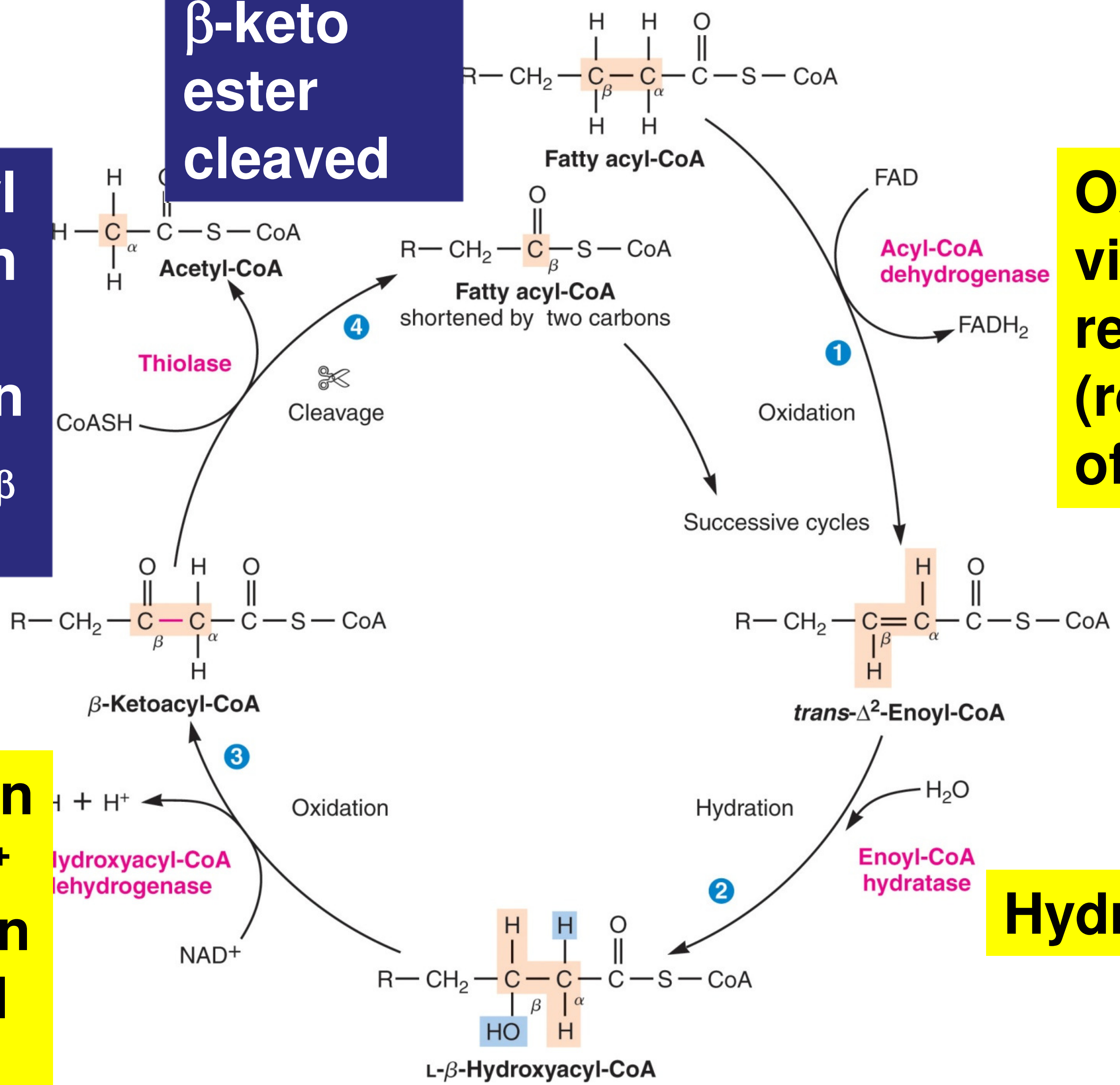
Acetyl-CoA released

Acyl-CoA synthetase, activates fatty acids for β-oxidation



Large negative ΔGº', drives the reaction forwards $\Delta G^{o\prime} = -33.6 \frac{kJ}{mol}$

β-oxidation of saturated fatty acids



β-keto ester cleaved

Carbonyl group on C_β via oxidation of C_α –C_β bond

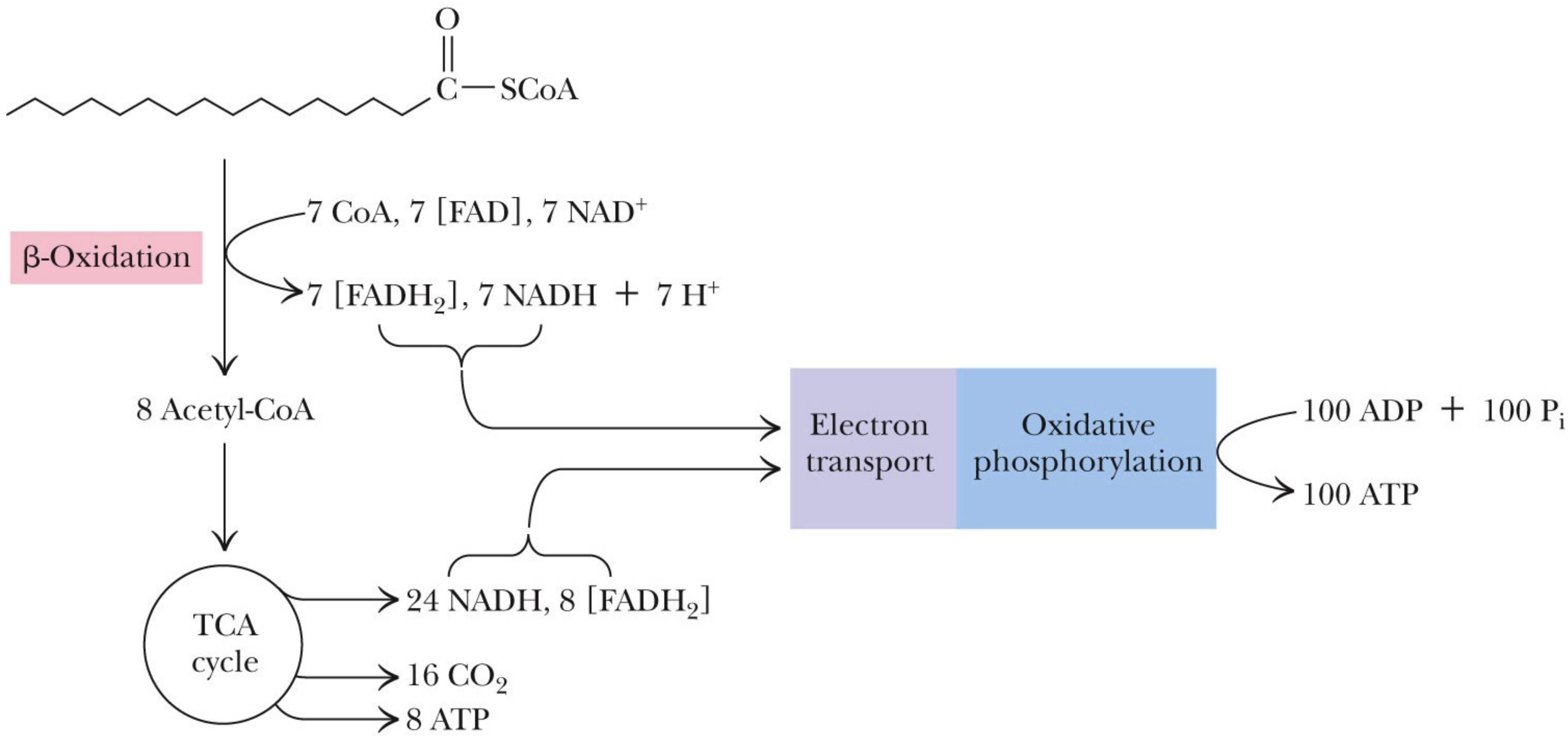
Oxidation via FAD reduction (removal of H_2)

Hydration

Oxidation via NAD^+ reduction (removal of H_2)

How many acetyl-coA, $FADH_2$ and NADH molecules, respectively are produced from complete oxidation of a 16C fatty acid?

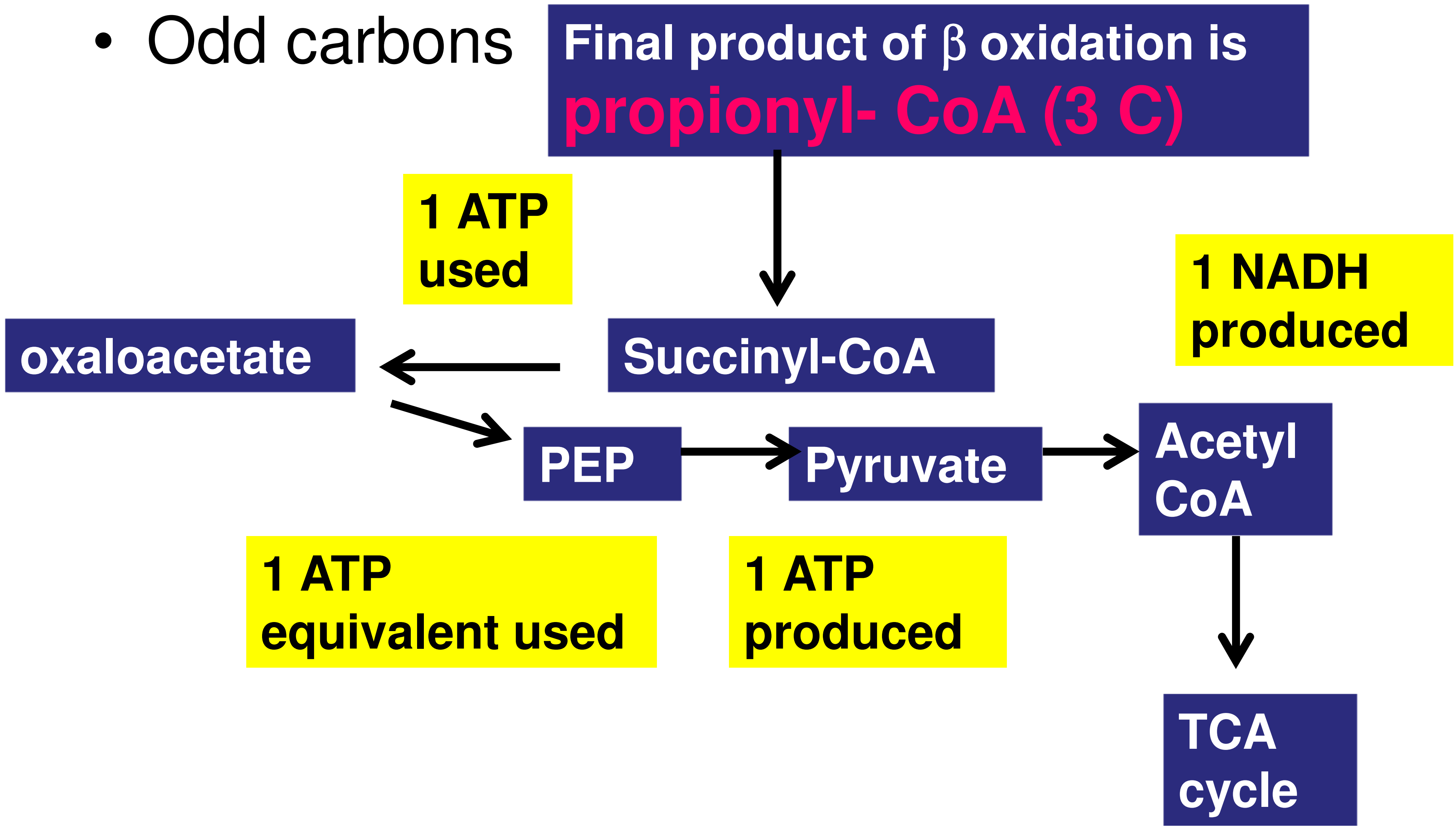
Complete β-oxidation of one palmitic acid (16 carbons)



What is the maximum number of ATP molecules that can be produced upon complete β-oxidation of palmitic acid (16 C)? (Assuming 2.5 ATP generated per NADH and 1.5 ATP generated per $FADH_2$)

β-oxidation of odd-carbon fatty acids

- Odd carbons



β-oxidation of unsaturated fatty acids

- Unsaturated fats

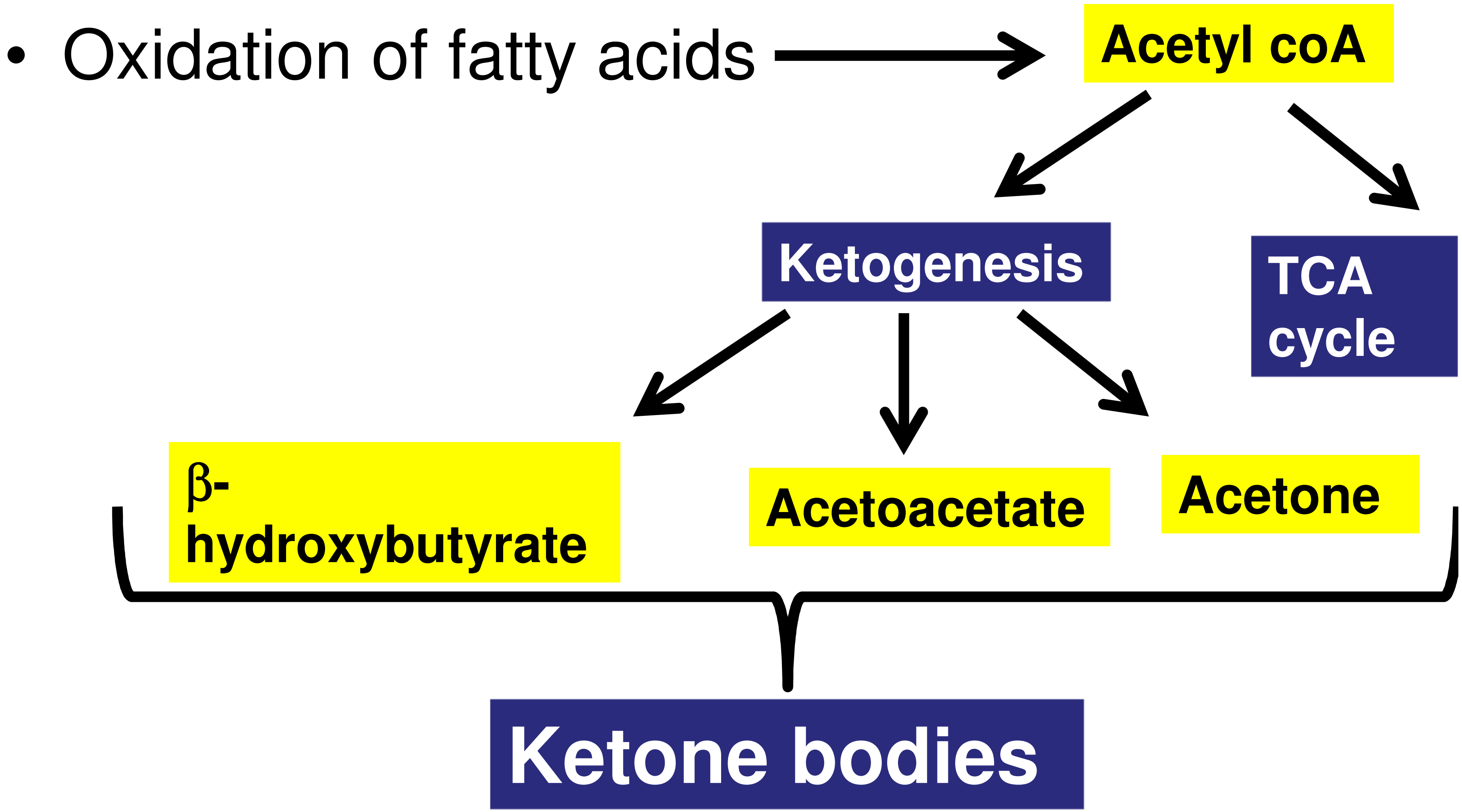
Also catabolised via β-oxidation

Acyl-CoA dehydrogenase can't oxidise *cis* bonds

The *cis* bonds are oxidised by 2 other enzymes

Calculate the approximate number of ATPs that can be obtained from the complete oxidation of the 17C cis-11-heptadeceonic acid to CO_2 and H_2O

Ketone bodies



Ketone bodies

- Step 1: condensation of 2 acetyl coA units → **acetoacetate**
- Step 2: Addition of a further acetyl coA to acetoacetate → **acetone** and **β-hydroxybutyrate**
- Ketone bodies: easily transportable FAs
- Transported from liver to tissues → acetyl-coA → TCA cycle → energy
- Diabetics: insufficient glucose in organs and tissues

Lipid Biosynthesis

Chapter 24

β-oxidation	Lipid biosynthesis
1. FAs linked to the SH group of **CoA**	1. Linked via SH groups to acyl carrier proteins **(ACPs)**
2. Occurs in **mitochondrion**	2. Occurs in the **cytosol**
3. Multiple individual enzymes	3. Multienxyme complex: FA synthase
4. NAD^+ **reduced** to NADH	4. NADPH **oxidised** to $NADP^+$

Fatty acid synthesis

1. FA chains constructed by **addition of 2C** units derived from acetyl-CoA
2. **ATP** is used to activate the acetyl units by forming **malonyl-CoA**
3. Malonyl-CoA is **decarboxylated** which drives the addition of each 2C unit to the chain
4. This is repeated until the chain reaches **16 C** in length
5. Other enzymes add double bonds and additional C to the chain

Substrate for FA synthesis

- **Acetyl CoA** and **NADPH**

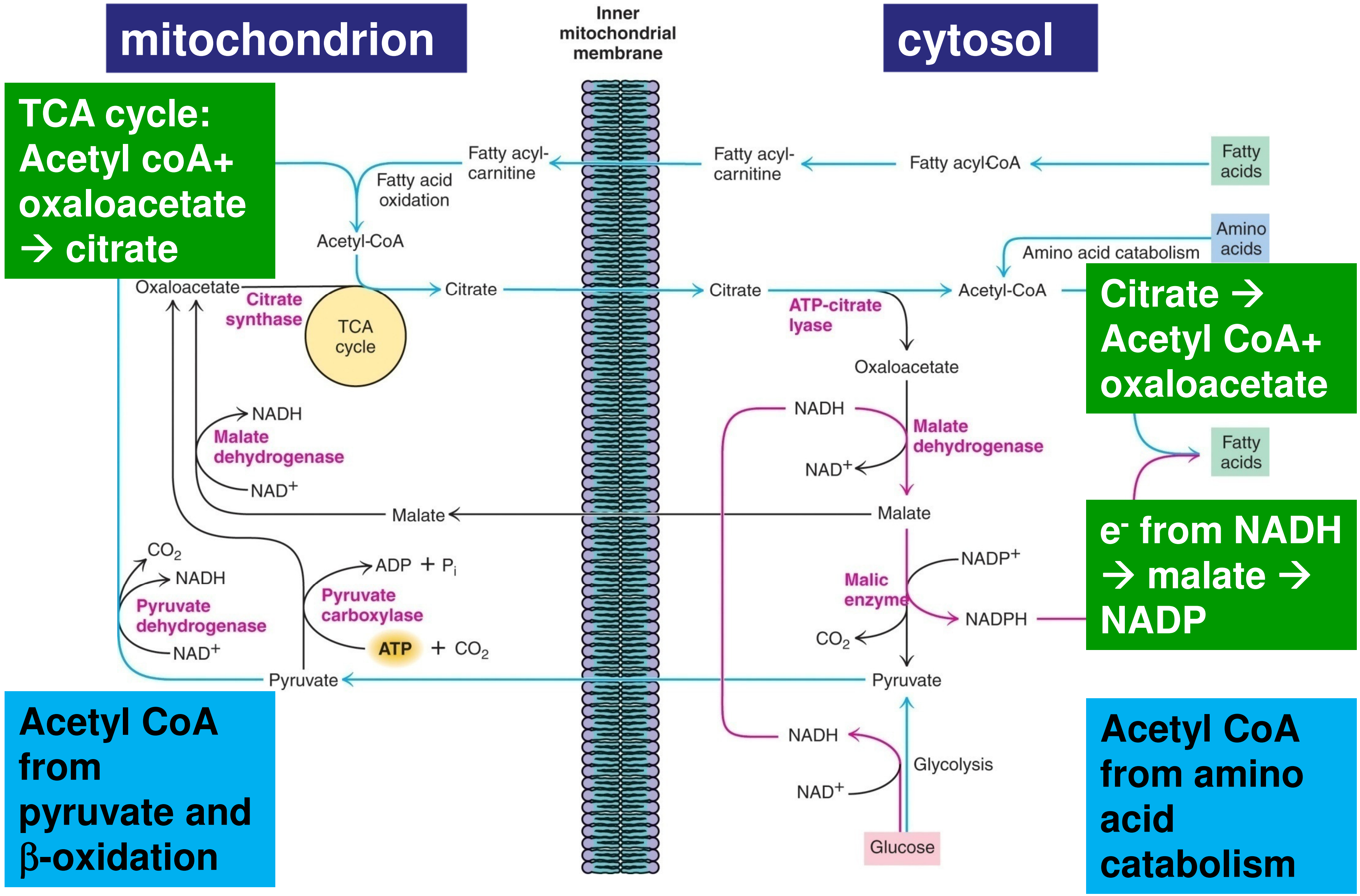
Acetyl CoA

- Amino acid degradation → cytosol → Insufficient for FA synthesis
- β-oxidation; Pyruvate decarboxylation after glycolysis → mitochondrion → Cannot directly cross the mitochondrial membrane

NADPH

- Pentose phosphate pathway
- Cytosolic malate → pyruvate (malic enzyme)

Citrate-malate-pyruvate shuttle

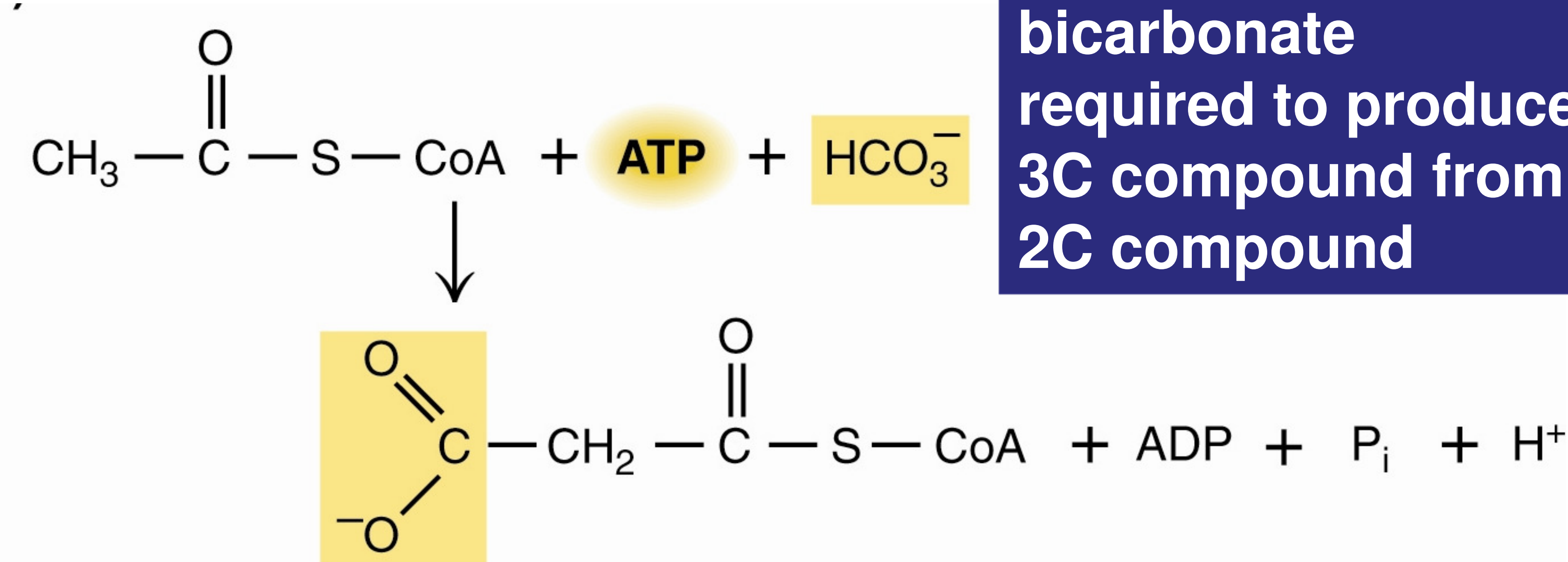


The committed step in FA synthesis

- Acetyl-CoA → Malonyl-CoA

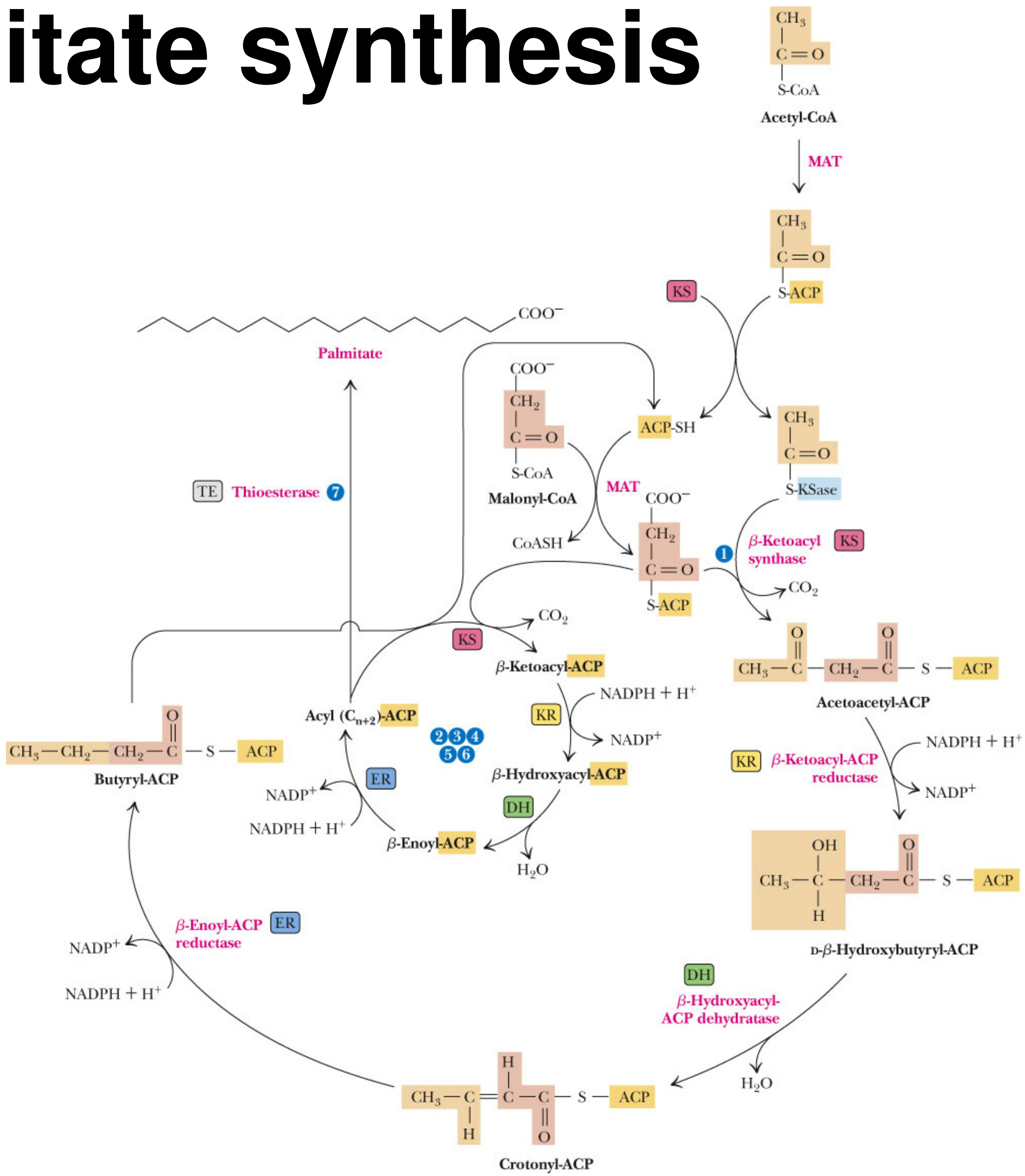
- ACC is the only enzyme in fatty acid synthesis that is not part of the multienzyme complex, fatty acid synthase
- Highly regulated by palmitoyl-CoA and citrate

The ACC reaction

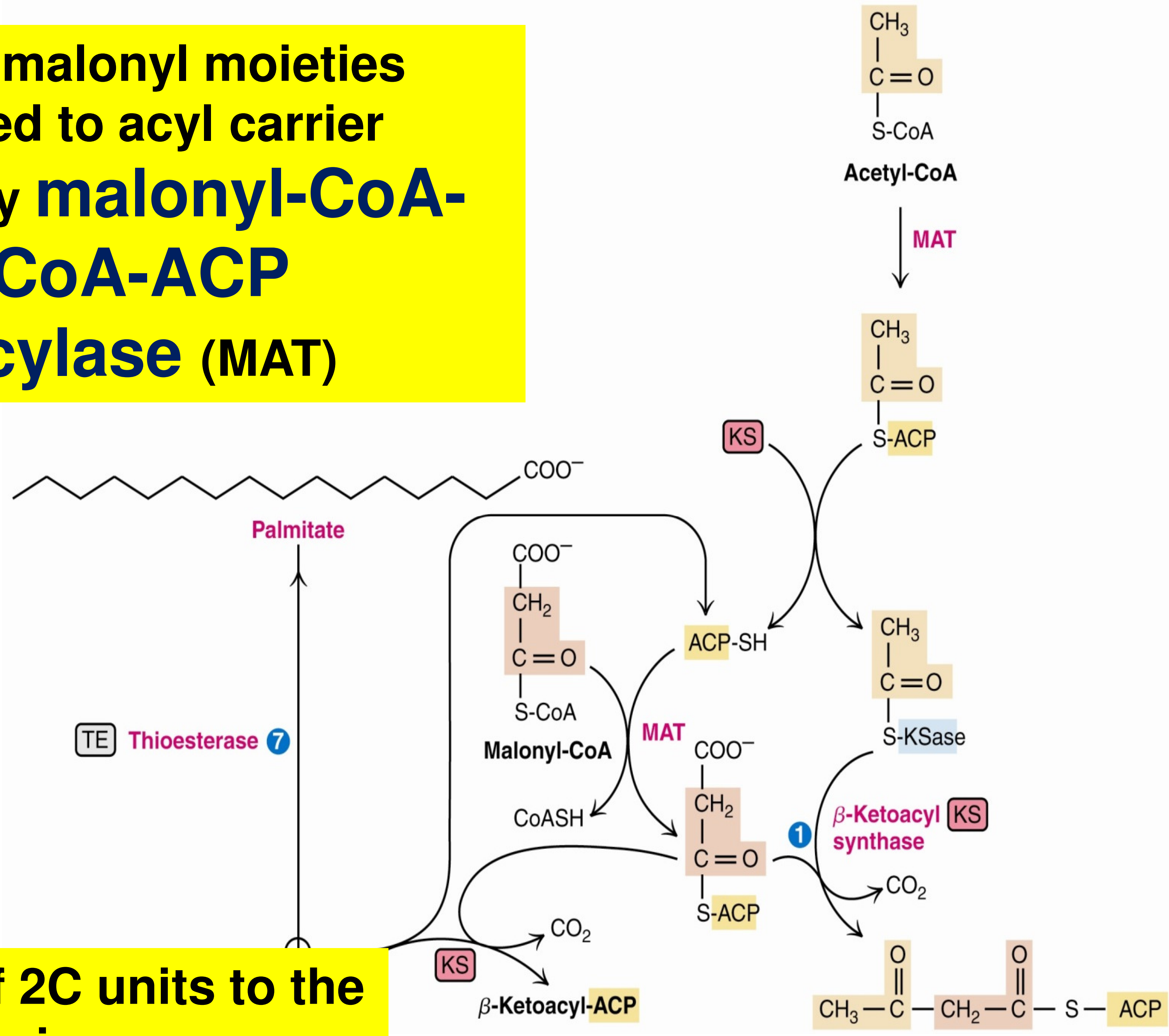


ATP and bicarbonate required to produce 3C compound from 2C compound

Palmitate synthesis



Acyl and malonyl moieties transferred to acyl carrier protein by malonyl-CoA-acetyl-CoA-ACP transacylase (MAT)



Addition of 2C units to the growing chain