
بسم الله الرحمن الرحيم

LIPID METABOLISM

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BY THE END OF THIS LESSON THE STUDENT WILL BE ABLE TO….

Inform Learner of Objectives

Know

- SOURCESES of FATTY ACIDS
- FATTY ACIDS OXIDATION
- BETA OXIDATION
- CARNITINE ,ROLE IN FA METABOLISM
- OXIDATION OF ODD NUMBER FATTY ACIDS
- METHYLMALONIC ACIDEMIA

FATTY ACIDS

CH3(CH 2)CH2 CH2 CH2 COO-

n

Degradation of FAs


KEEP
CALM
AND
ACTIVATE PRIOR
KNOWLEDGE

- Classify fatty acids according to the chain length ?

TYPES OF FATTY ACIDS

Length of fatty acids

- Short-chain fatty acids(SCFA) are fatty acids with aliphatic tails of five or fewer carbons e.g. butyric acid.
- Medium-chain fatty acids (MCFA) are fatty acids with aliphatic tails of 6 to 12 carbons, which can form medium-chain triglycerides.
- Long-chain fatty acids (LCFA) are fatty acids with aliphatic tails of 13 to 21 carbons.
- Very long chain fatty acids (VLCFA) are fatty acids with aliphatic tails of 22 or more carbons.

- What are sourceses of fatty acids?

SOURCESES of FATTY ACIDS

- Lypolysis of adipose tissues

  TG $\xrightarrow{\text{Lipase}}$ 3FFA + glycerol

- Degradation of chylomicron and VLDL by enzyme lipoprotein lipase
- Small and medium chain FA from diet
- FFA can be synthesis(de novo) from acetyl-Co A in liver.

Uptake OF FREE FAYTY ACIDS

The FFA diffuse through the cell membrane and in the plasma they form

1. Complex with albumin.
2. Associated with HDL.
3. As unionized FA anion.
4. In the cell they are attached to FA binding protein the Z-PROTEIN.

From these forms they enter in the degradation or oxidation for the production of energy.

- The turnover rate or ½ life of 1-3min.
- Complete oxidation of FA …….CO_2 + H_2O +9.1Kcal/gm.

FATTY ACIDS OXIDATION

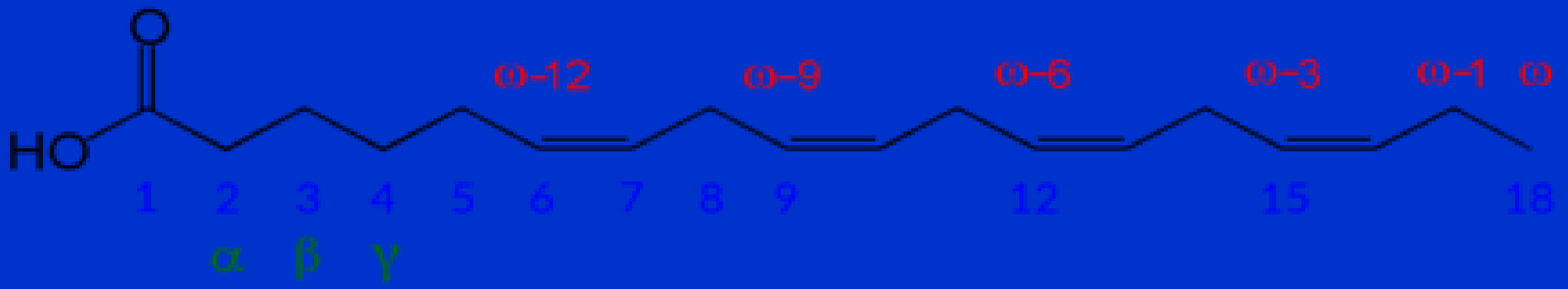
- Alpha oxidation
- **Beta oxidation**
- Gamma oxidation
- Peroxisomal FA oxidation.

BETA OXIDATION

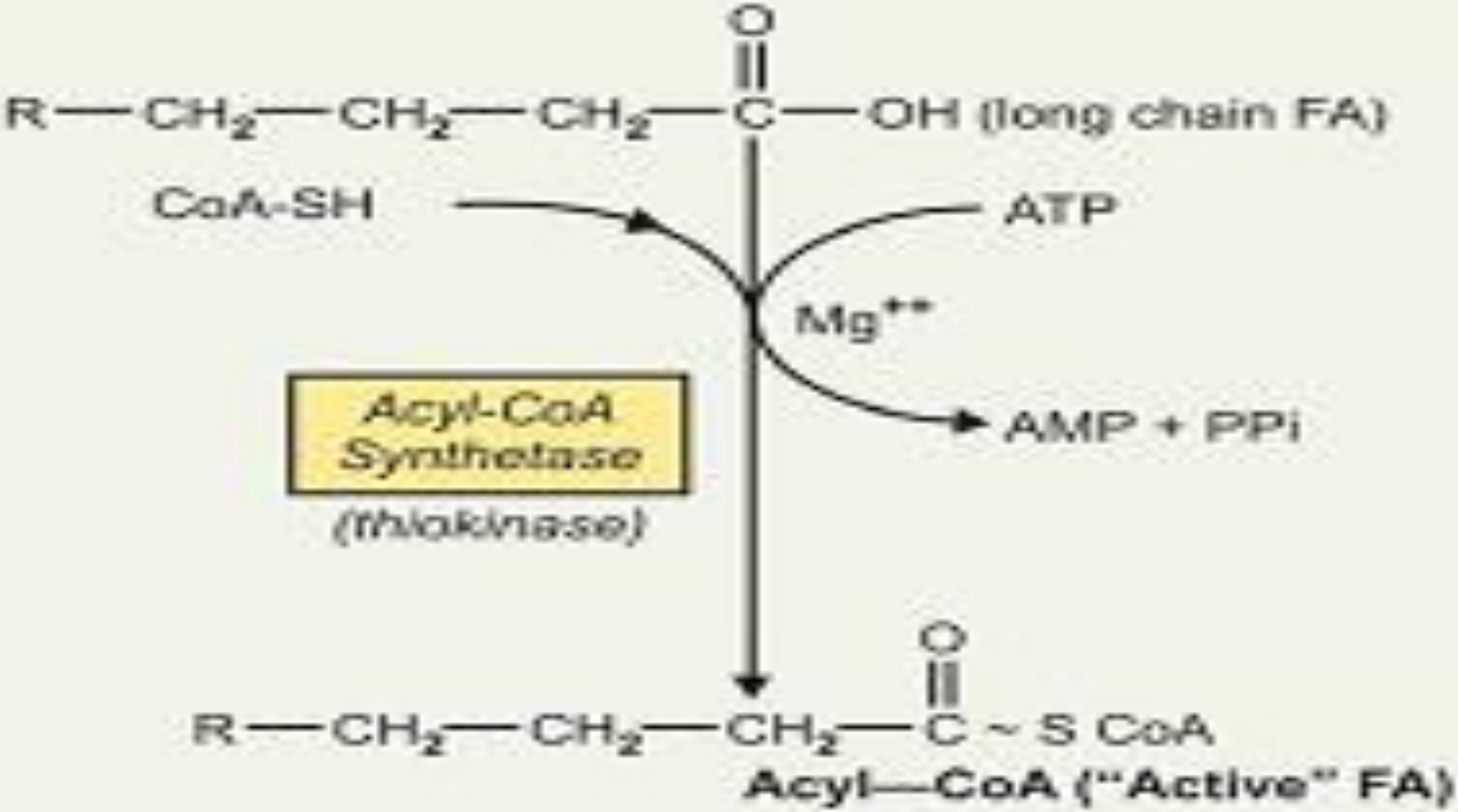
Oxidation of FA at Beta carbon atom, results in sequential removal of a two carbon fragment, acetyl CoA.

Beta oxidation of FAs involves three stages.

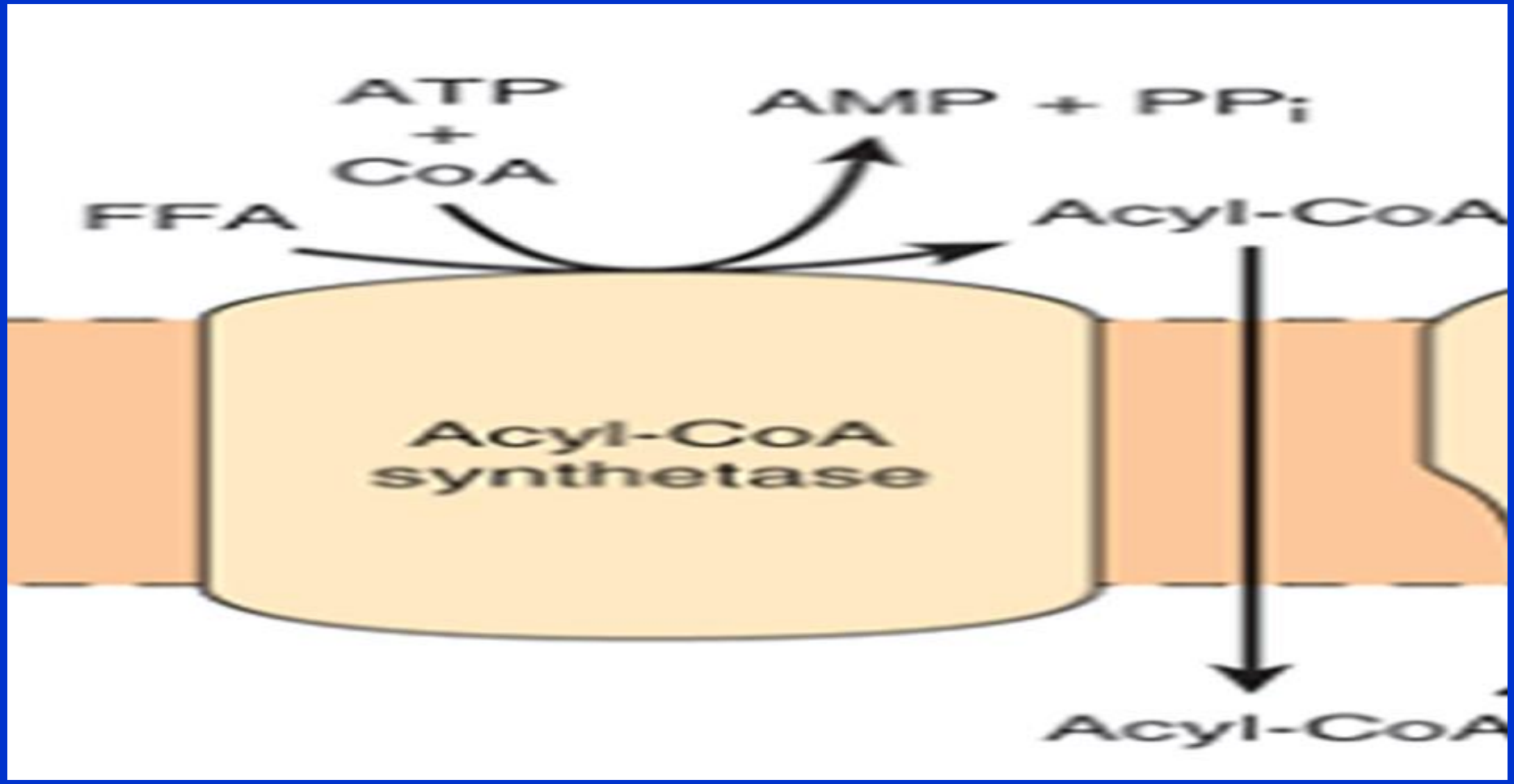
- 1. Activation of FAs in cytosol.
- 2. Transport of FAs into mitochondria
- 3.Beta oxidation proper in mitochondria



1.Activation of FAs in cytosol



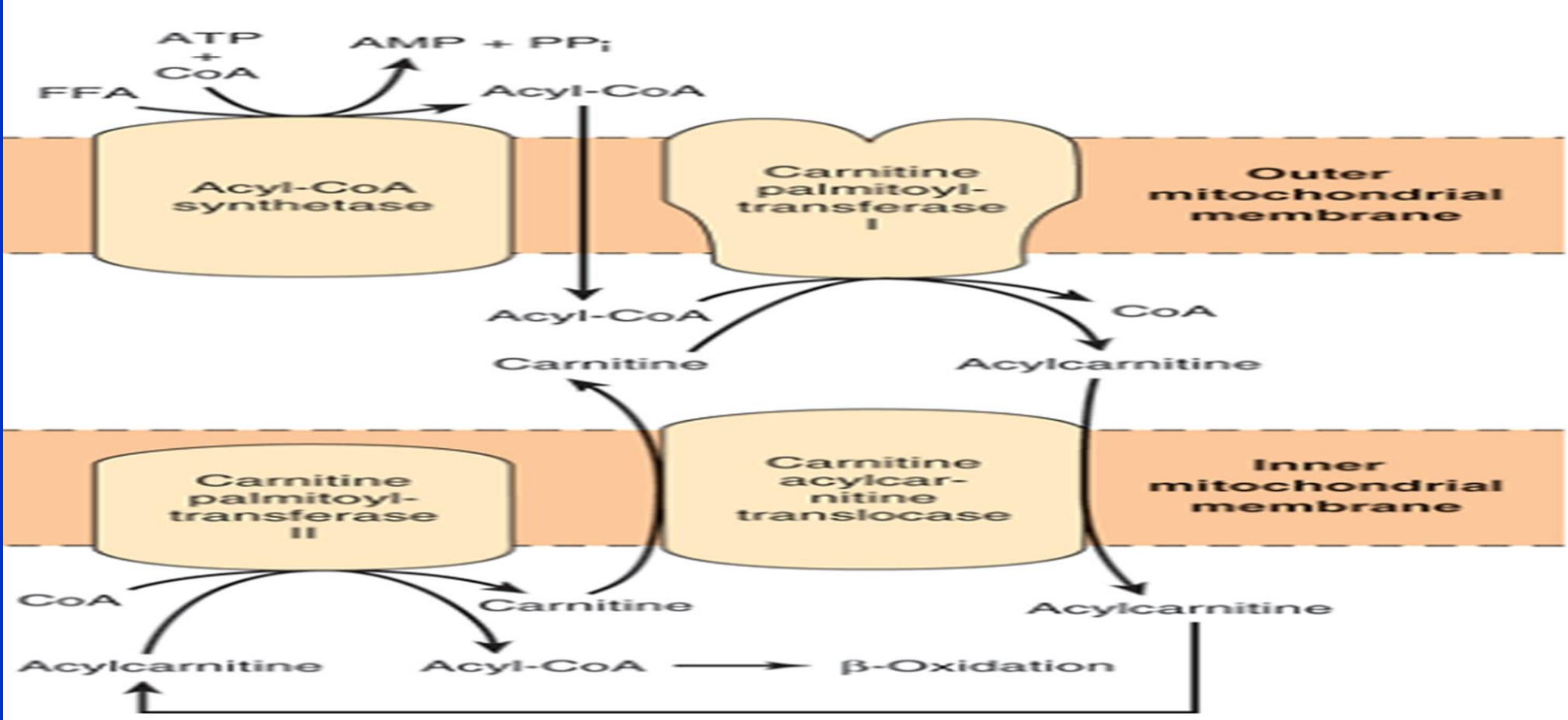
1.Activation of FAs in cytosol



Location and types of Acyl-CoA synthetases: The enzymes are found in the endoplasmic reticulum and inside (for short-chain FA) and outside (for long-chain FA) of the mitochondria. Several varieties of the enzyme have been described, each specific for FA of different chain lengths.

- *Acetyl-CoA synthetase* → acts on acetic acid and butyric acid
- *Second medium chain synthetase* → acts on FA with chain length C_4 to C_{12}
- *Long chain acyl-CoA synthetase* → Acts on FA with chain length C_8 to C_{22}

2. Transport of FAs into mitochondria



"Active" FA (acyl-CoA) are formed in cytosol, whereas β-oxidation of FA occurs in mitochondrial matrix. *Acyl-CoA are impermeable to mitochondrial membrane*. Long-chain activated FA penetrate the inner mitochondrial membrane only in combination with carnitine.

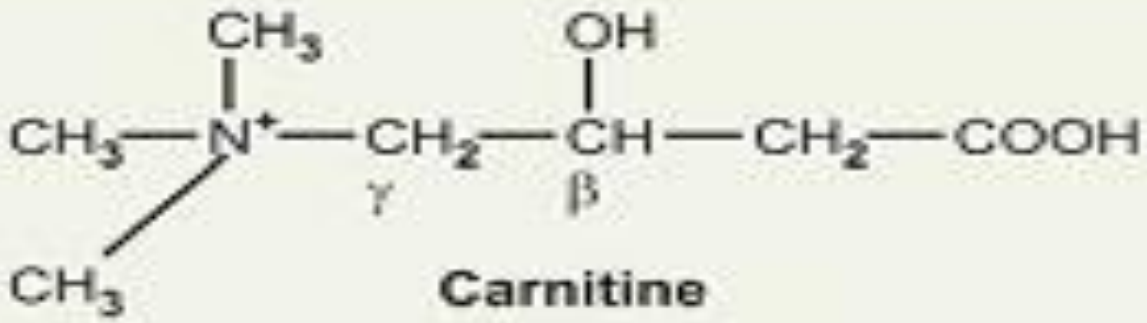
CHEMICAL STRUCTURE OF CoA

$C_{21}H_{36}N_7O_{16}P_3S$

CARNITINE AND ITS ROLE IN FA METABOLISM

Carnitine: Chemistry and functions

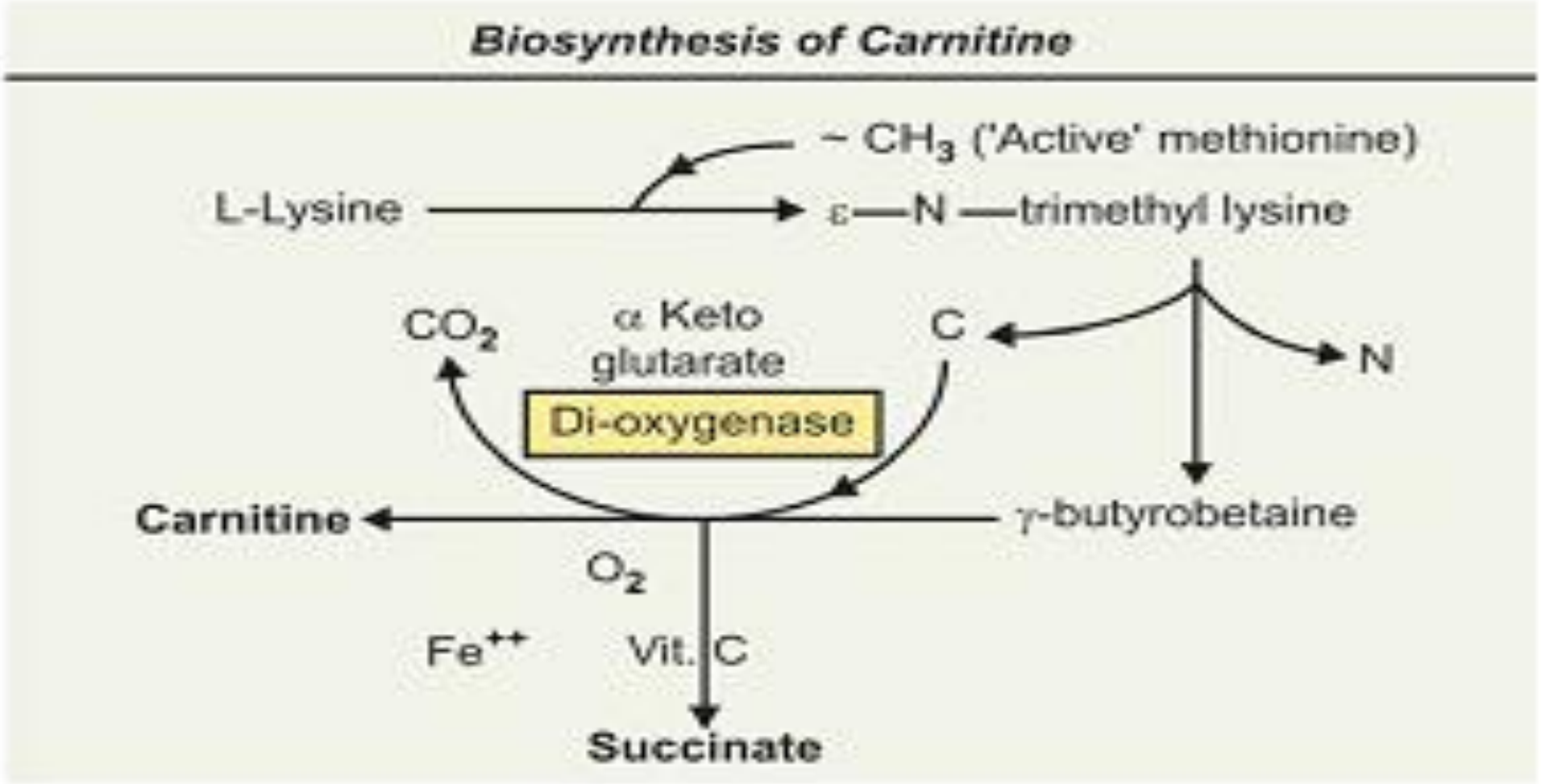
Carnitine is chemically "β–OH–γ–trimethyl ammonium butyrate"



Carnitine

Distribution: Carnitine is widely distributed in yeast, milk, liver and particularly large quantities in muscles and in meat extracts.

Biosynthesis of carnitine: It is synthesised from lysine and methionine in liver principally, also in kidneys.



CONCENTRATION

- Skeletal muscle: 1 mg/gm dry weight
- Heart muscle: 560 mcg/gm
- Kidneys: 412 mcg/gm
- Liver: 280 mcg/gm

Blood: Small amounts in blood 7-14 mcg/ml.

Excretion in 24 hrs urine: 50 to 100 mcg/ml.

FUNCTION

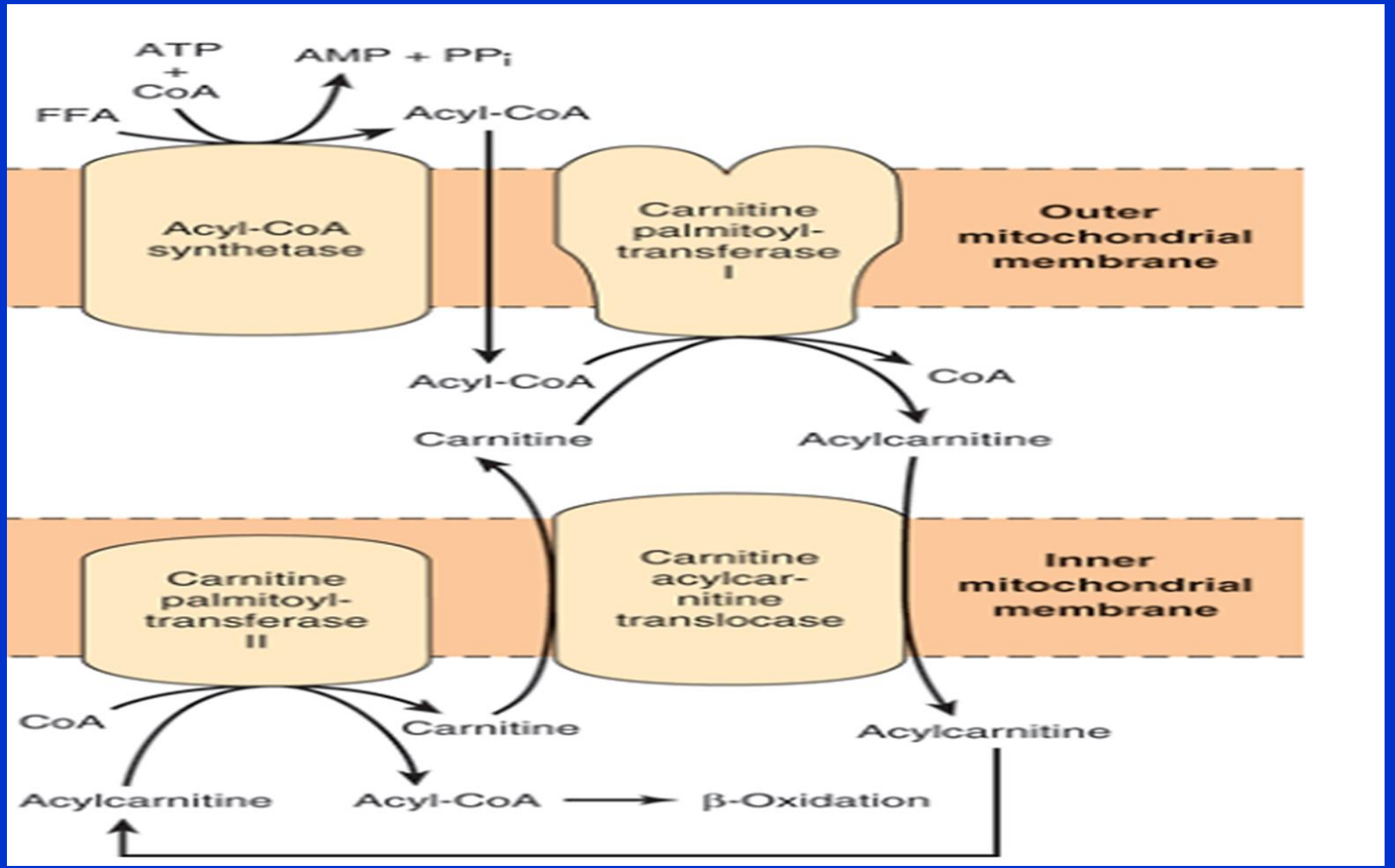
Functions: Carnitine is considered as a **"carrier molecule"; it *acts like a ferry-boat.*** It transports long-chain acyl-CoA across mitochondrial membrane which is impermeable to acyl-CoA.

- Facilitates transport of long-chain acyl-CoA for oxidation in mitochondria.
- Facilitates exit of acetyl-CoA and acetoacetyl-CoA from within mitochondria to cytosol, where FA synthesis takes place.

Inhibitor of Carnitine

- Malonyl CoA inhibits carnitine acyl transferase 1 (FAs synthesis metabolite) in the cytosol.

2. Transport of FAs into mitochondria

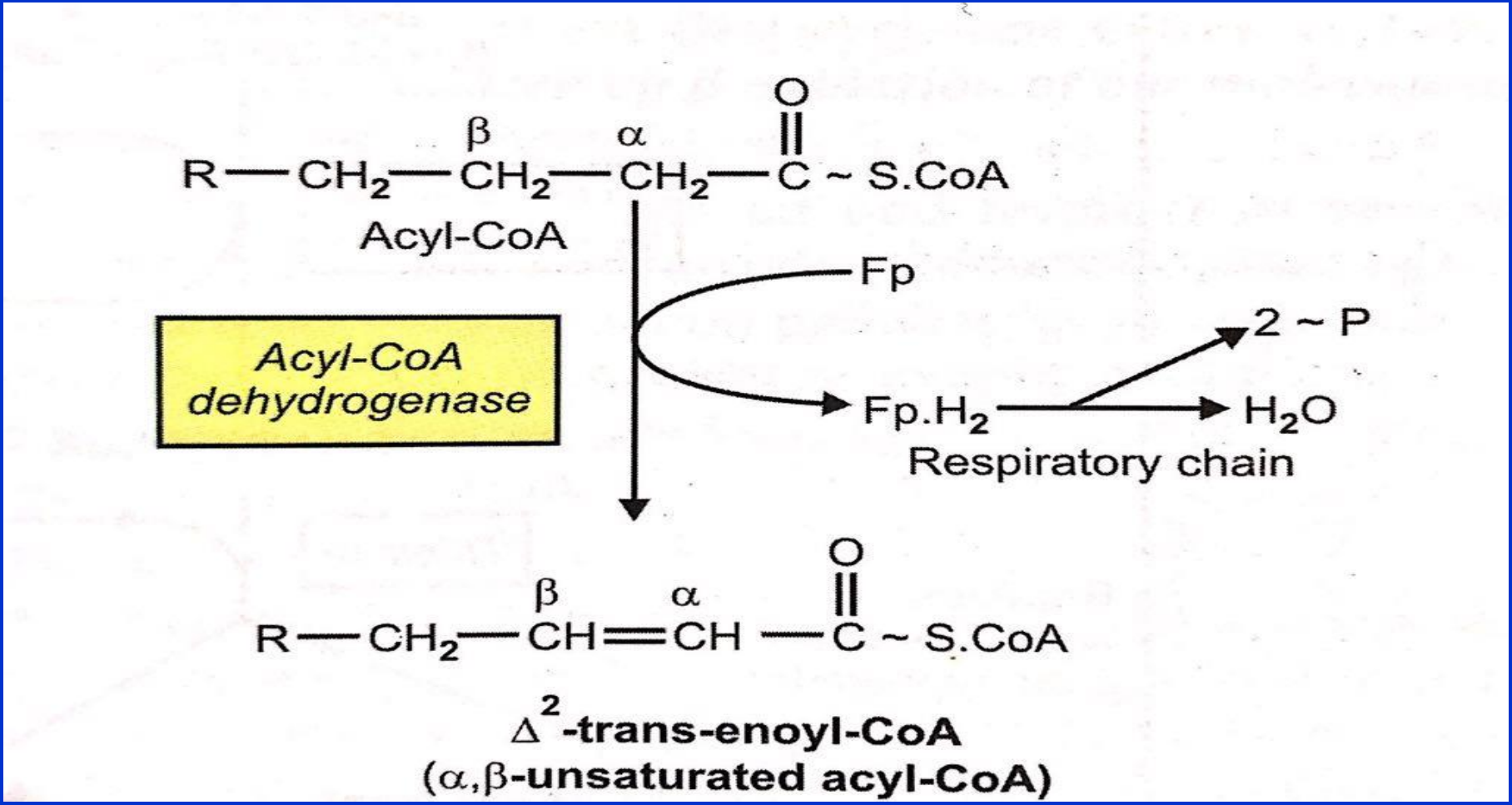


BETA OXIDATION

- Once acyl co A is transported by carnitine in the mitrochondrial matrix it undergoes ß oxidation by fatty acid oxidase complex enzyme.

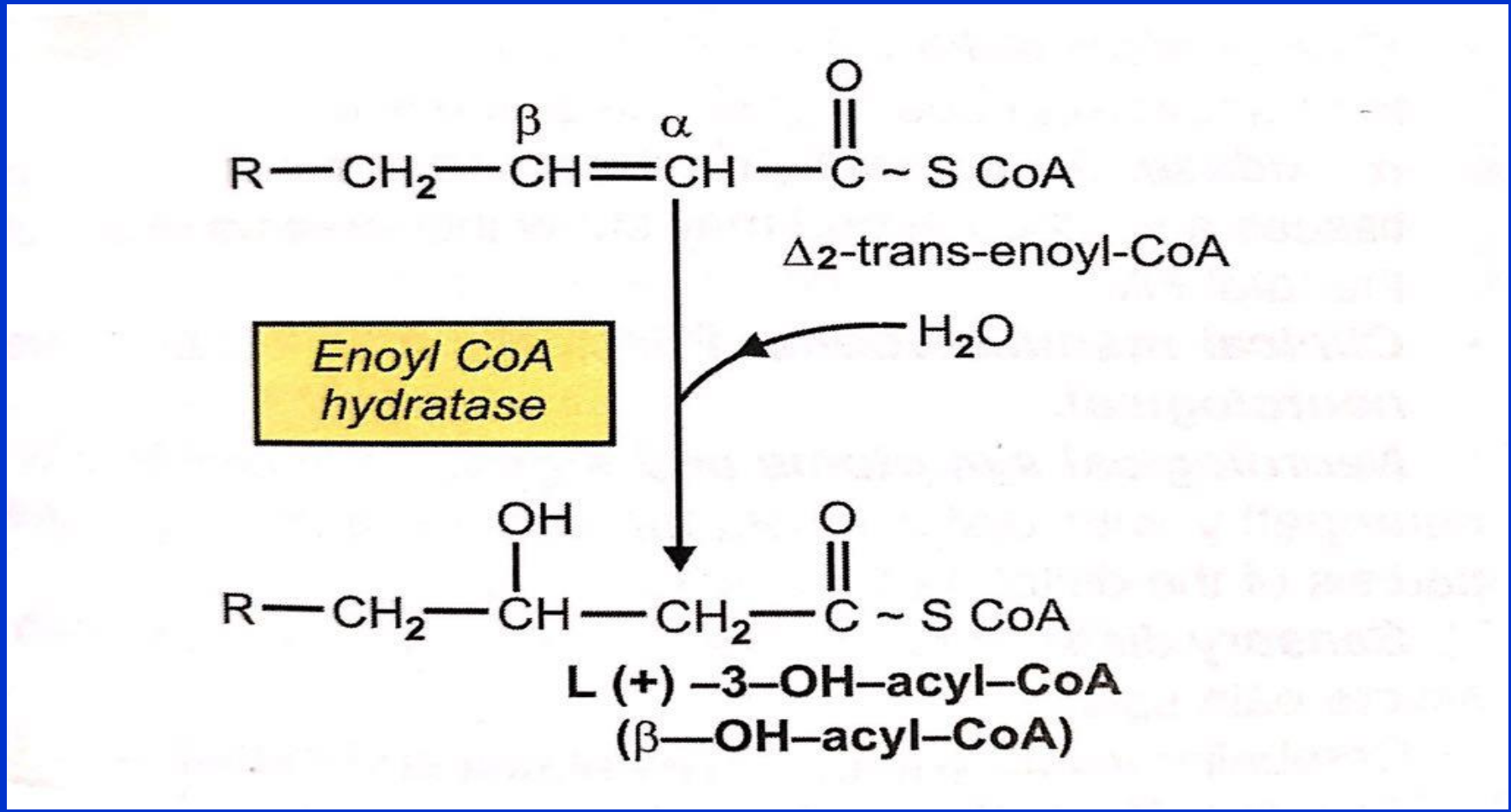
Steps of Beta oxidation

- **1. Dehydrogenation(oxidation): - 2 H atoms + 2 ATP**



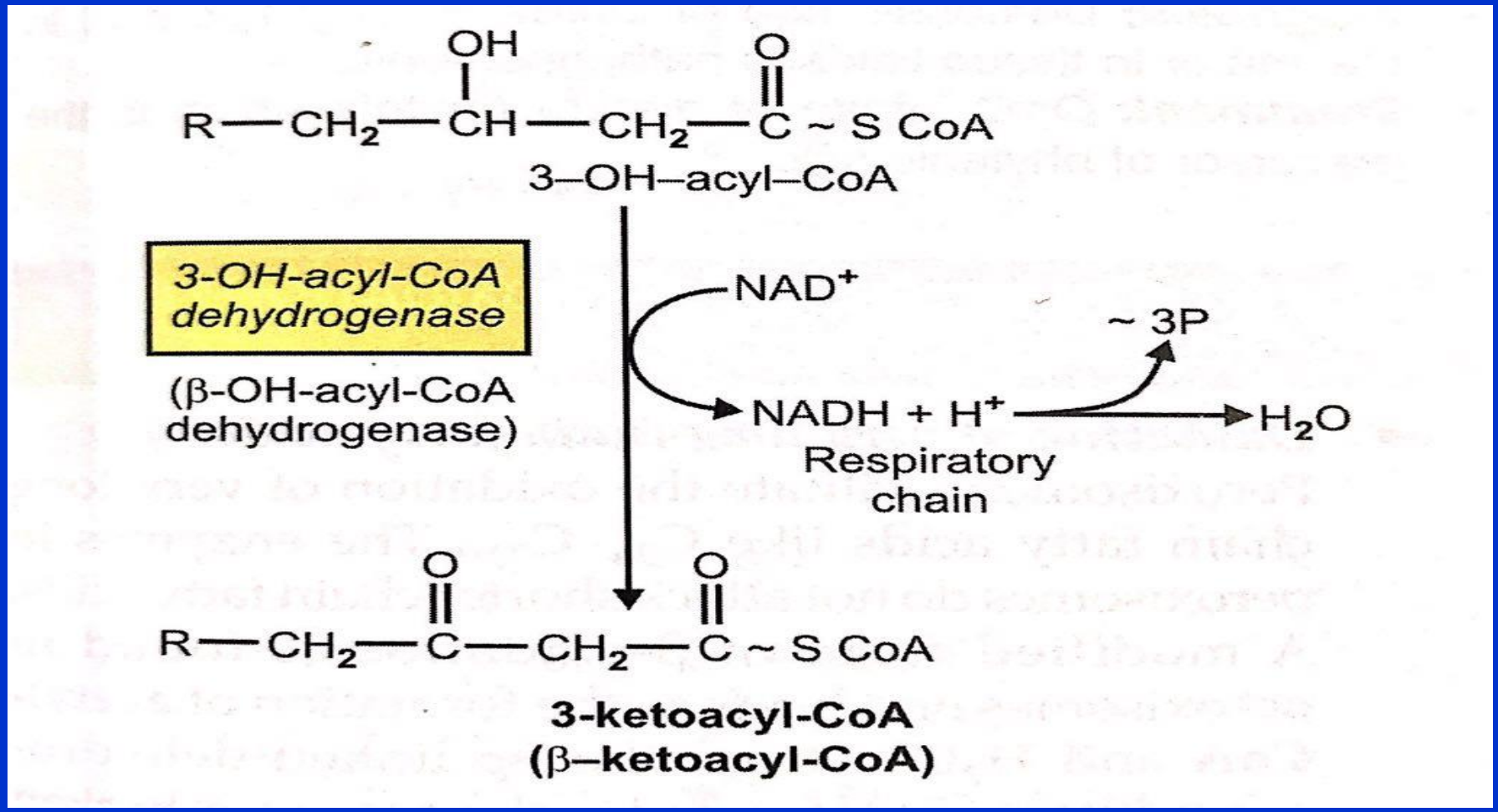
Steps of Beta oxidation

2. Hydration: + 1 H_2O



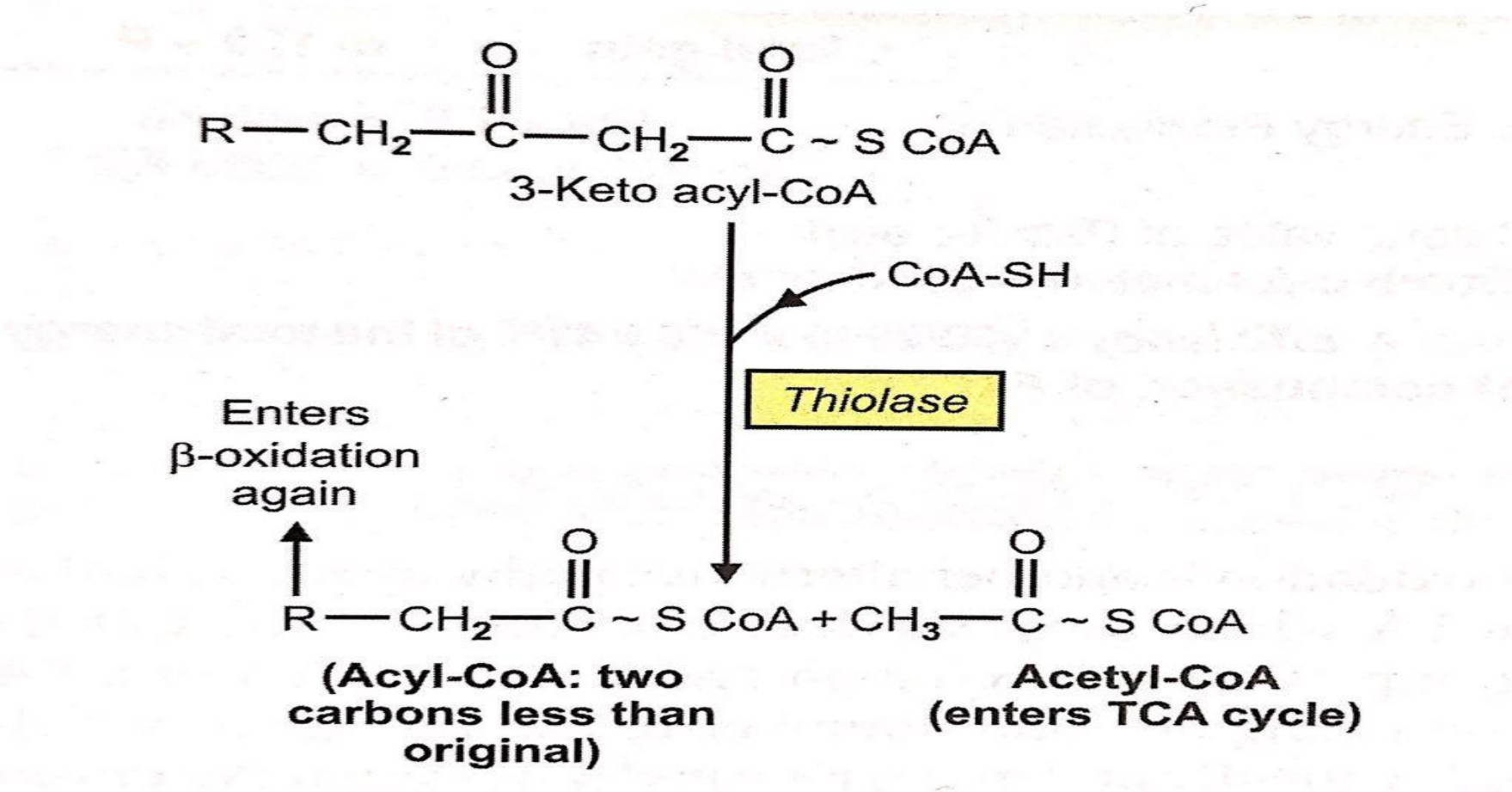
Steps of Beta oxidation

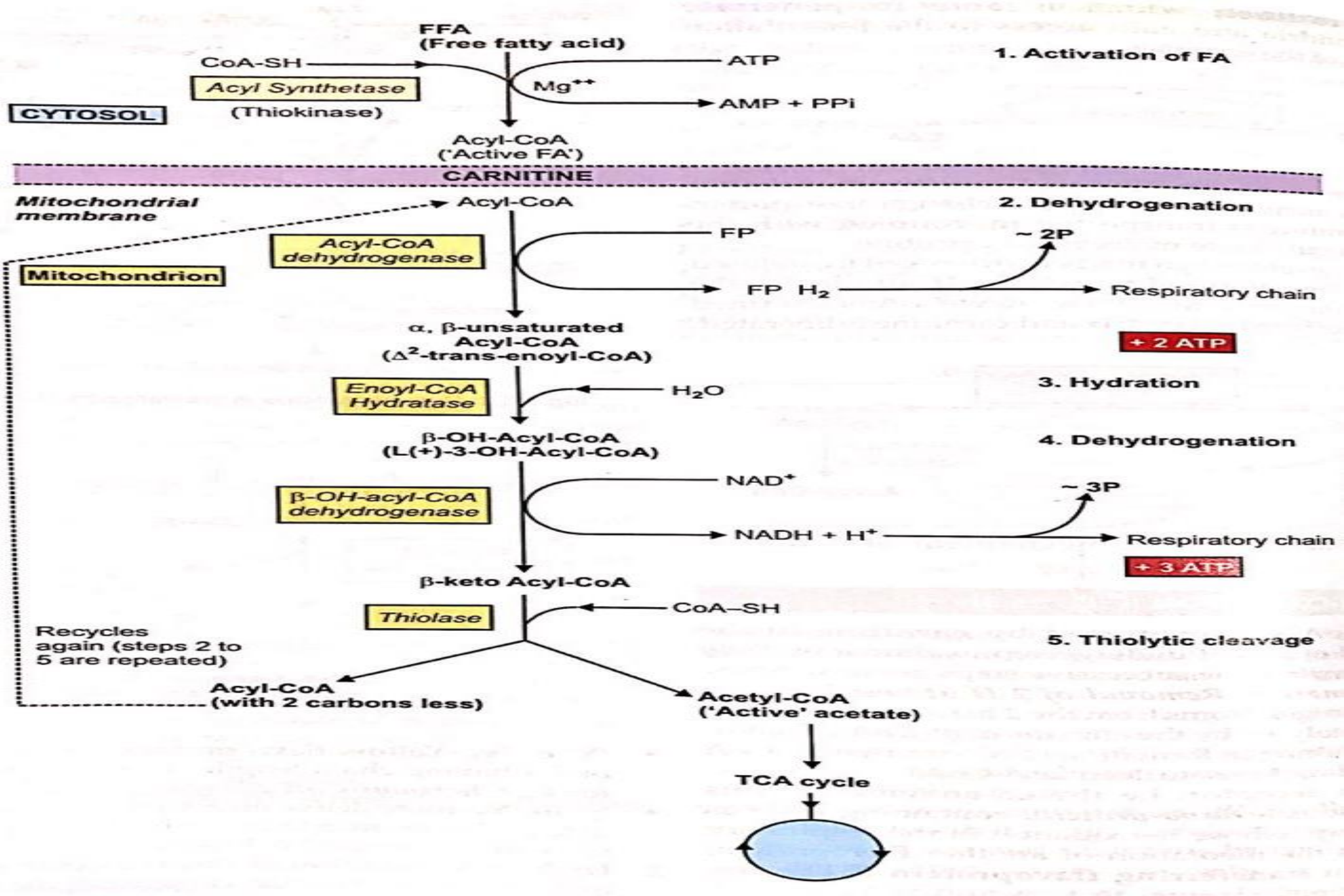
3. Dehydrogenation: - 2H atoms .....> 3ATP

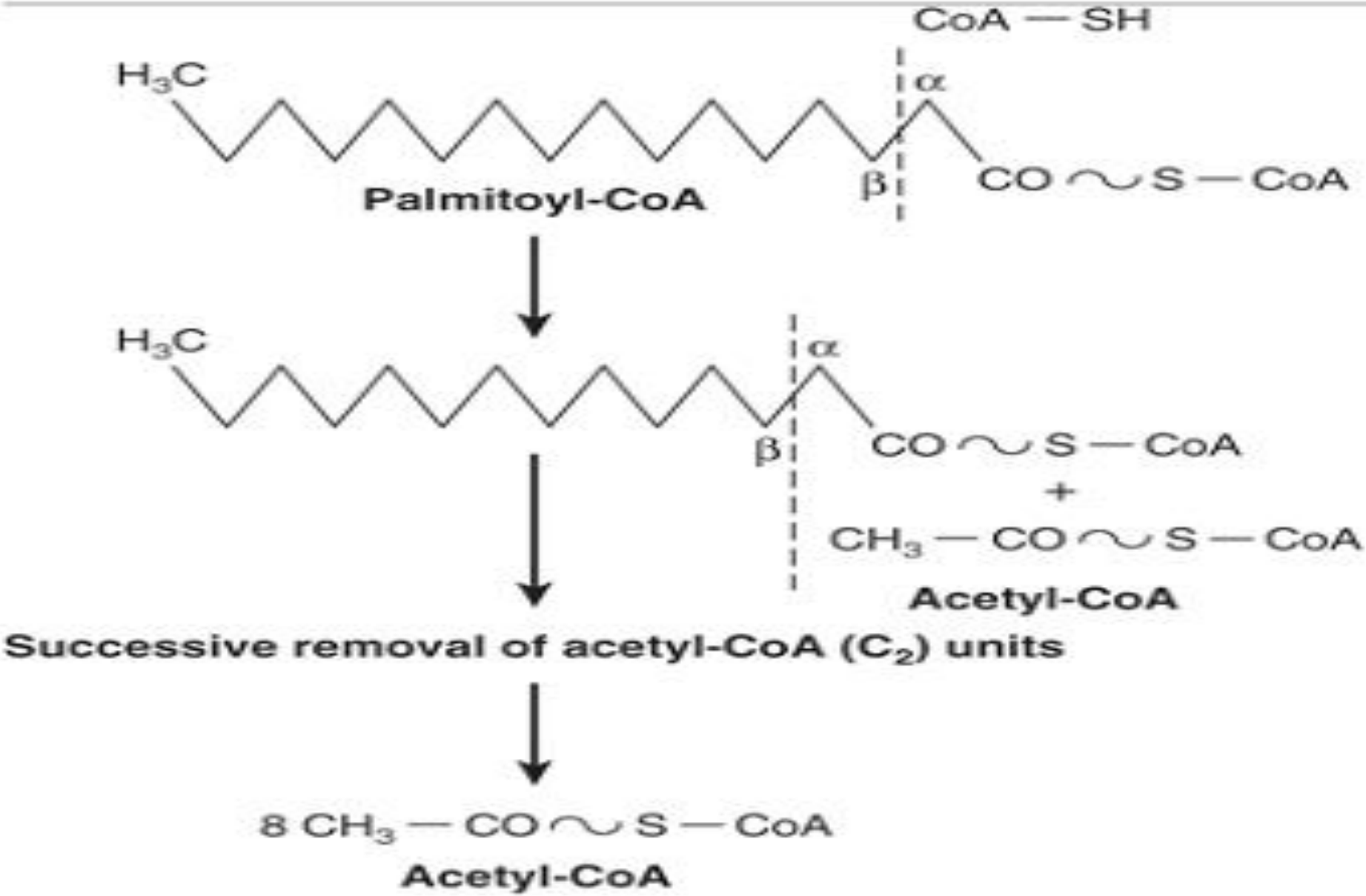


Steps of Beta oxidation

4. Thiolytic cleavage:




FFA
(Free fatty acid)
CoA-SH
Acyl Synthetase
(Thiokinase)
CYTOSOL
ATP
Mg++
AMP + PPi
1. Activation of FA
Acyl-CoA
('Active FA')
CARNITINE
Mitochondrial membrane
Acyl-CoA
2. Dehydrogenation
Acyl-CoA dehydrogenase
FP
~ 2P
Mitochondrion
FP H2
Respiratory chain
+ 2 ATP
α, β-unsaturated Acyl-CoA
(Δ2-trans-enoyl-CoA)
Enoyl-CoA Hydratase
H2O
3. Hydration
β-OH-Acyl-CoA
(L(+)-3-OH-Acyl-CoA)
4. Dehydrogenation
β-OH-acyl-CoA dehydrogenase
NAD+
~ 3P
NADH + H+
Respiratory chain
+ 3 ATP
β-keto Acyl-CoA
Thiolase
CoA–SH
Recycles again (steps 2 to 5 are repeated)
5. Thiolytic cleavage
Acyl-CoA
(with 2 carbons less)
Acetyl-CoA
('Active' acetate)
TCA cycle


CoA — SH
H3C
α
β
CO ~ S — CoA
Palmitoyl-CoA
H3C
α
β
CO ~ S — CoA
+
CH3 — CO ~ S — CoA
Acetyl-CoA
Successive removal of acetyl-CoA (C2) units
8 CH3 — CO ~ S — CoA
Acetyl-CoA

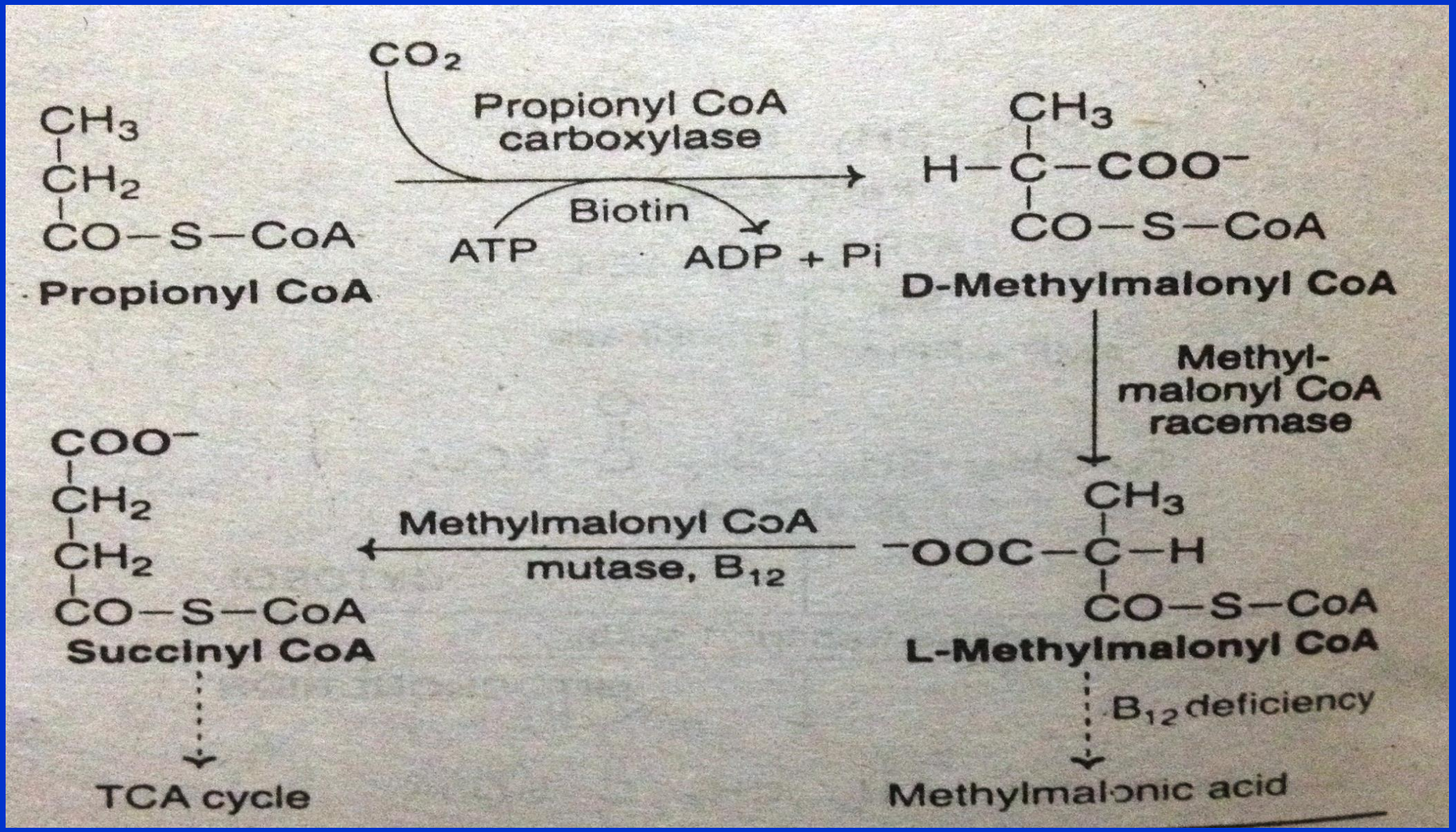
ENERGY YIELD FROM ß-OXIDATION

- From PalmitoylCoA 16carbon chain FA ATP Yield

7NADH x 3 ATP by ETC oxidation	21
7 $FADH_2$ x 2 ATP by ETC oxidation	14
8 Acetyl CoA x 12 ATP via Krebs CAC	96
Total (Gross)	131 ATP
Less	2 ~PP
NET	129 ATP

From one molecule of palmitoylCoA

Oxidation of odd carbon chain fatty acids


CO2
Propionyl CoA carboxylase
Biotin
ATP
ADP + Pi
Propionyl CoA
D-Methylmalonyl CoA
Methyl-malonyl CoA racemase
Methylmalonyl CoA mutase, B12
Succinyl CoA
L-Methylmalonyl CoA
B12 deficiency
TCA cycle
Methylmalonic acid

Oxidation of unsaturated carbon chain fatty acids

.Beta oxidation
.Isomerase and epimarase
.It provide less energy than even number FAs.

disorders of FA Oxidation

1. Acly Co A dehydrogenase deficiency(Jamaican vomiting sickness)
2.Carnitine deficiency
3.congenital deficiency of Carnitine palmityl transferase system.
4. Congenital absence of peroxisoms

Akee fruit

Methylmalonic acidemia

Two types
1. Due to deficiency of vit B12
2. Due to defect in the methymalonyl CoA mutase

ANY QUESTION

- CHATTERJEA BIOCHEMISTRY
- LIPPINCOTT BIOCHEMISTRY
- HARPERS BIOCHEMISTRY
- SATYANARAYANA BIOCHEMISTRY
- INTERNET

Thank you