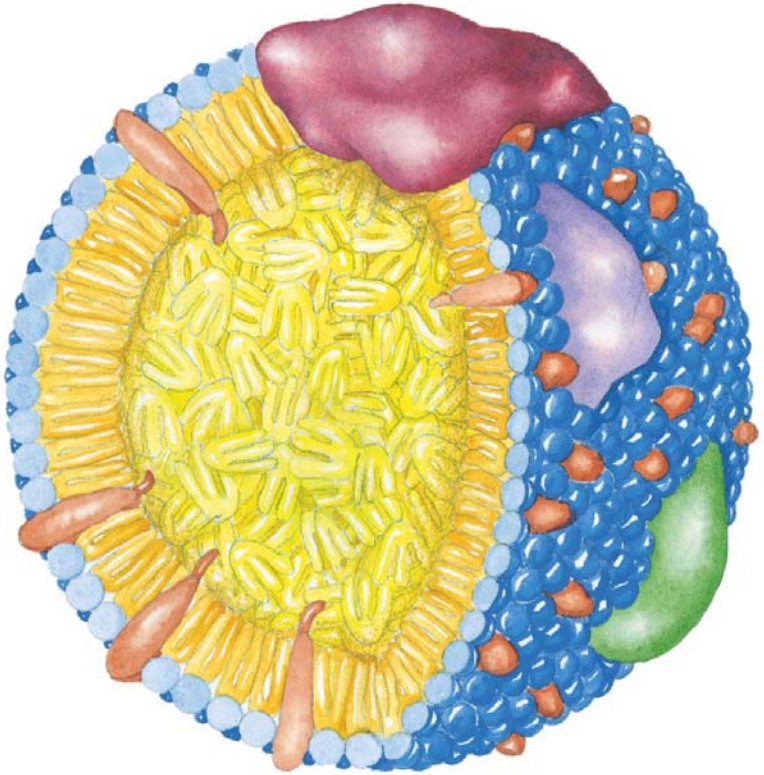
Chpt. 17

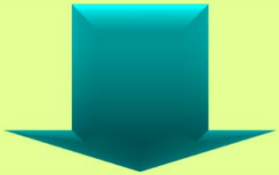
Fatty Acid Catabolism

17.1 Digestion, Mobilization, and Transport of Fats
17.2 Oxidation of Fatty Acids
17.3 Ketone Bodies



Lipids

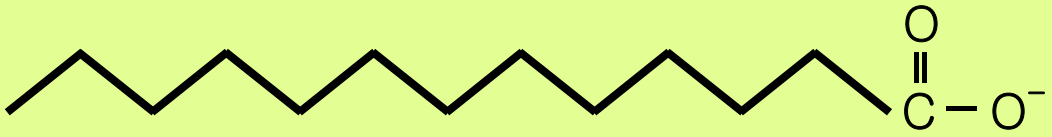
- **Fats or Oils:** stored forms of energy
- **Phospholipids, Sterols:** major structural elements of biological membrane
- **Other lipids:** roles as enzyme cofactor, electron carrier, hydrophobic anchor, hormones, intracellular messengers



Storage lipids
Structural lipids in membranes
Lipids as signals, cofactors, and pigments

Fatty acids

Fatty acids: carboxylic acids with hydrocarbon chains (C_4 to C_{36})



Saturated fatty acids
Unsaturated fatty acids

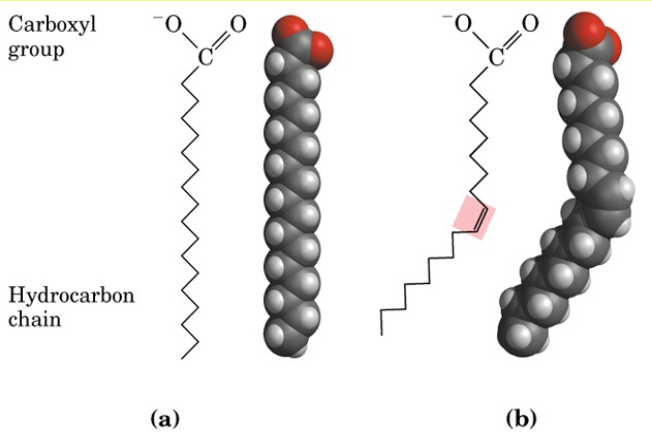


TABLE 10–1 Some Naturally Occurring Fatty Acids: Structure, Properties, and Nomenclature

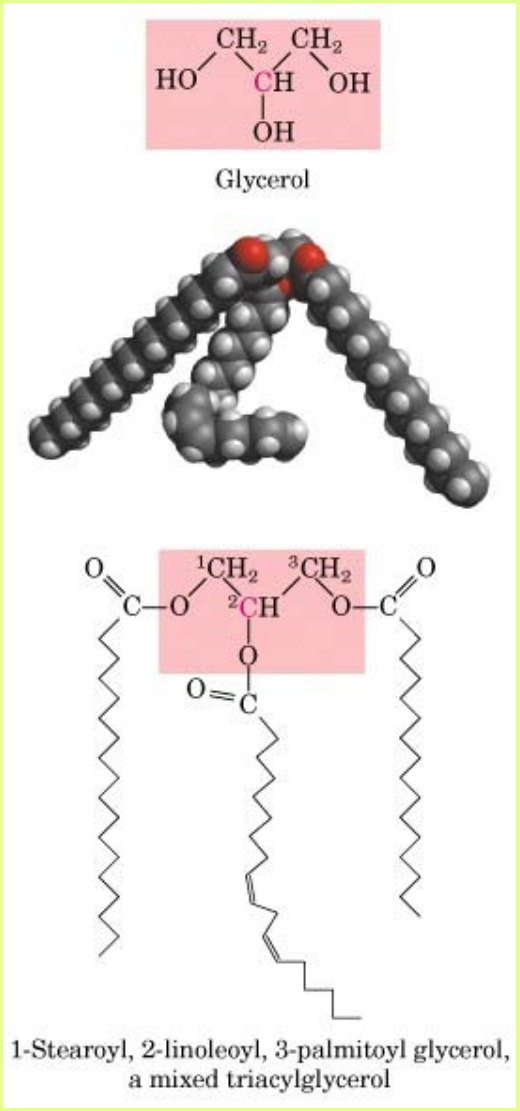
Carbon skeleton	Structure*	Systematic name†	Common name (derivation)	Melting point (°C)	Solubility at 30 °C (mg/g solvent)	
					Water	Benzene
12:0	$CH_3(CH_2)_{10}COOH$	*n*-Dodecanoic acid	Lauric acid (Latin *laurus*, "laurel plant")	44.2	0.063	2,600
14:0	$CH_3(CH_2)_{12}COOH$	*n*-Tetradecanoic acid	Myristic acid (Latin *Myristica*, nutmeg genus)	53.9	0.024	874
16:0	$CH_3(CH_2)_{14}COOH$	*n*-Hexadecanoic acid	Palmitic acid (Latin *palma*, "palm tree")	63.1	0.0083	348
18:0	$CH_3(CH_2)_{16}COOH$	*n*-Octadecanoic acid	Stearic acid (Greek *stear*, "hard fat")	69.6	0.0034	124
20:0	$CH_3(CH_2)_{18}COOH$	*n*-Eicosanoic acid	Arachidic acid (Latin *Arachis*, legume genus)	76.5		
24:0	$CH_3(CH_2)_{22}COOH$	*n*-Tetracosanoic acid	Lignoceric acid (Latin *lignum*, "wood" + *cera*, "wax")	86.0		
16:1(Δ^9)	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$	*cis*-9-Hexadecenoic acid	Palmitoleic acid	1–0.5		
18:1(Δ^9)	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$	*cis*-9-Octadecenoic acid	Oleic acid (Latin *oleum*, "oil")	13.4		
18:2($\Delta^{9,12}$)	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$	*cis*-,*cis*-9,12-Octadecadienoic acid	Linoleic acid (Greek *linon*, "flax")	1–5		
18:3($\Delta^{9,12,15}$)	$CH_3CH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$	*cis*-,*cis*-,*cis*-9,12,15-Octadecatrienoic acid	α-Linolenic acid	−11		
20:4($\Delta^{5,8,11,14}$)	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_3COOH$	*cis*-,*cis*-,*cis*-,*cis*-5,8,11,14-Icosatetraenoic acid	Arachidonic acid	−49.5		

*All acids are shown in their nonionized form. At pH 7, all free fatty acids have an ionized carboxylate. Note that numbering of carbon atoms begins at the carboxyl carbon.

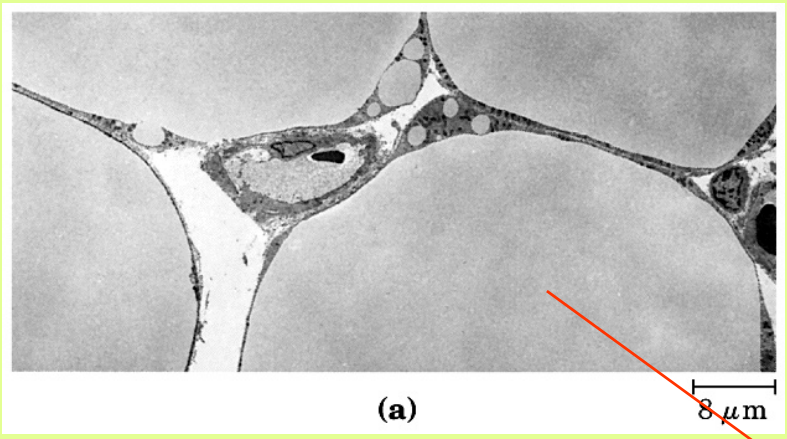
†The prefix *n*- indicates the "normal" unbranched structure. For instance, "dodecanoic" simply indicates 12 carbon atoms, which could be arranged in a variety of branched forms; "*n*-dodecanoic" specifies the linear, unbranched form. For unsaturated fatty acids, the configuration of each double bond is indicated; in biological fatty acids the configuration is almost always cis.

Triacylglycerol

Storage lipids (derivatives of fatty acids)

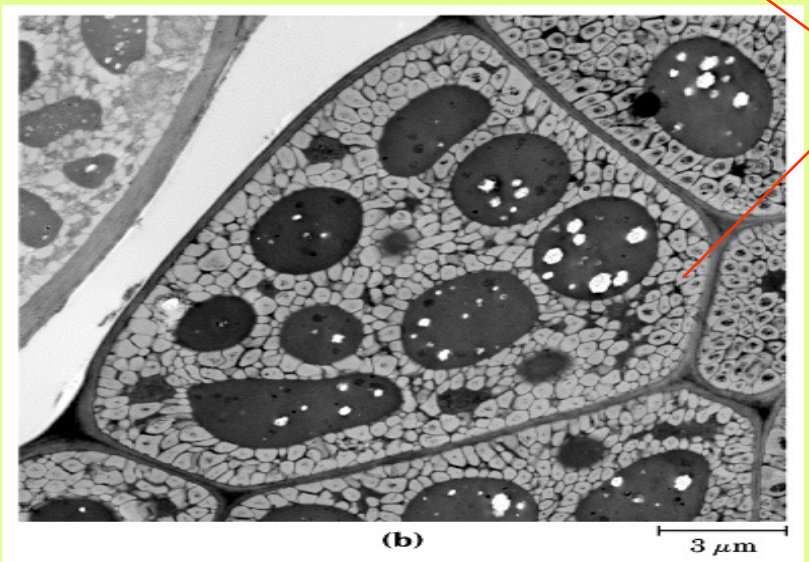


provide stored energy and insulation

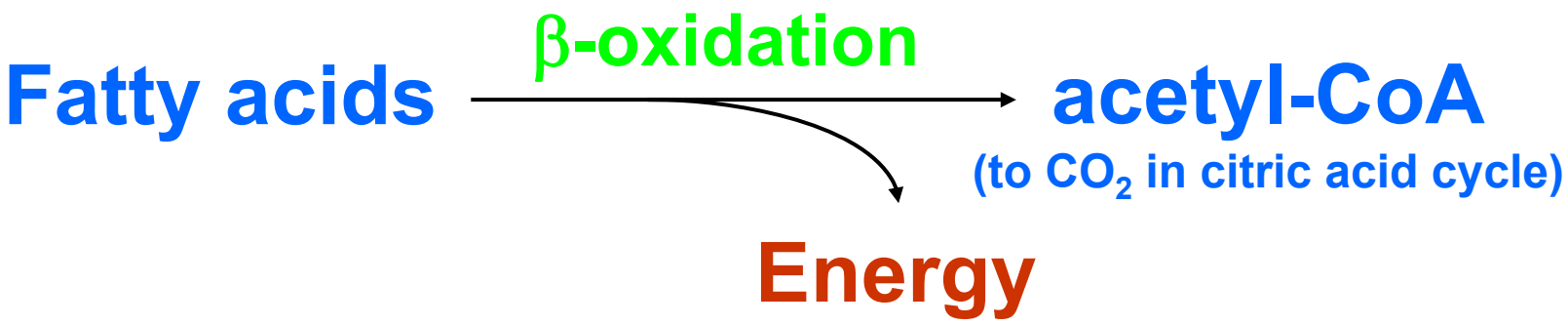


adipocytes

fat



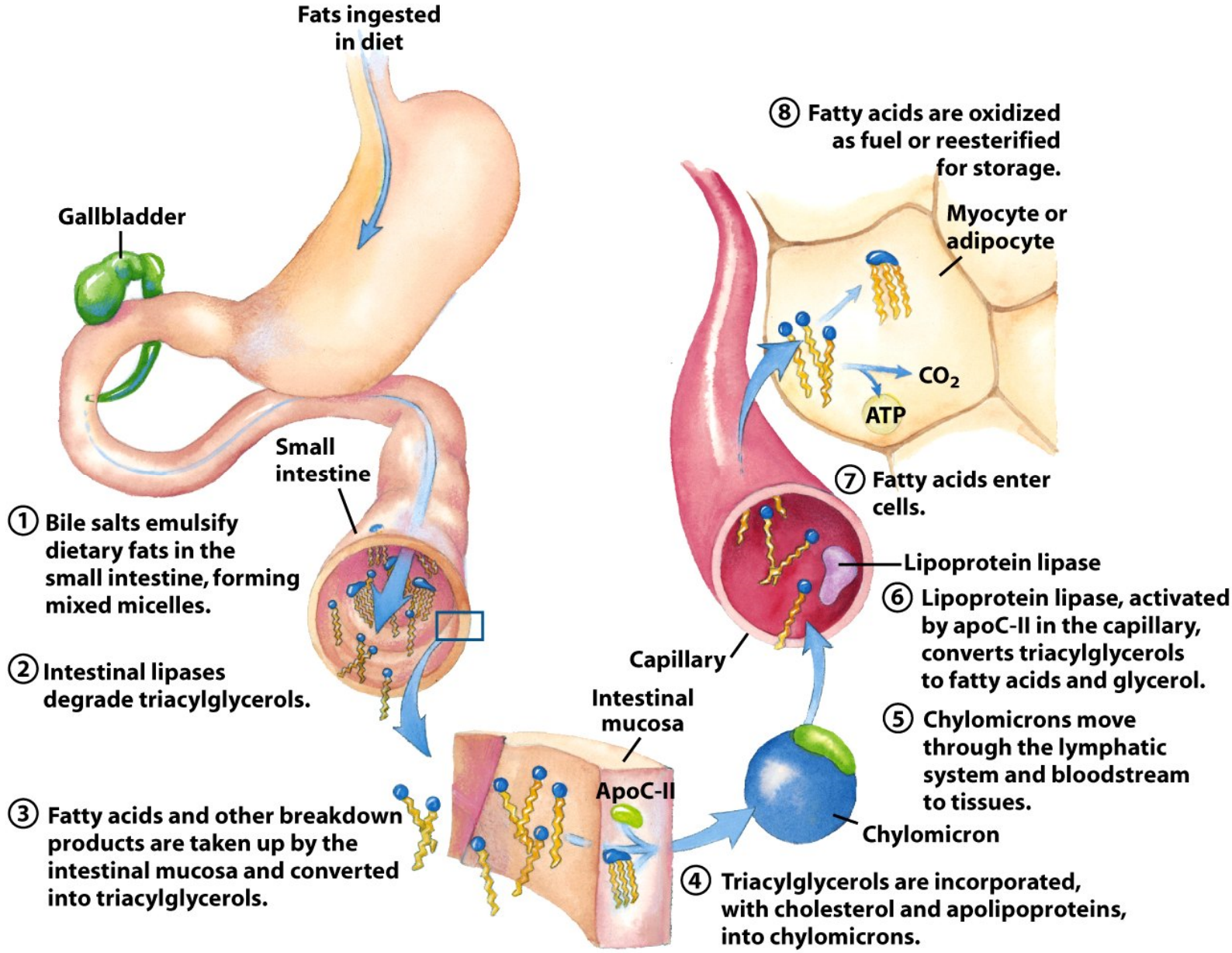
seed

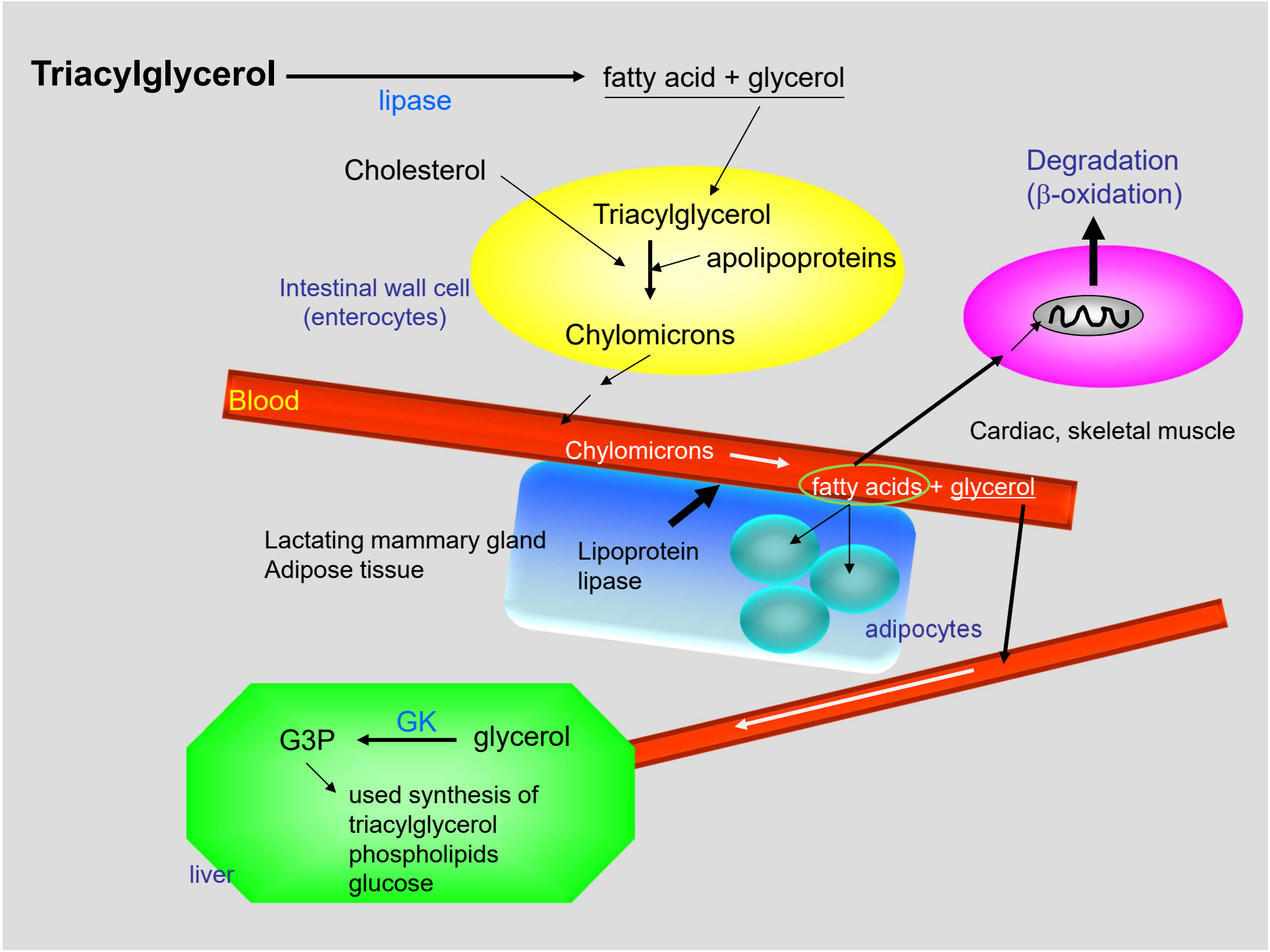


Palmitic acid : 106 ATP/ 16 carbon = 6.6 ATP/carbon

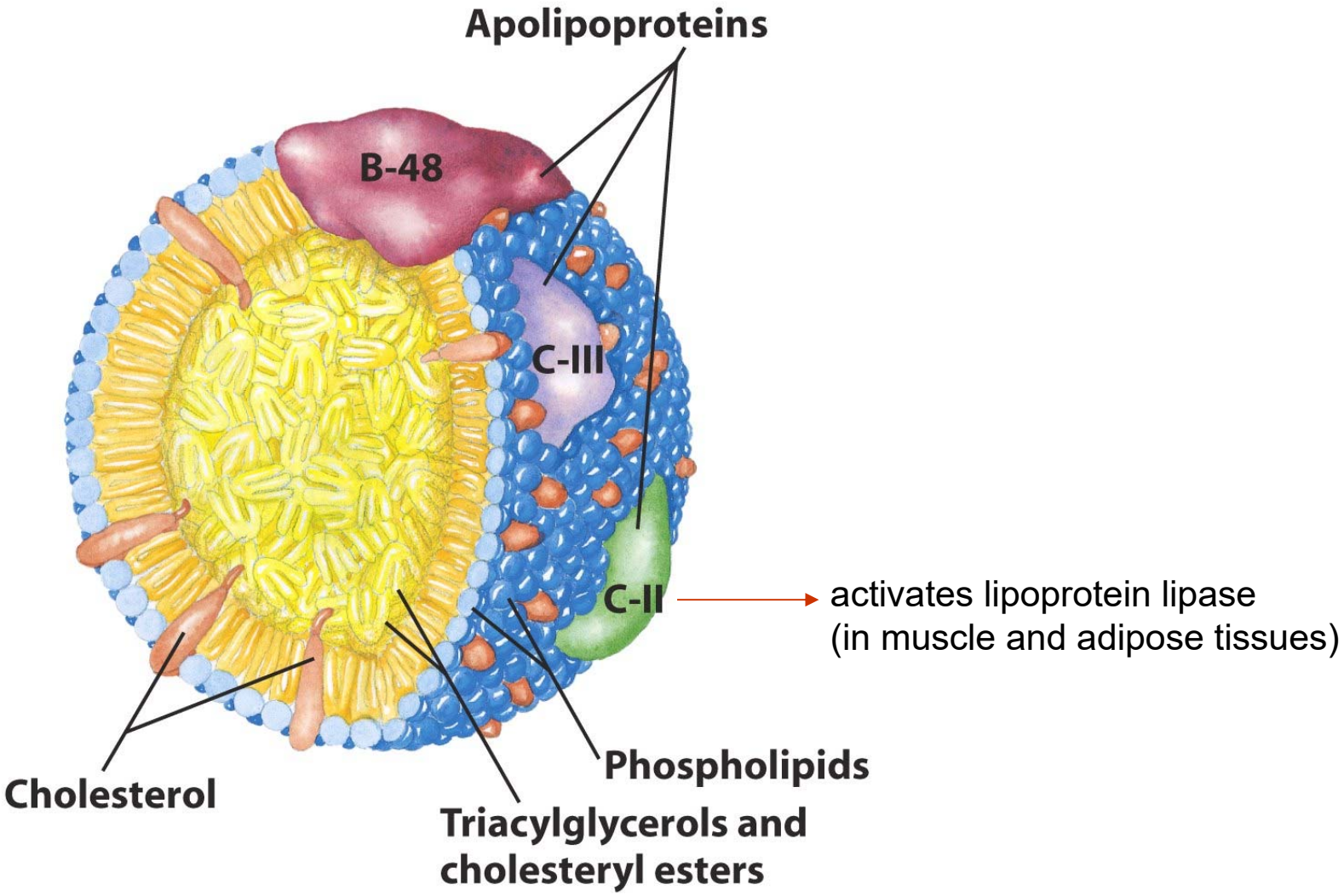
Glucose : 31 ATP/ 6 carbon = 5.2 ATP/carbon

Processing of dietary lipids in vertebrates




Triacylglycerol
lipase
fatty acid + glycerol
Cholesterol
Triacylglycerol
apolipoproteins
Chylomicrons
Intestinal wall cell
(enterocytes)
Degradation
(β-oxidation)
Blood
Chylomicrons
fatty acids + glycerol
Cardiac, skeletal muscle
Lactating mammary gland
Adipose tissue
Lipoprotein
lipase
adipocytes
GK
G3P
glycerol
used synthesis of
triacylglycerol
phospholipids
glucose
liver

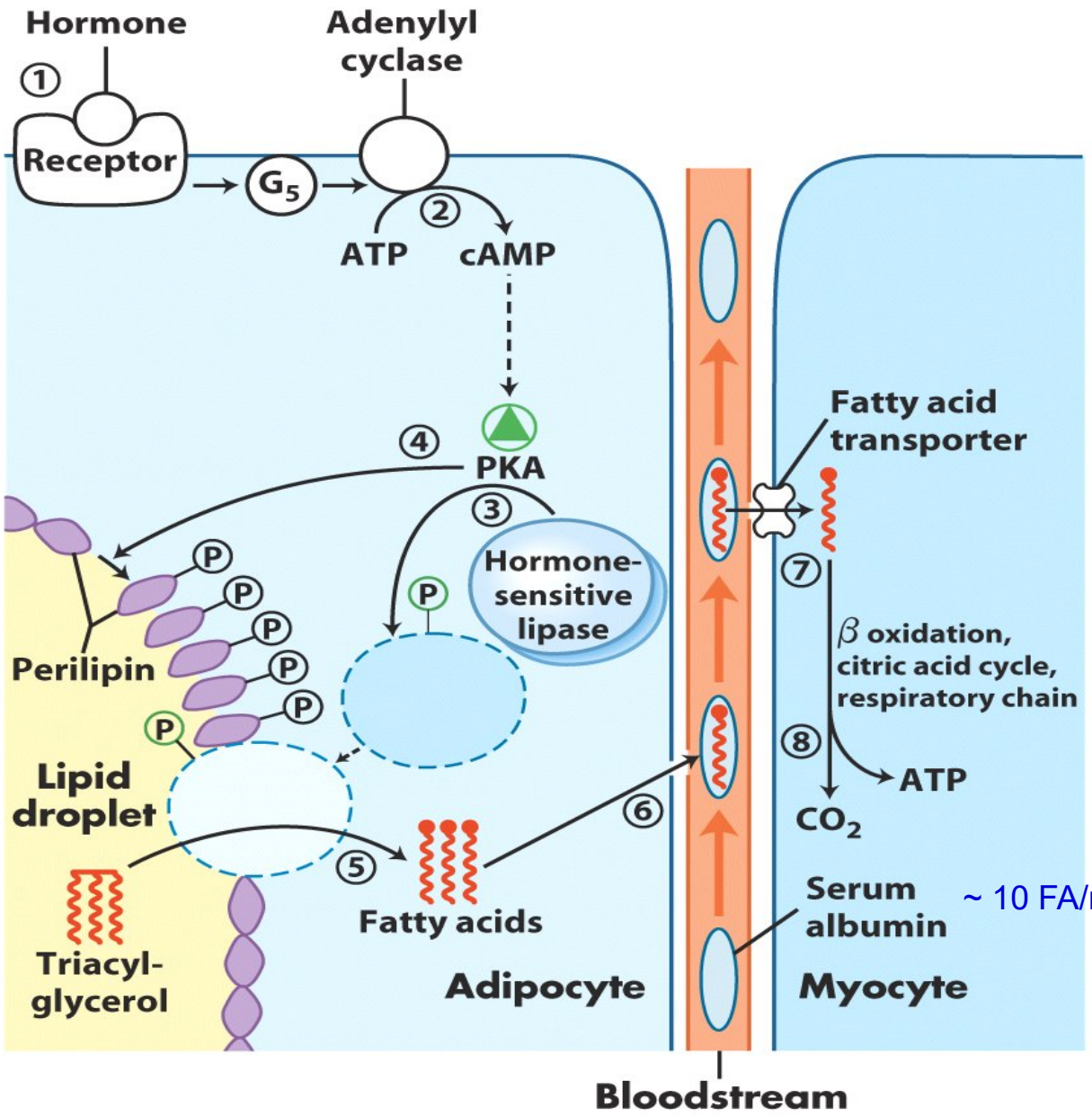
Molecular structure of a chylomicron



Mobilization of TAGs stored in adipose tissue

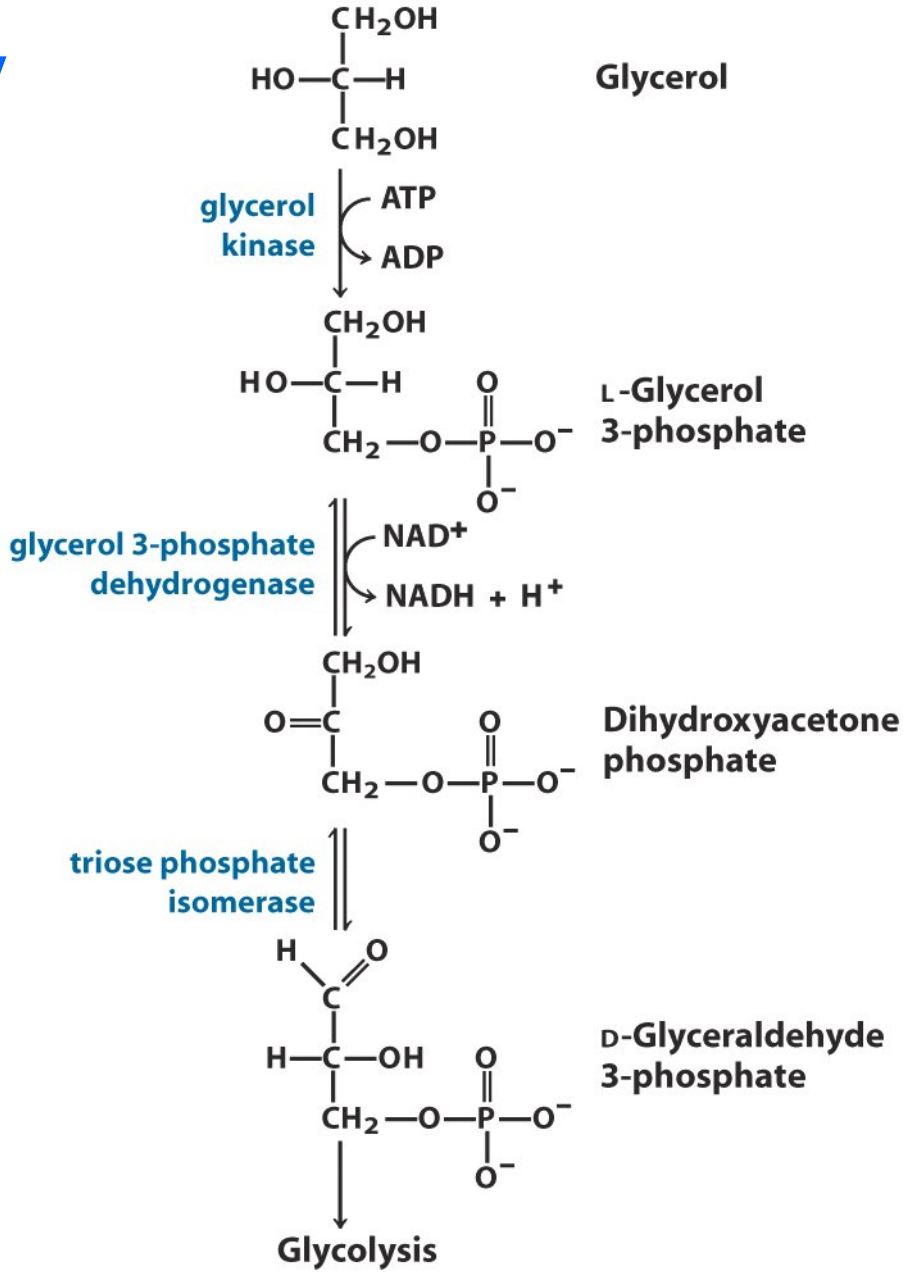
Serum glucose level (H):
[insulin]
TAG synthesis (lipogenesis)

Serum glucose level (L):
[glucagon, epinephrine]
TAG breakdown (lipolysis)

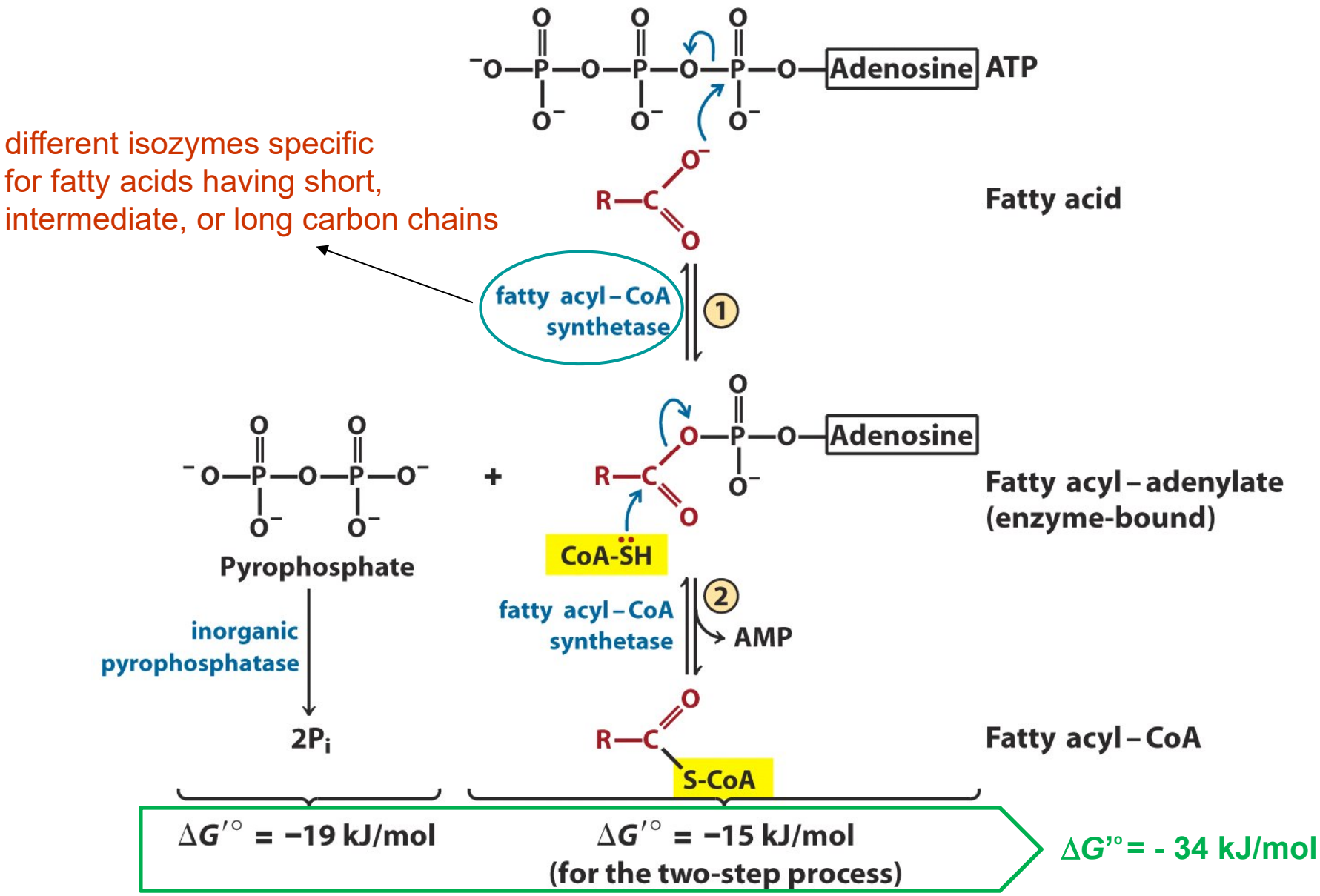


~ 10 FA/monomer

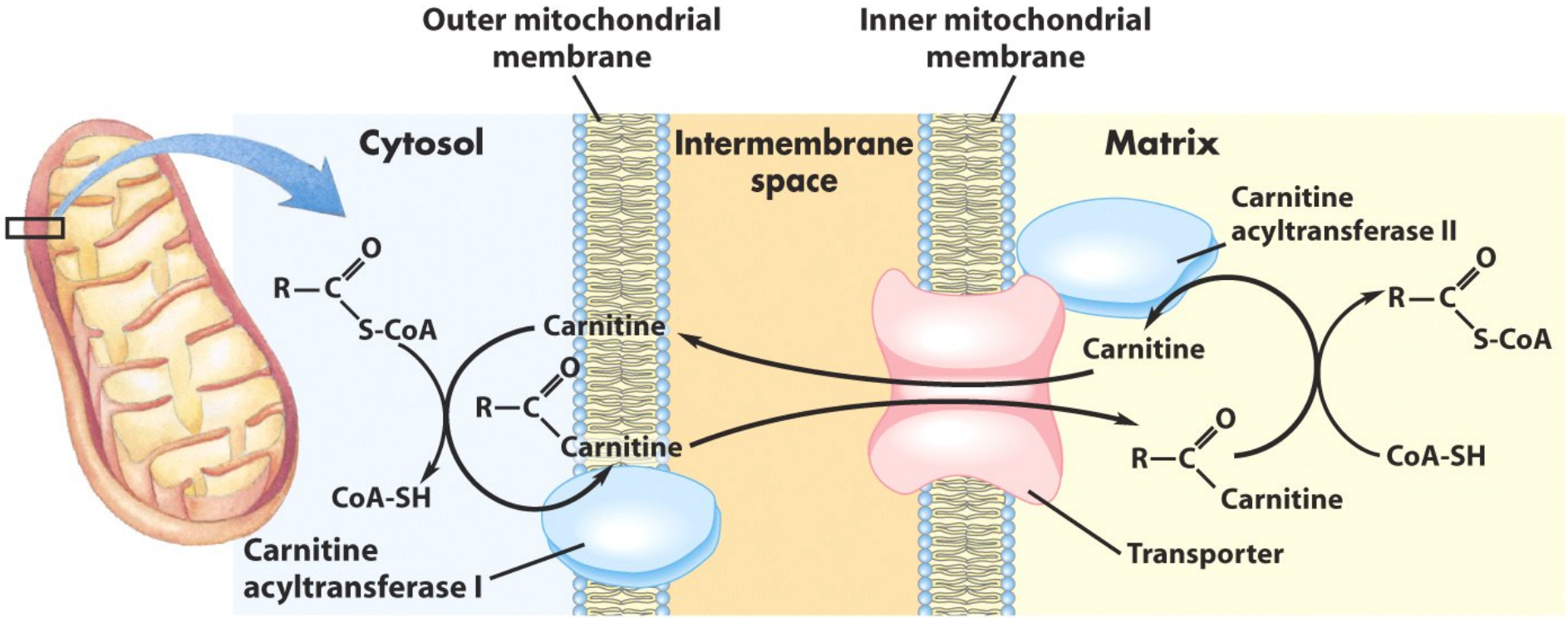
Entry of glycerol into the glycolytic pathway



Conversion of fatty acid to a fatty acyl-CoA



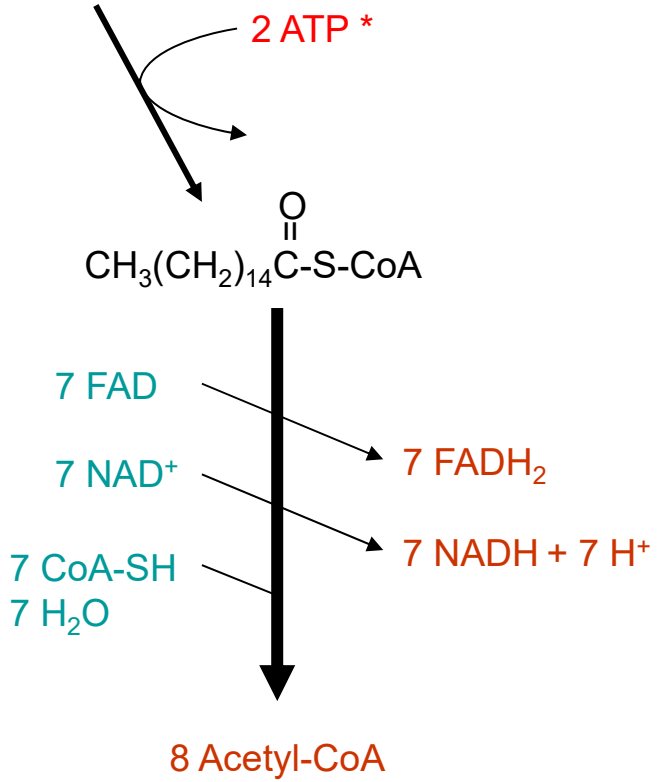
Fatty acids (> 14 carbon) entry into mitochondria via the acyl-carnitine/carnitine transporter



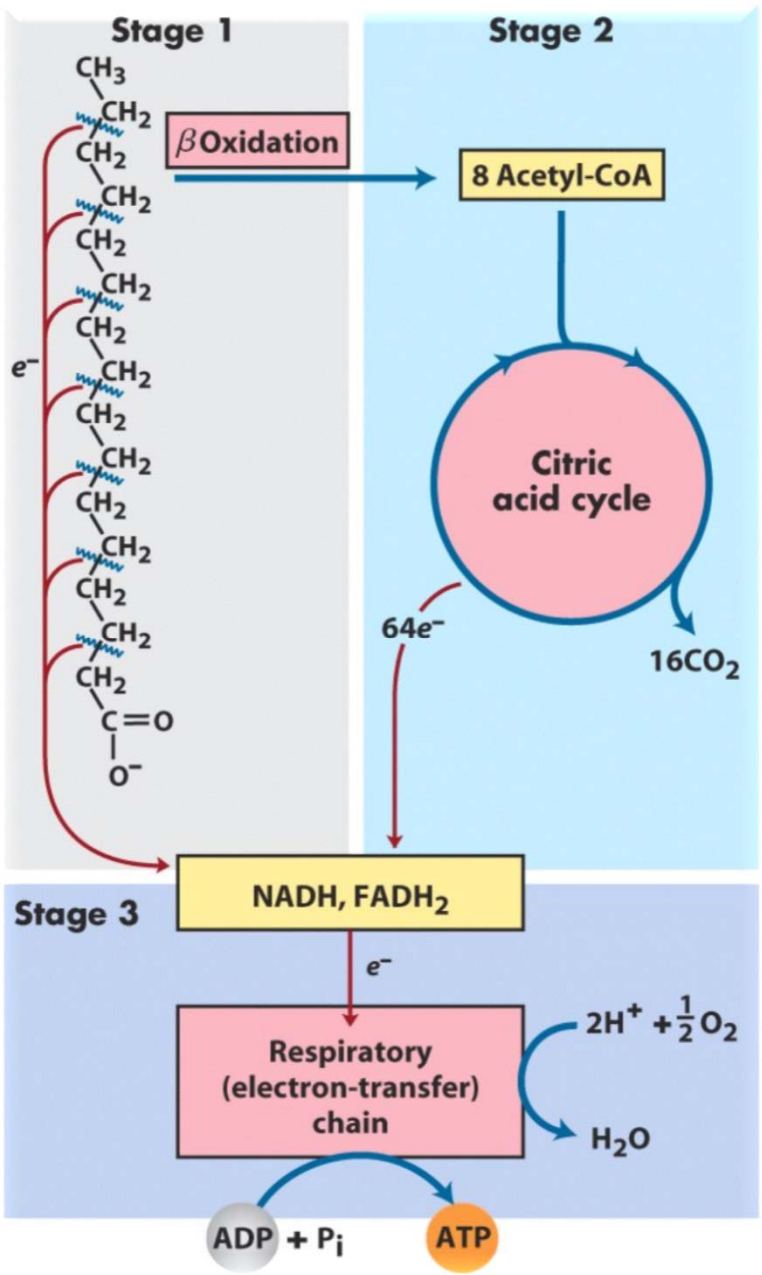
Fatty Acids
(12 or fewer carbons)

Stages of fatty acid oxidation

(eg. Palmitic acid)



7 $FADH_2$	x	1.5 ATP/$FADH_2$	=	10.5 ATP
7 NADH	x	2.5 ATP/NADH	=	17.5 ATP
8 acetyl-CoA	x	10 ATP/acetyl-CoA	=	80 ATP
				108 ATP
				- 2 ATP *
				106 ATP

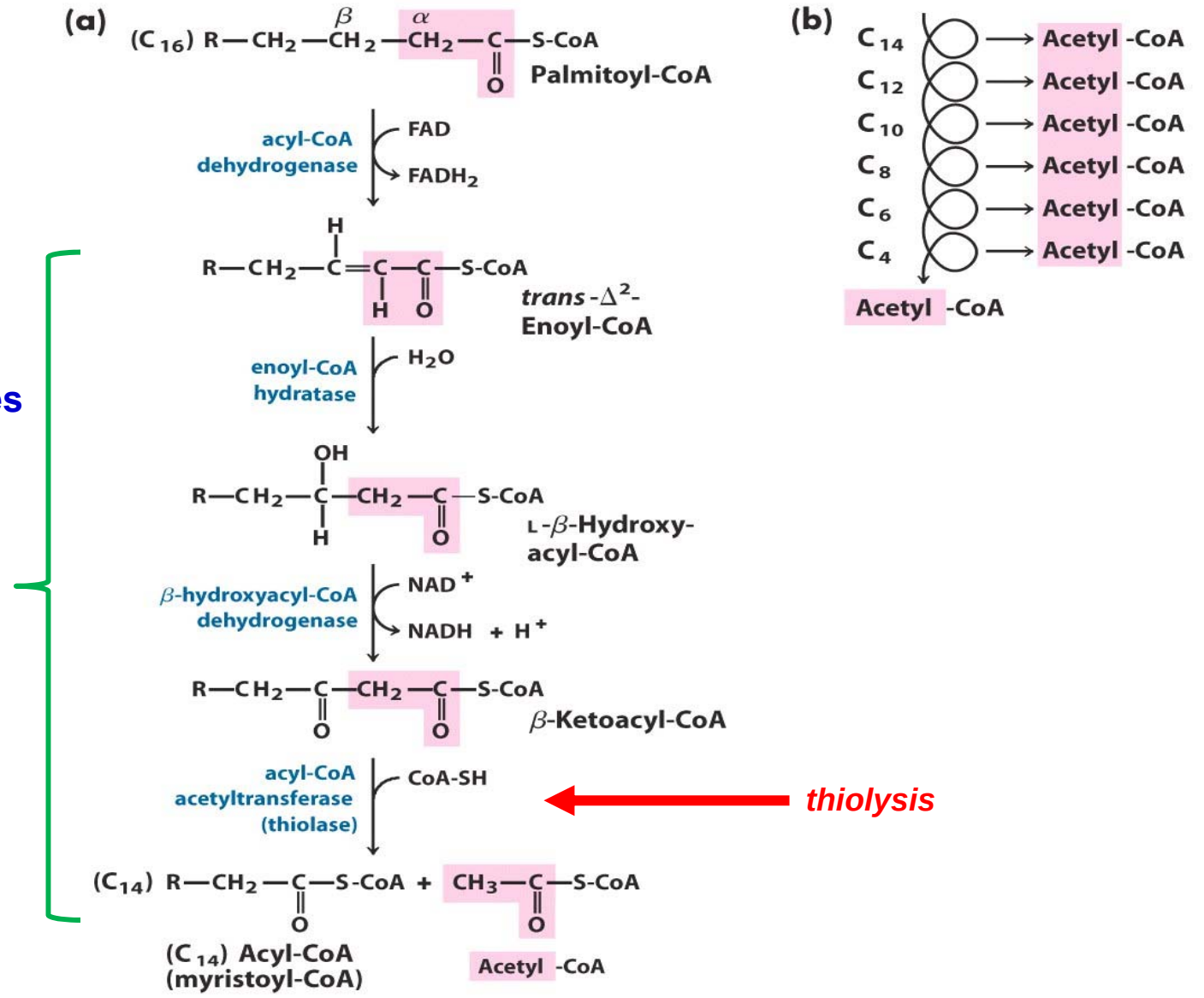


The β-oxidation pathway (of saturated fatty acids)

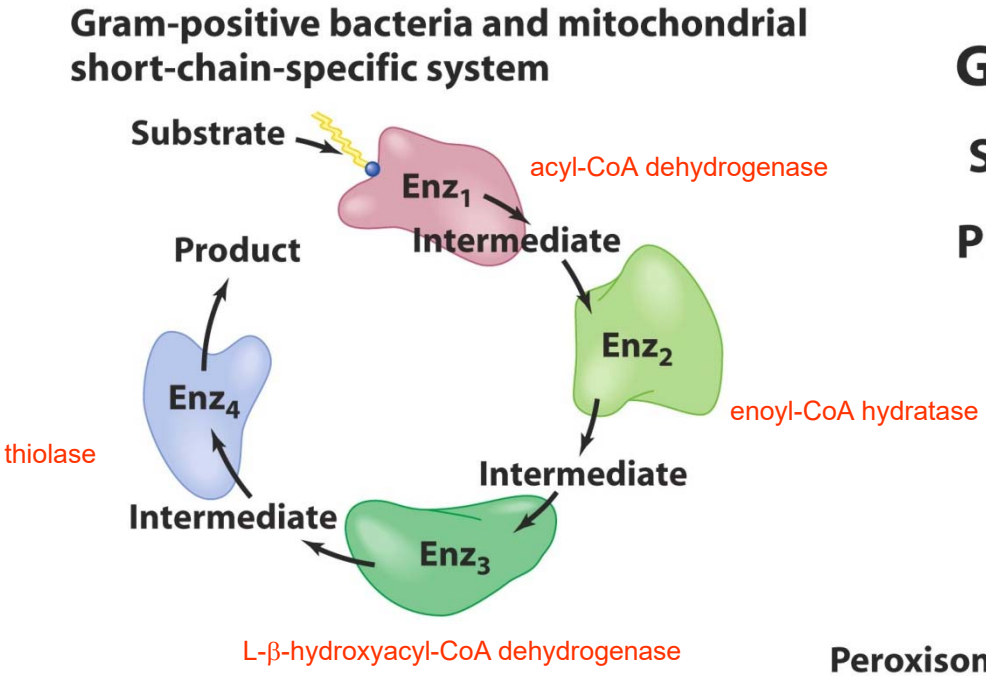
Two sets of enzymes

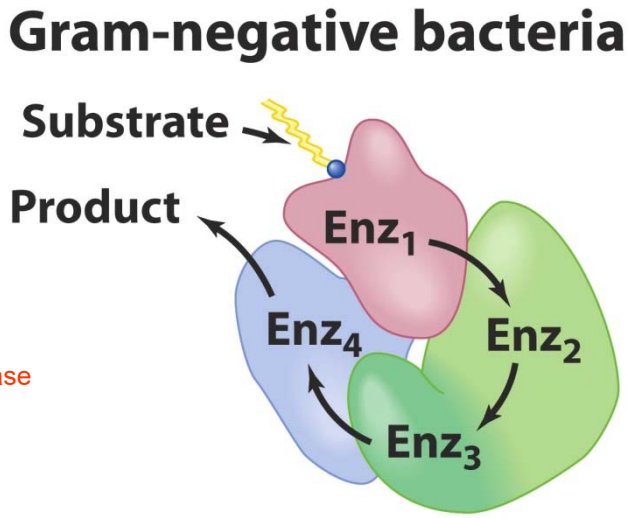
TFP complex ($\alpha_4\beta_4$)
(> 12 carbons)

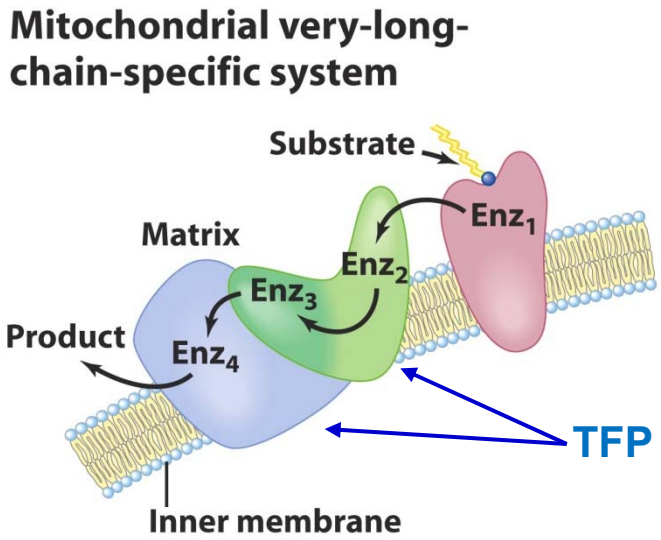
Soluble enzymes
(< 12 carbons)

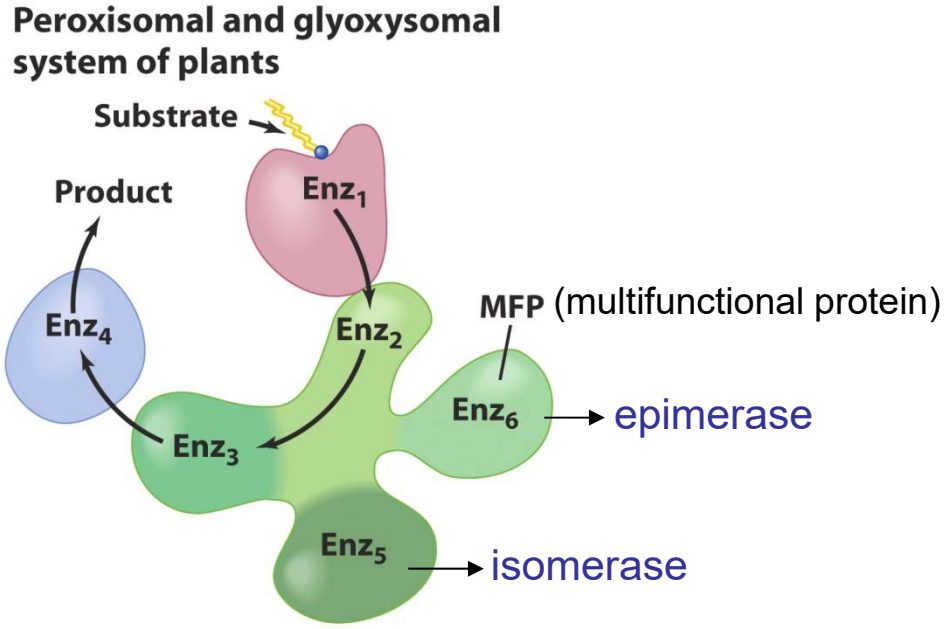


The enzymes of β-oxidation

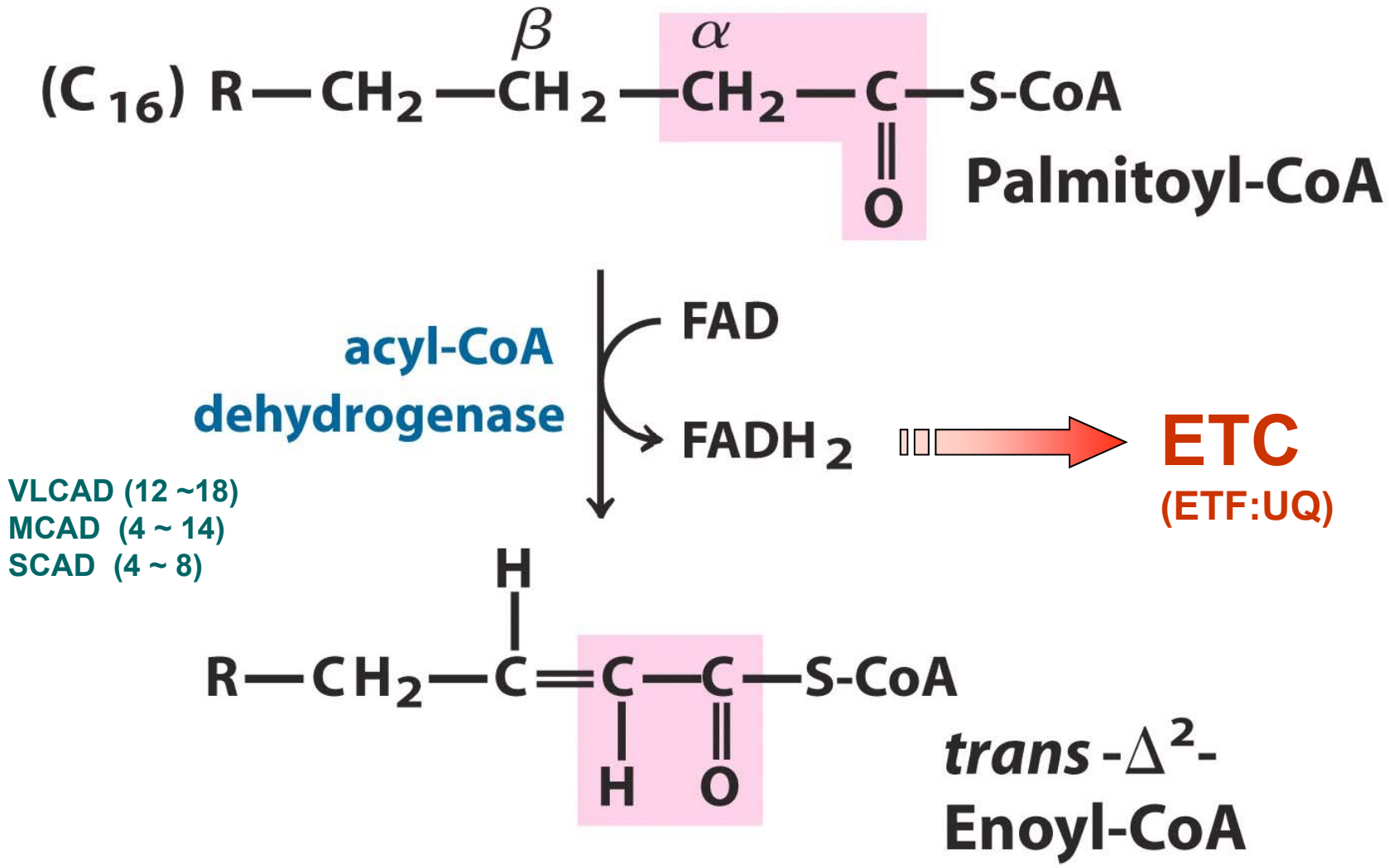




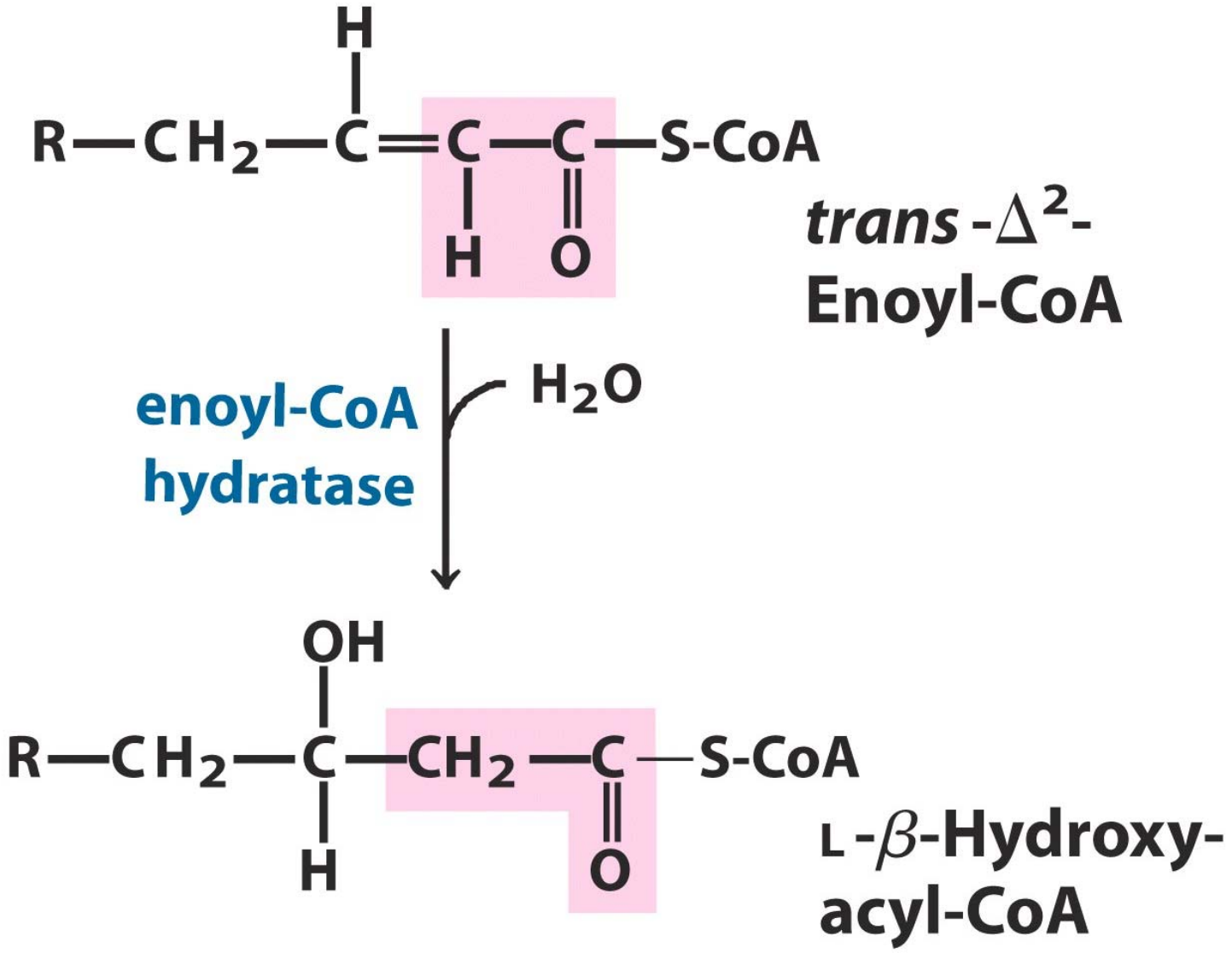




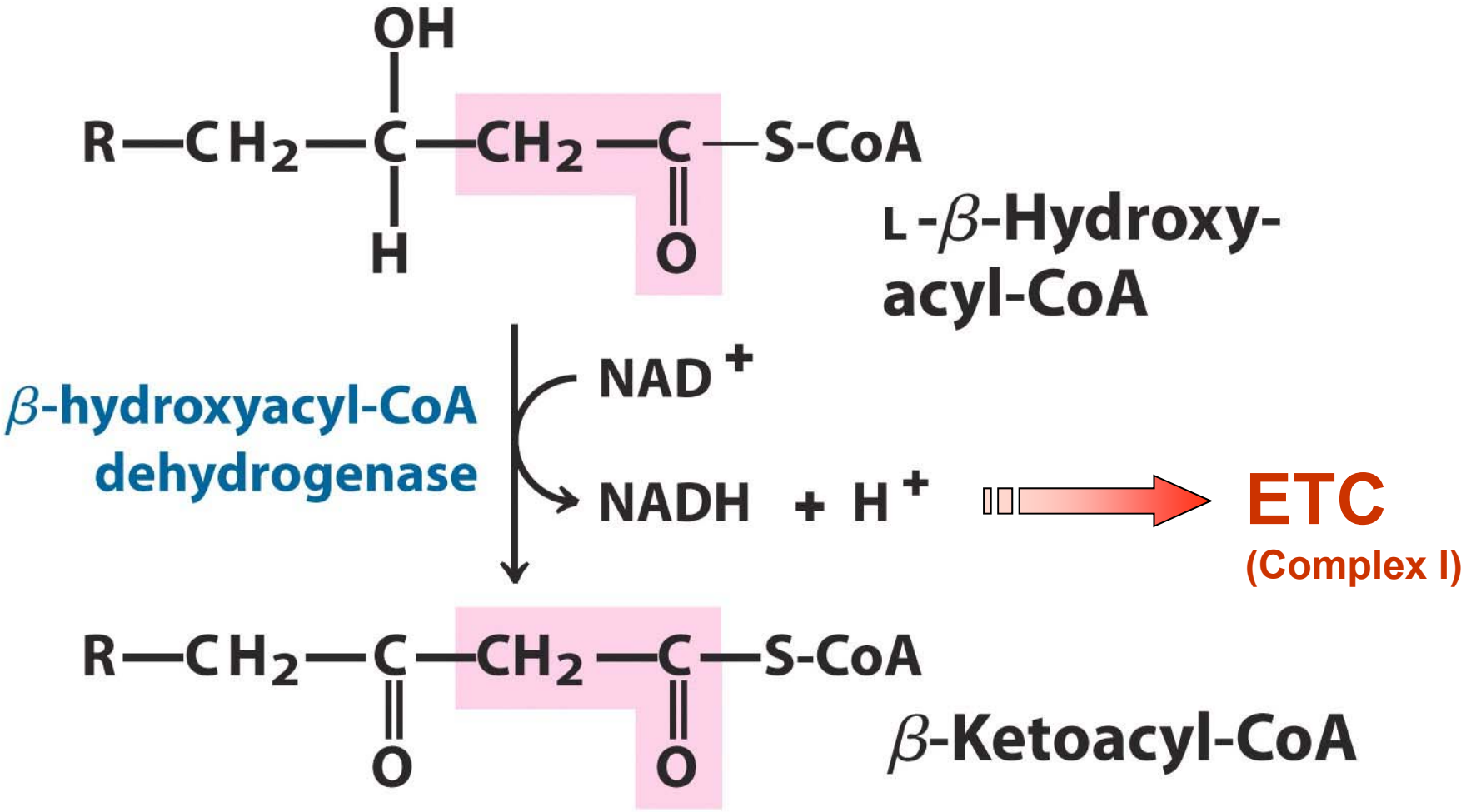
Step 1


β
α
(C16) R—CH2—CH2—CH2—C—S-CoA
O
Palmitoyl-CoA
acyl-CoA
dehydrogenase
FAD
FADH2
ETC
(ETF:UQ)
VLCAD (12 ~18)
MCAD (4 ~ 14)
SCAD (4 ~ 8)
H
R—CH2—C=C—C—S-CoA
H
O
trans -Δ2-
Enoyl-CoA

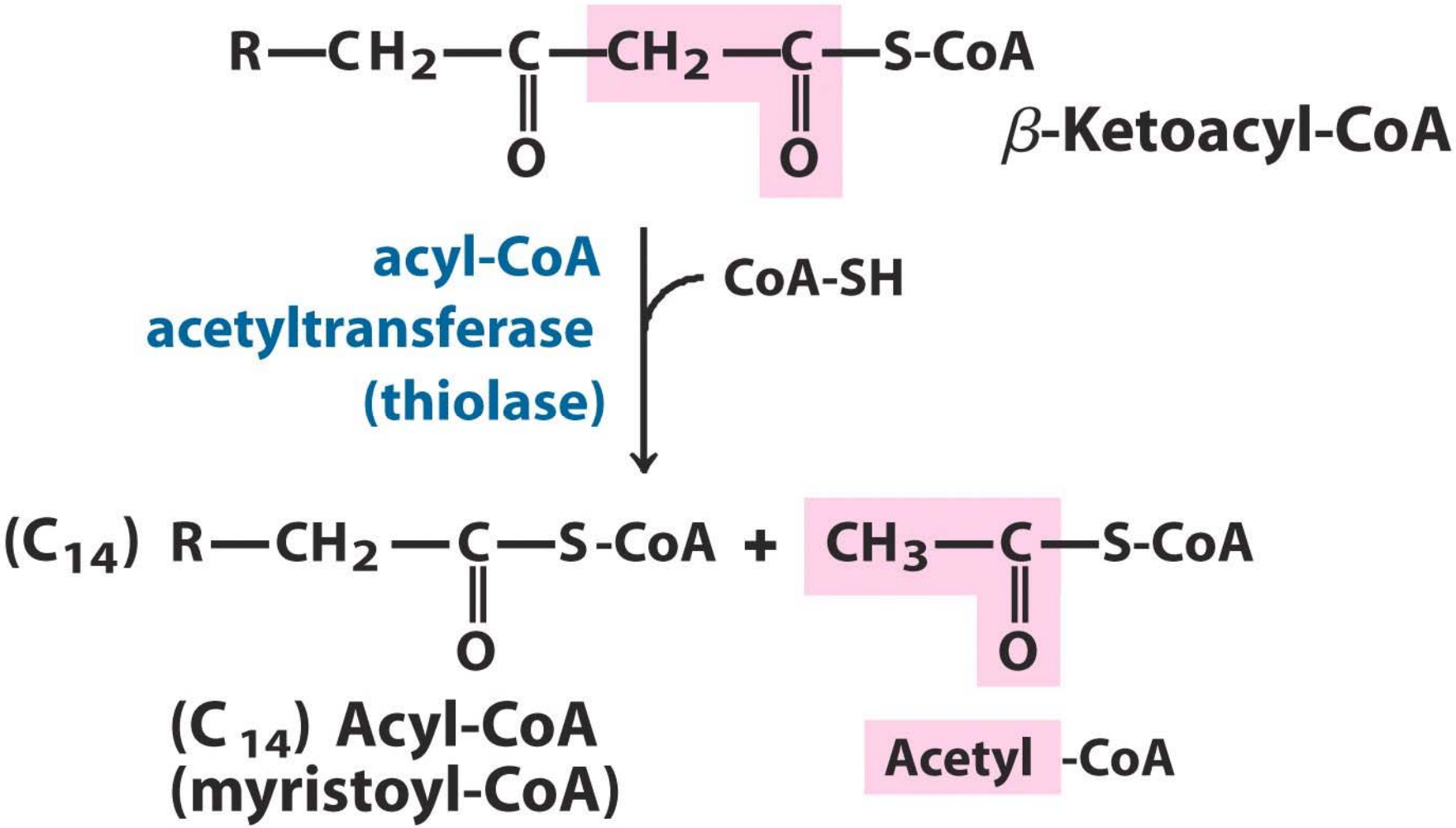
Step 2

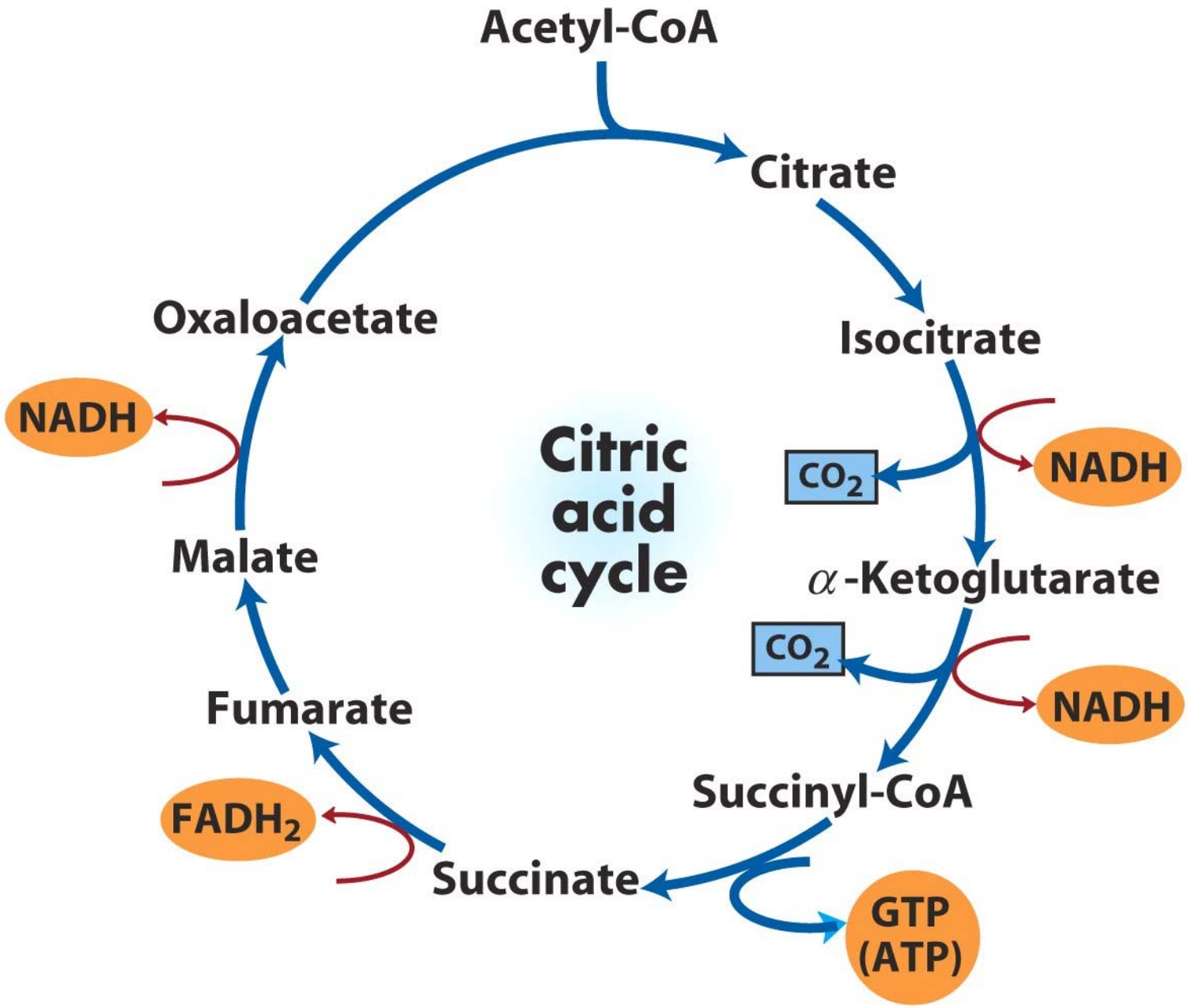

H
R—CH2—C=C—C—S-CoA
H
O
trans-Δ2-
Enoyl-CoA
enoyl-CoA
hydratase
H2O
OH
R—CH2—C—CH2—C—S-CoA
H
O
L-β-Hydroxy-
acyl-CoA

Step 3


OH
R—CH2—C—CH2—C—S-CoA
H
O
L-β-Hydroxy-acyl-CoA
β-hydroxyacyl-CoA dehydrogenase
NAD+
NADH + H+
ETC
(Complex I)
R—CH2—C—CH2—C—S-CoA
O
O
β-Ketoacyl-CoA

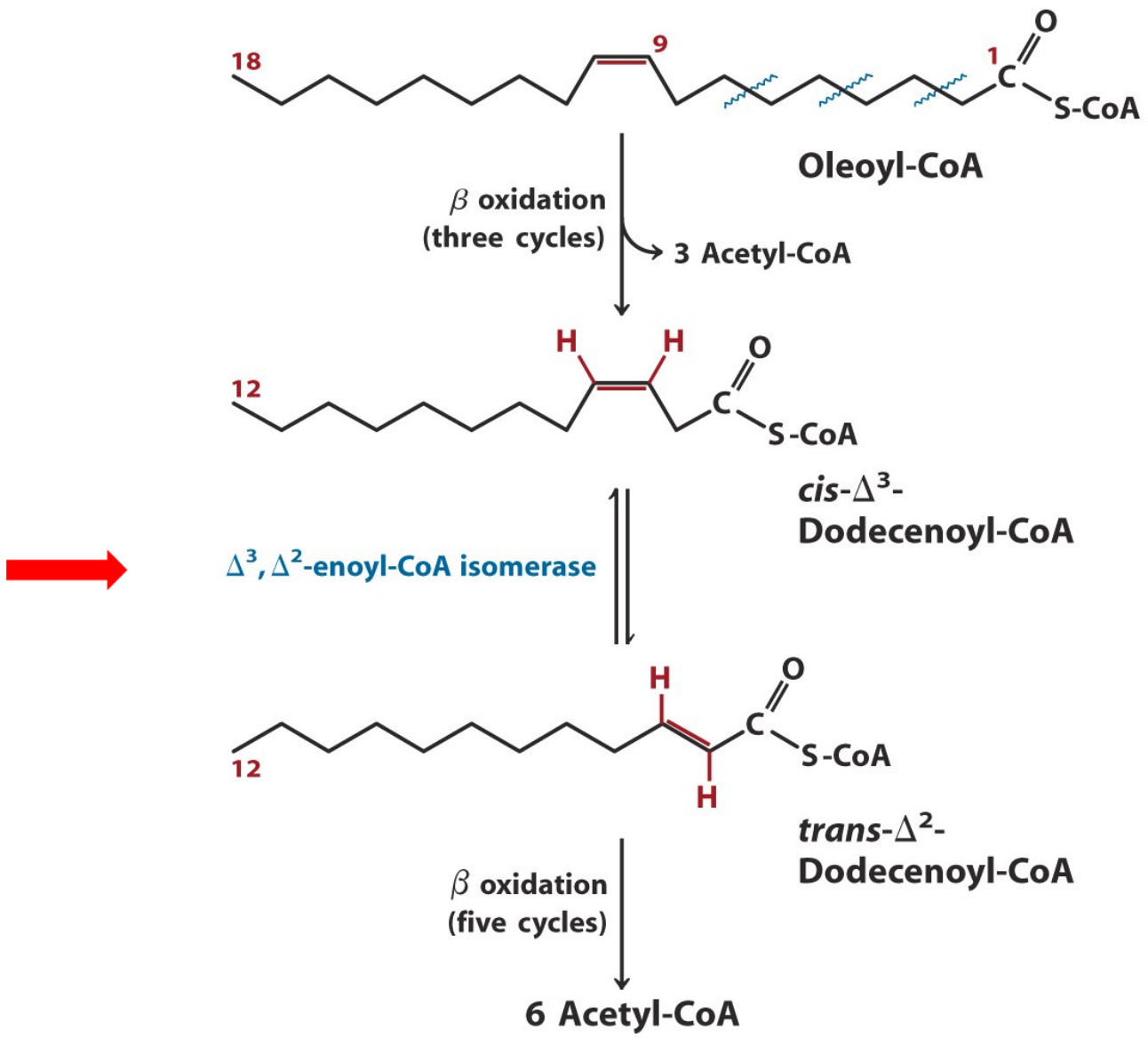
Step 4


R—CH2—C—CH2—C—S-CoA
O
O
β-Ketoacyl-CoA
acyl-CoA
acetyltransferase
(thiolase)
CoA-SH
(C14) R—CH2—C—S-CoA + CH3—C—S-CoA
O
O
(C14) Acyl-CoA
(myristoyl-CoA)
Acetyl -CoA


Acetyl-CoA
Citrate
Isocitrate
NADH
CO_2
α-Ketoglutarate
CO_2
NADH
Succinyl-CoA
GTP
(ATP)
Succinate
$FADH_2$
Fumarate
Malate
NADH
Oxaloacetate
Citric
acid
cycle

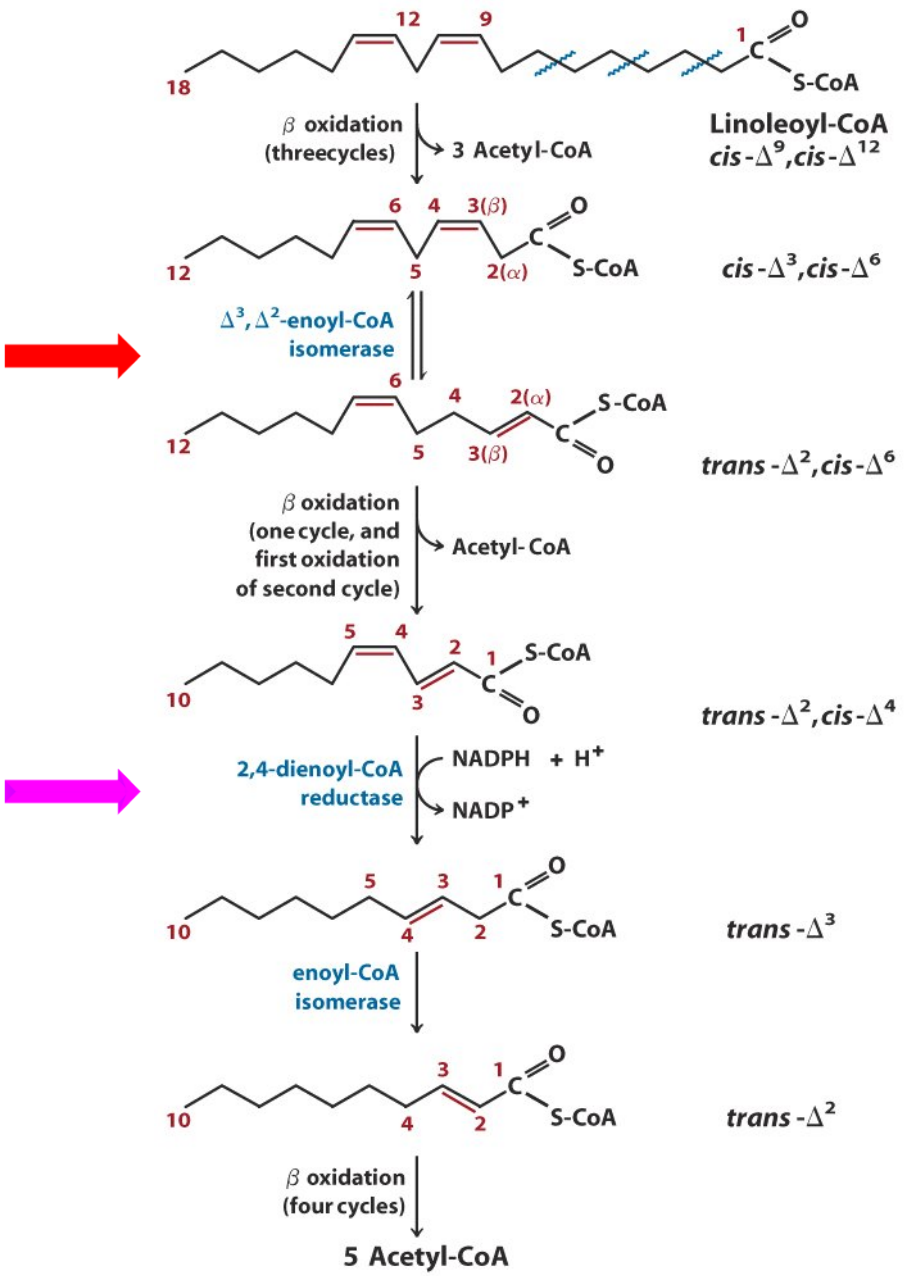
Fat bears carry out β-oxidation in their sleep

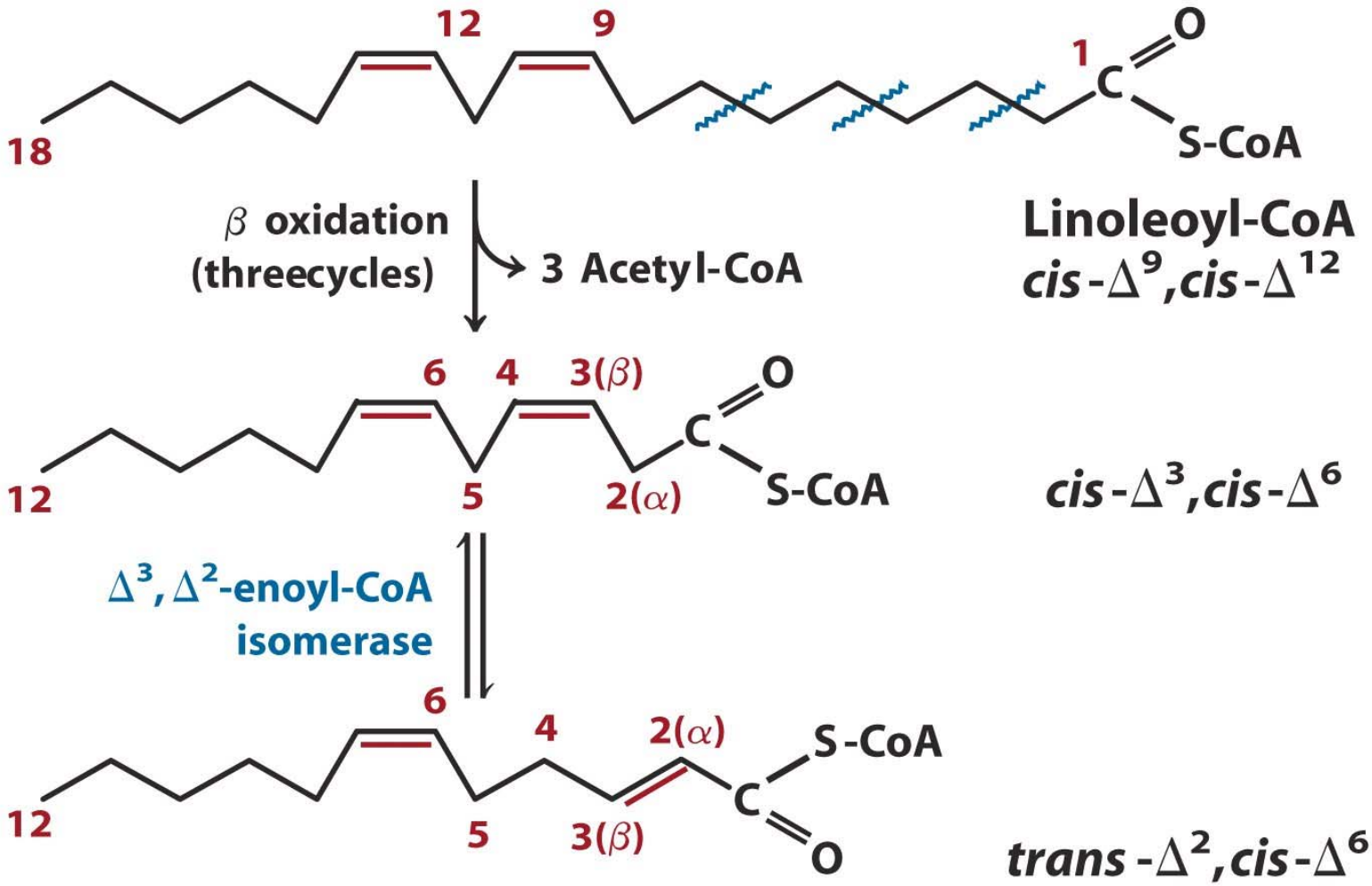
Oxidation of monounsaturated fatty acid

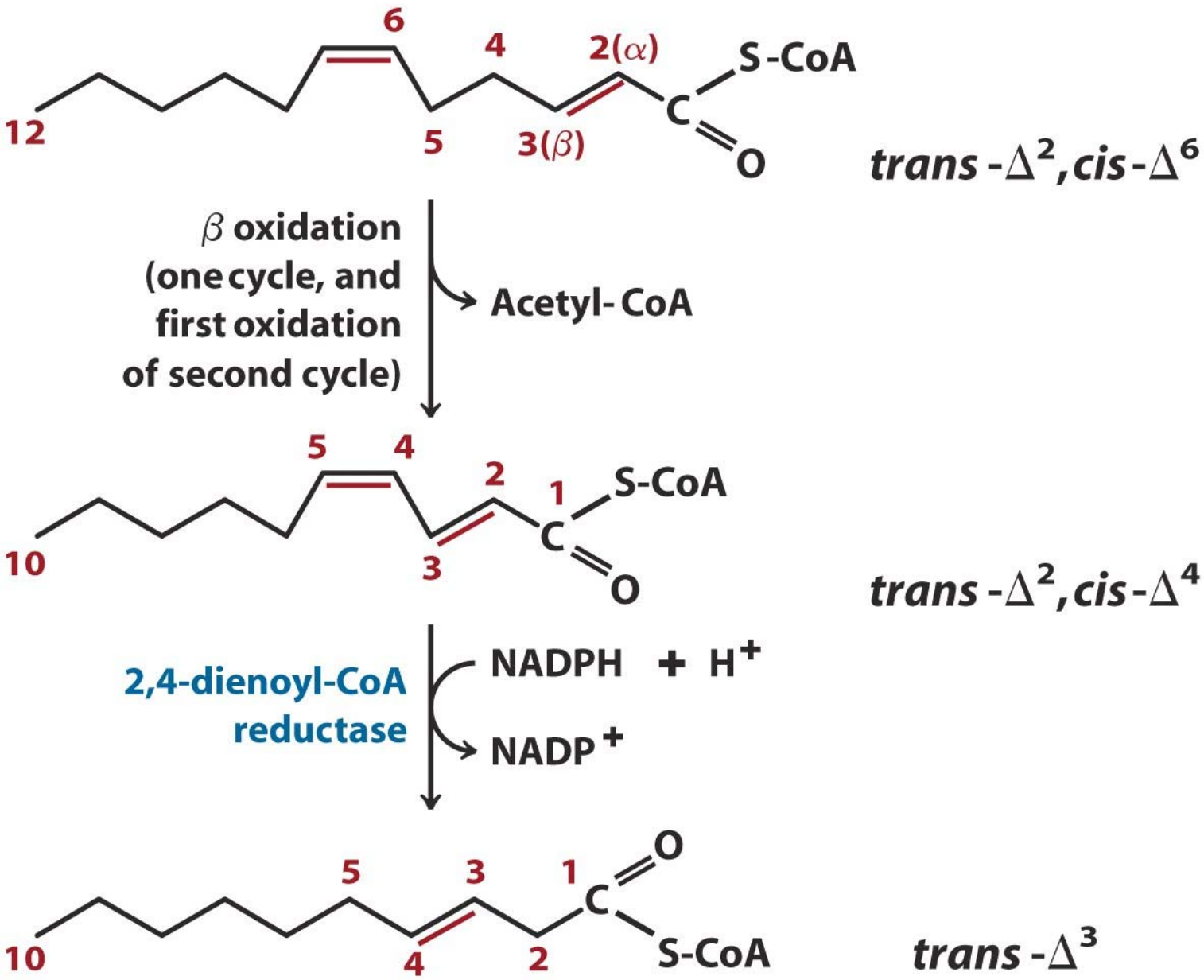


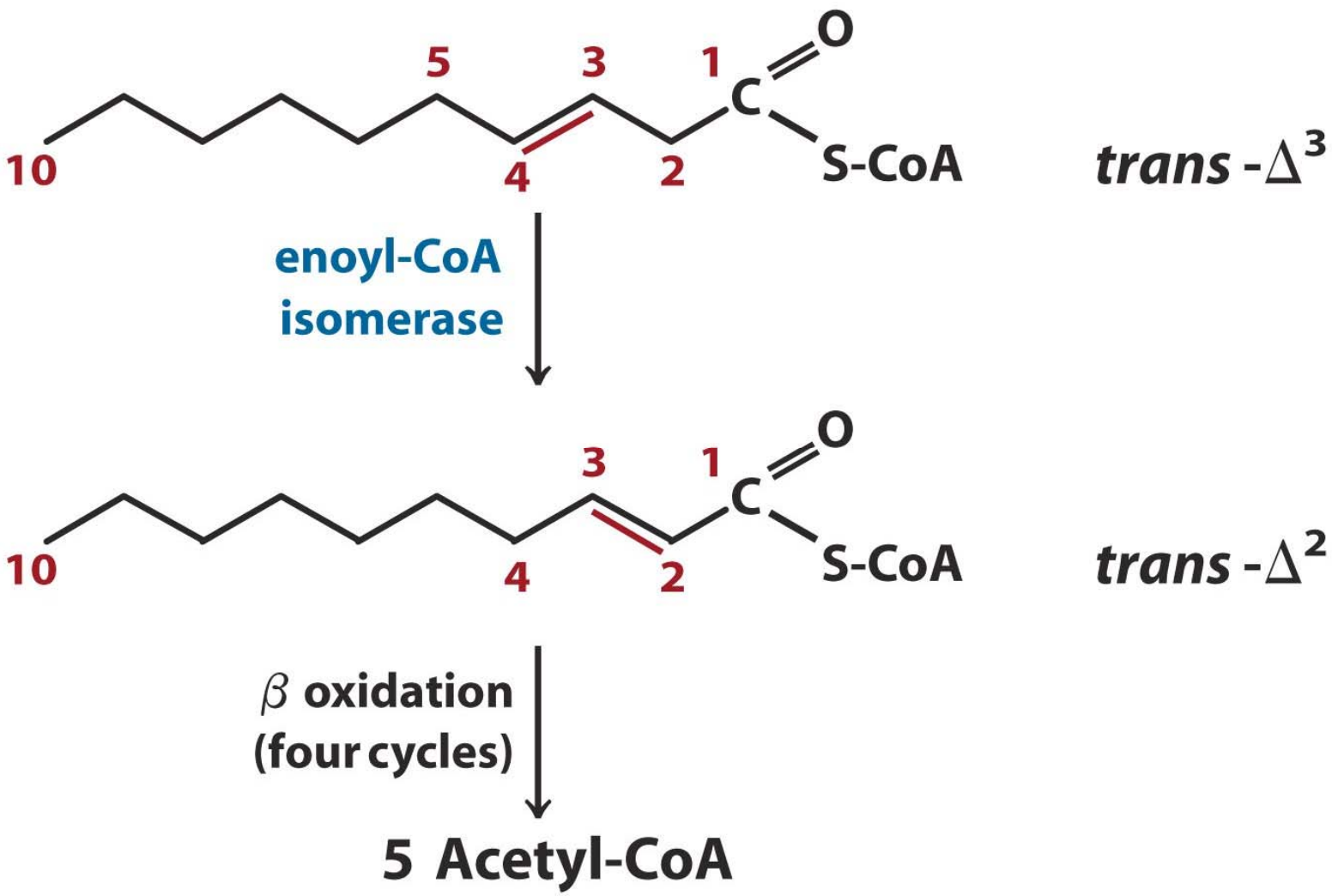
Oxidation of polyunsaturated fatty acid

(Linoleic acid, 18:2$\Delta^{9,12}$)



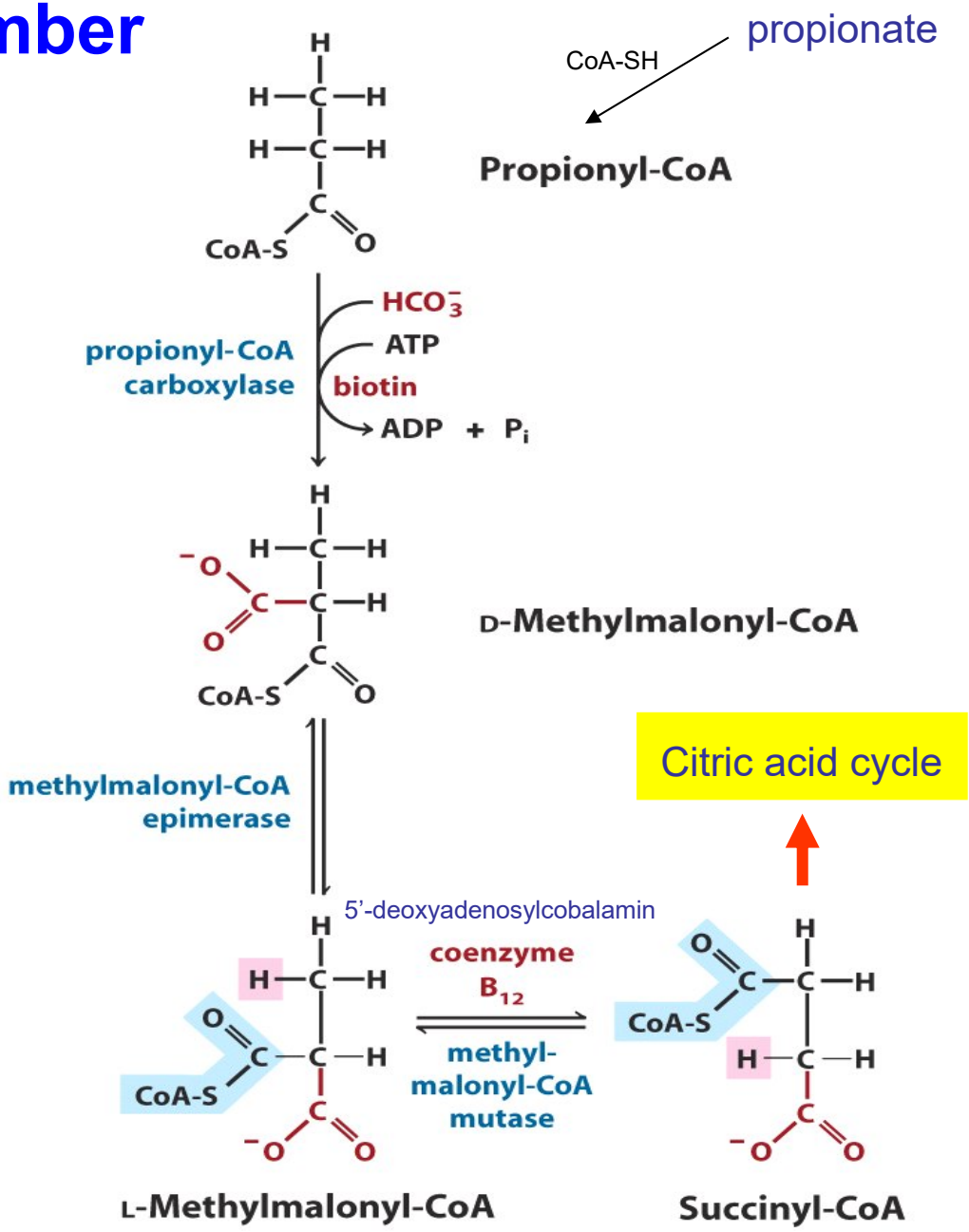

12
9
1
O
C
S-CoA
18
β oxidation
(threecycles)
3 Acetyl-CoA
Linoleoyl-CoA
cis-Δ9,cis-Δ12
6
4
3(β)
O
C
12
5
2(α)
S-CoA
cis-Δ3,cis-Δ6
Δ3, Δ2-enoyl-CoA
isomerase
6
4
2(α)
S-CoA
C
12
5
3(β)
O
trans-Δ2,cis-Δ6


6
4
2(α)
S-CoA
12
5
3(β)
C
O
trans -Δ2, cis -Δ6
β oxidation
(one cycle, and
first oxidation
of second cycle)
Acetyl- CoA
5
4
2
1
S-CoA
10
3
C
O
trans -Δ2, cis -Δ4
2,4-dienoyl-CoA
reductase
NADPH + H+
NADP+
5
3
1
O
10
4
2
C
S-CoA
trans -Δ3


10
5
4
3
2
1
C
O
S-CoA
trans -Δ3
enoyl-CoA
isomerase
10
4
3
2
1
C
O
S-CoA
trans -Δ2
β oxidation
(four cycles)
5 Acetyl-CoA

Oxidation of odd-number fatty acid

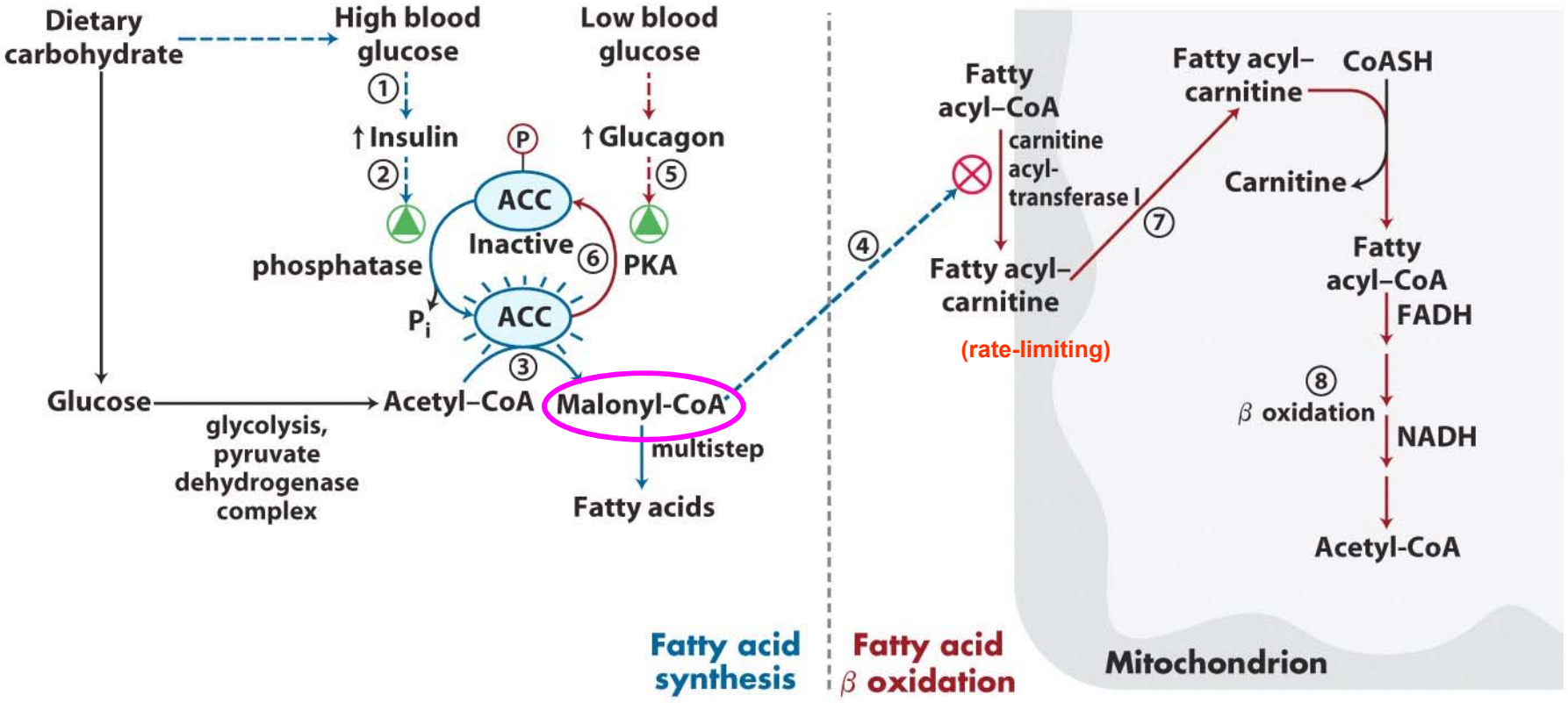
(in the lipids of many plants
and some marine organisms)



* Pernicious anemia
(intrinsic factor ↓)

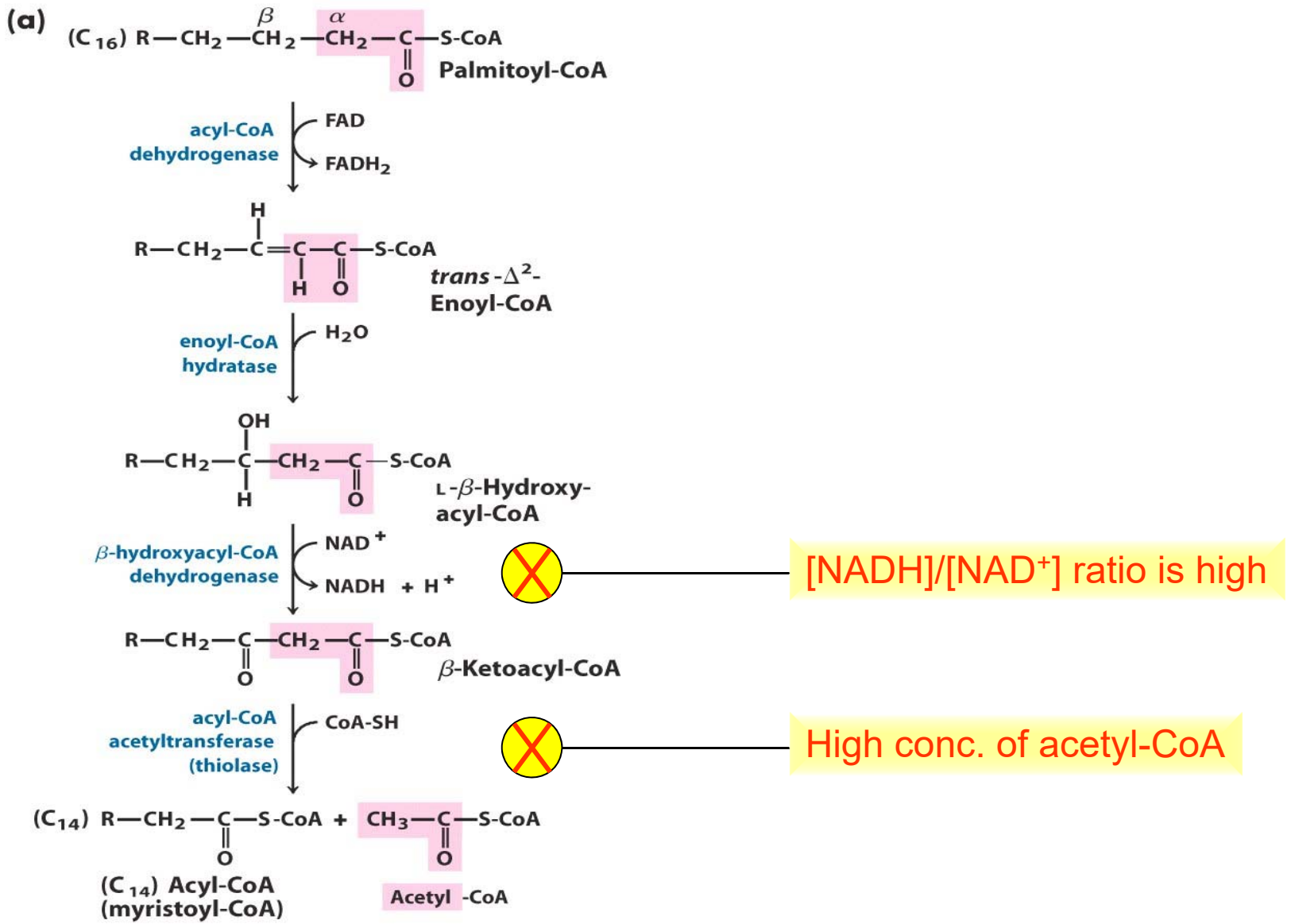
Coordinated regulation of fatty acid synthesis and breakdown

TAG or phospholipids ← Fatty acyl-CoA → β-oxidation



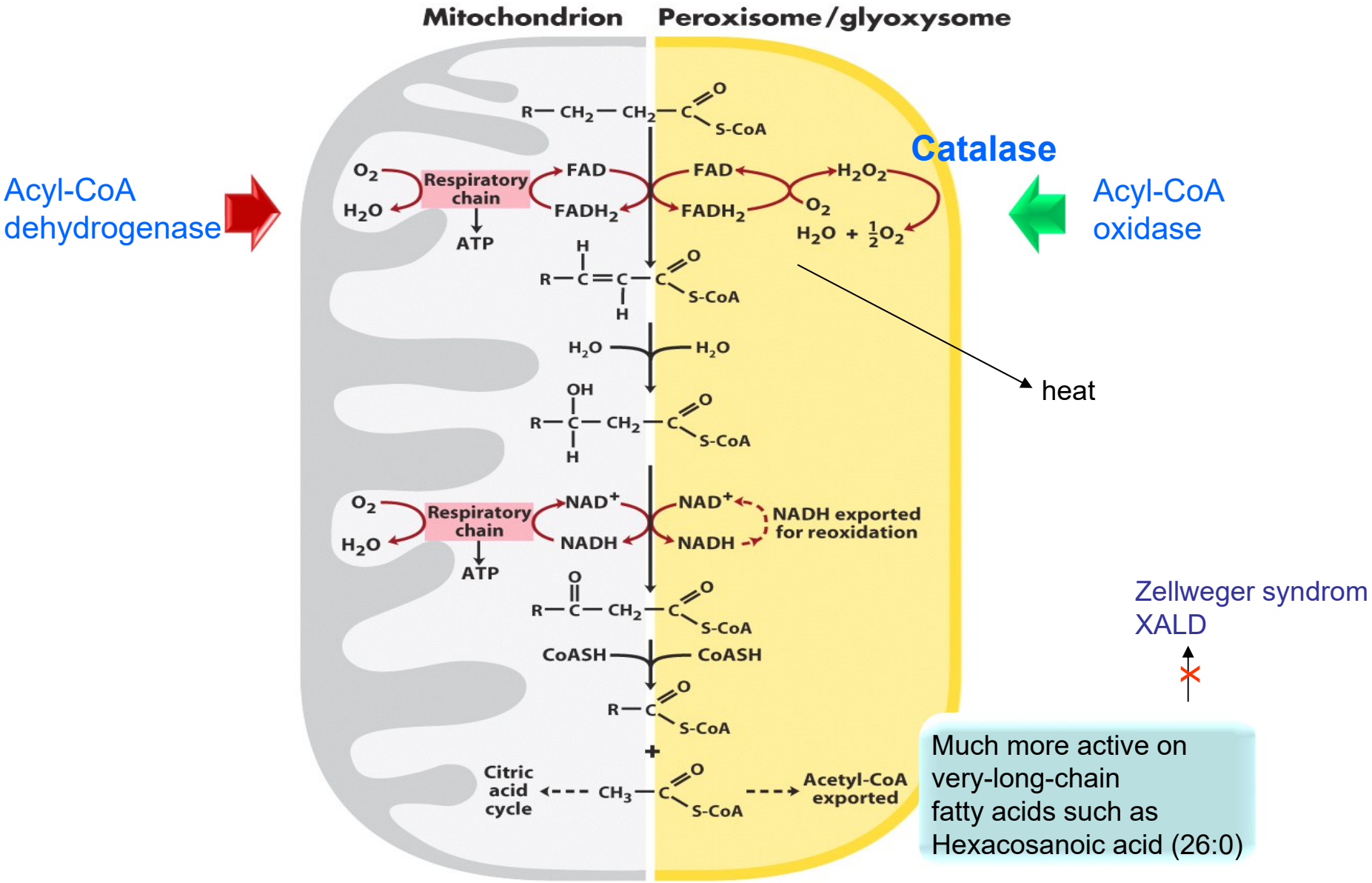
ACC : acetyl-CoA caboxylase

Two inhibition steps for β-oxidation



Peroxisome also carry out β-oxidation

(major site of β-oxidation in plant)



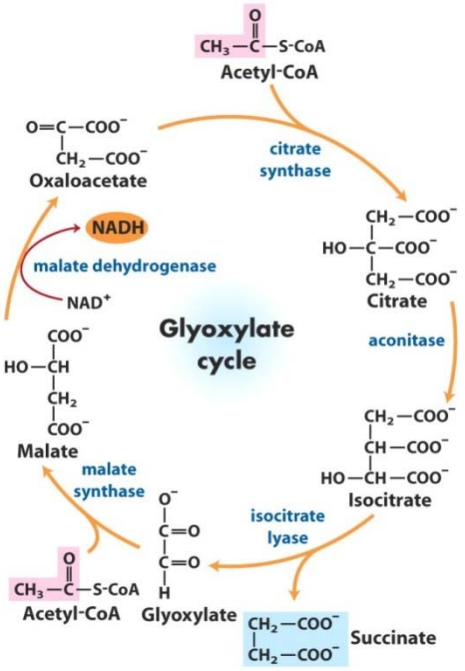
Triacylglycerols as glucose source in seeds

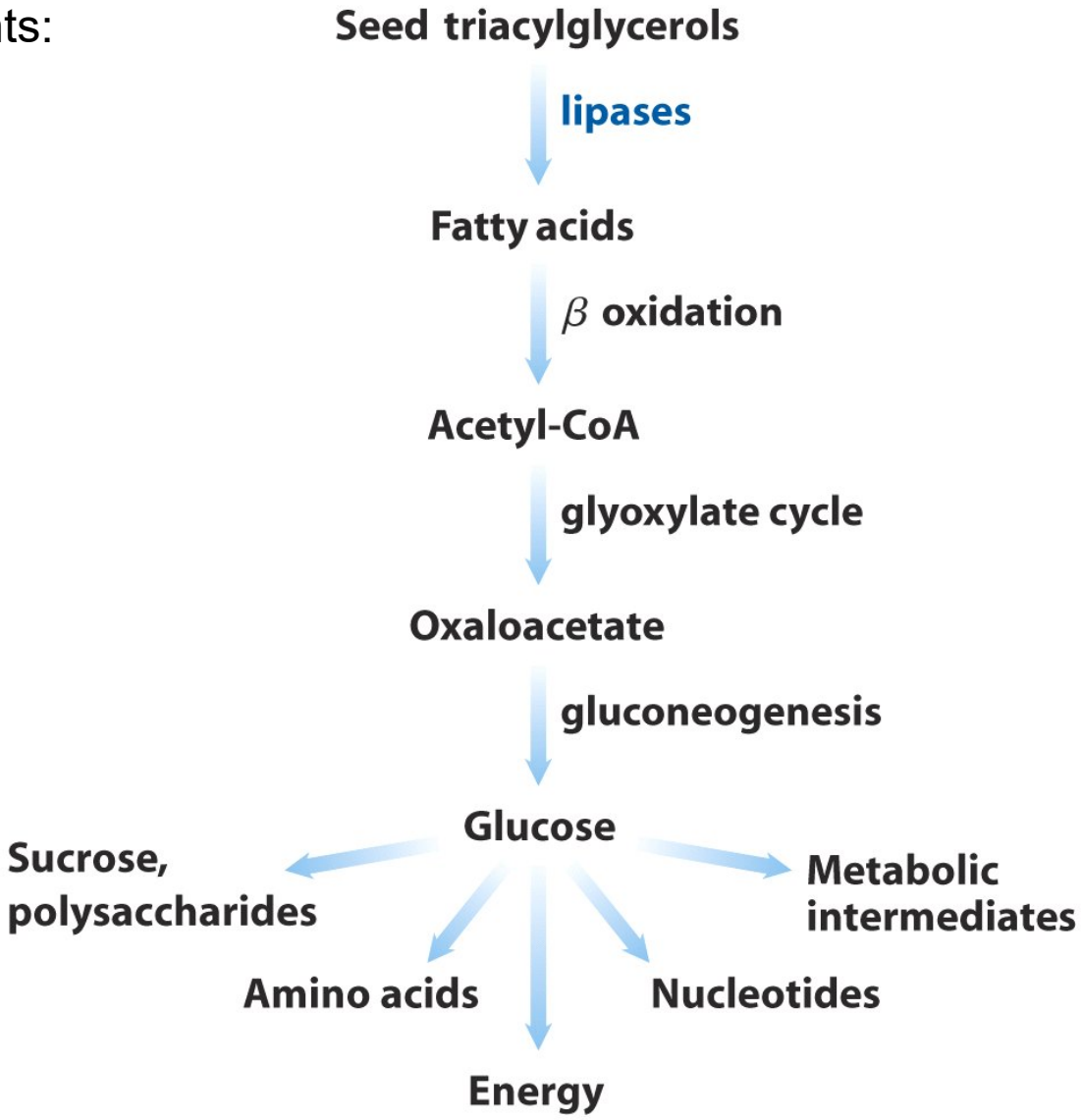
Fatty acid oxidation in plants:

not in mitochondria

but in the peroxisomes

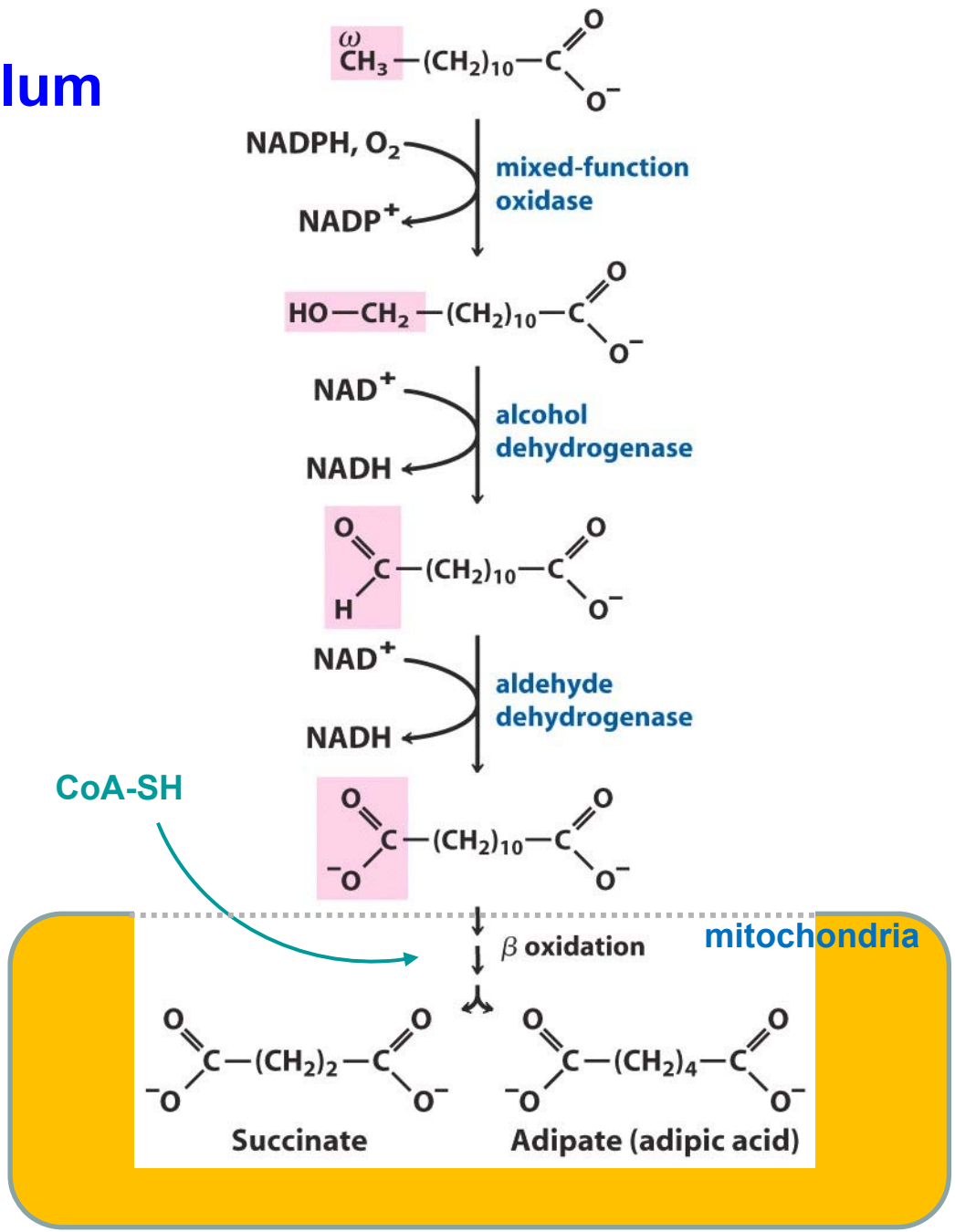
(and the glyoxysomes of germinating seeds)





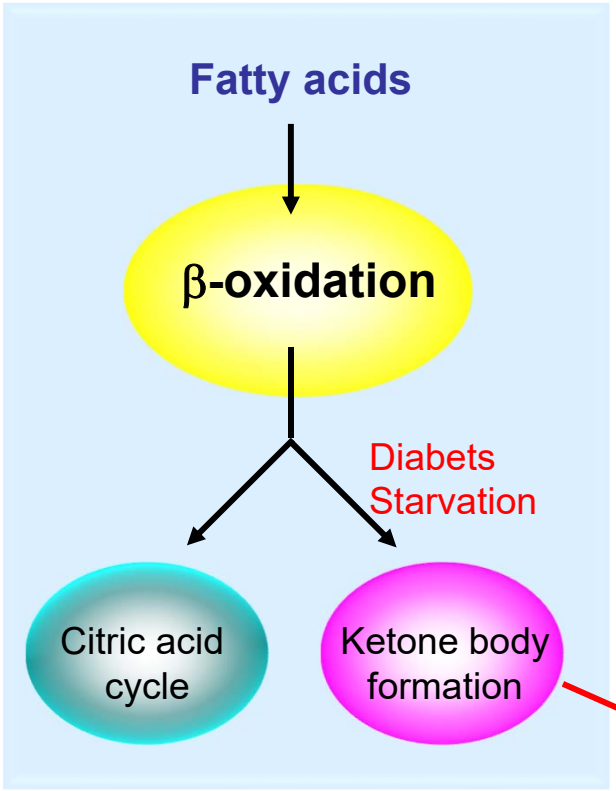
ω-oxidation
in the endoplasmic reticulum
(liver and kidney in animal)

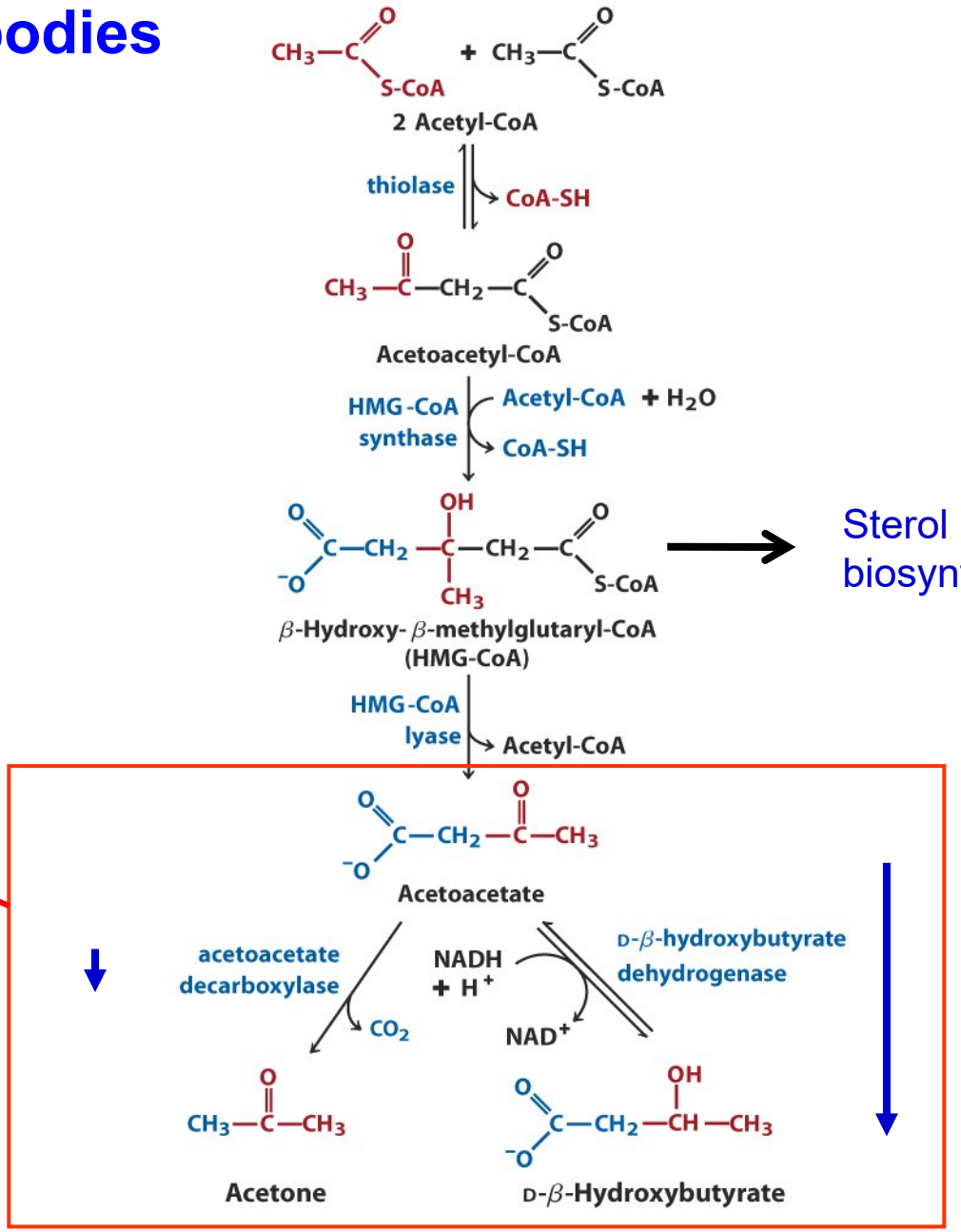
(10:0 or 12:0)



α-oxidation:
- branched-chain fatty acids
- in peroxisome of animal cells

Formation of ketone bodies from acetyl-CoA

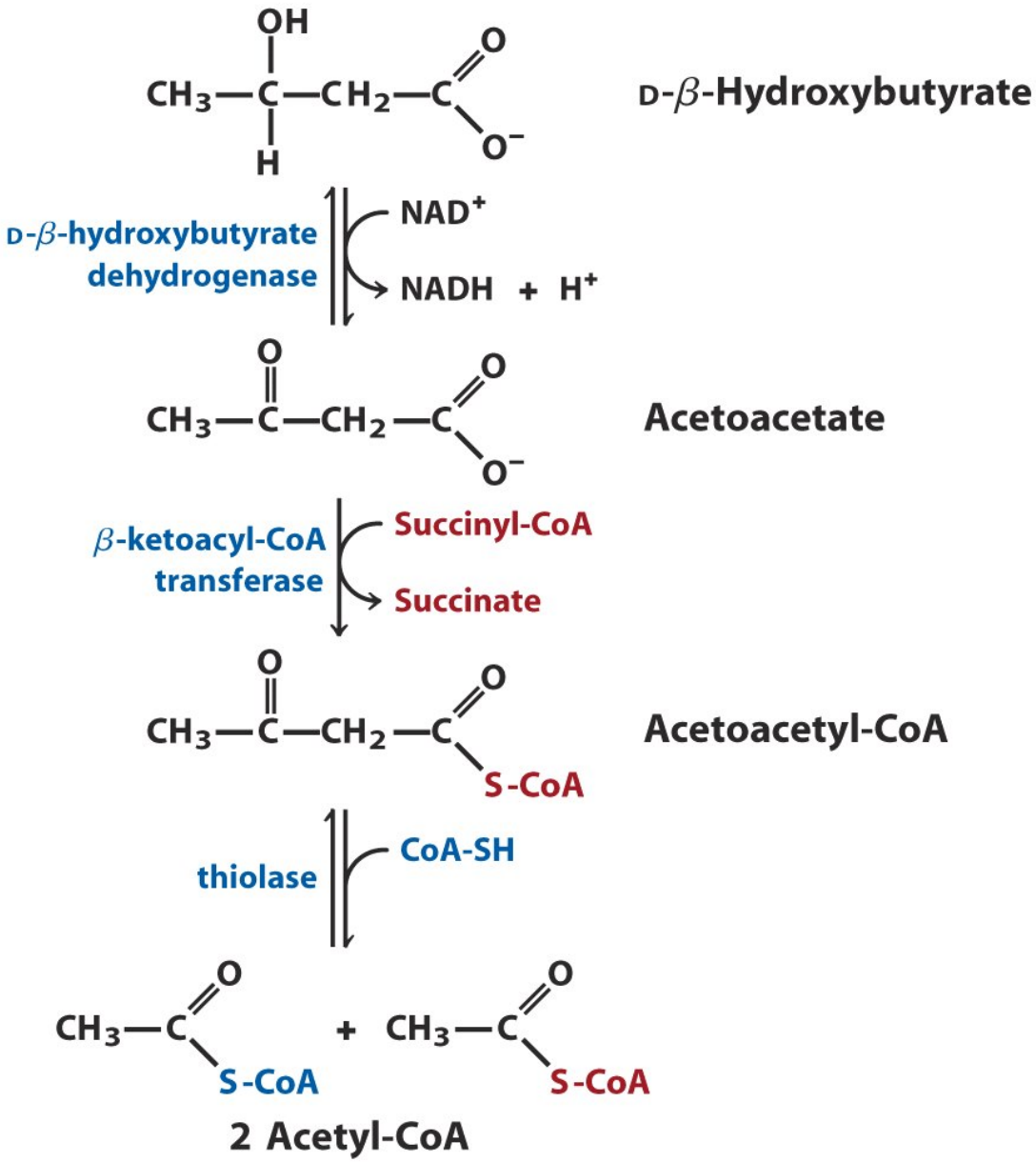




Sterol biosynthesis

β-Hydroxybutyrate as a fuel

(in extrahepatic tissues)



Ketone body formation and export from the liver

Acidosis

Ketosis

90 mg/100 ml in blood
(<3 mg/100 ml)
5000 mg/24 h urinary excretion
(<125 mg/24 h)