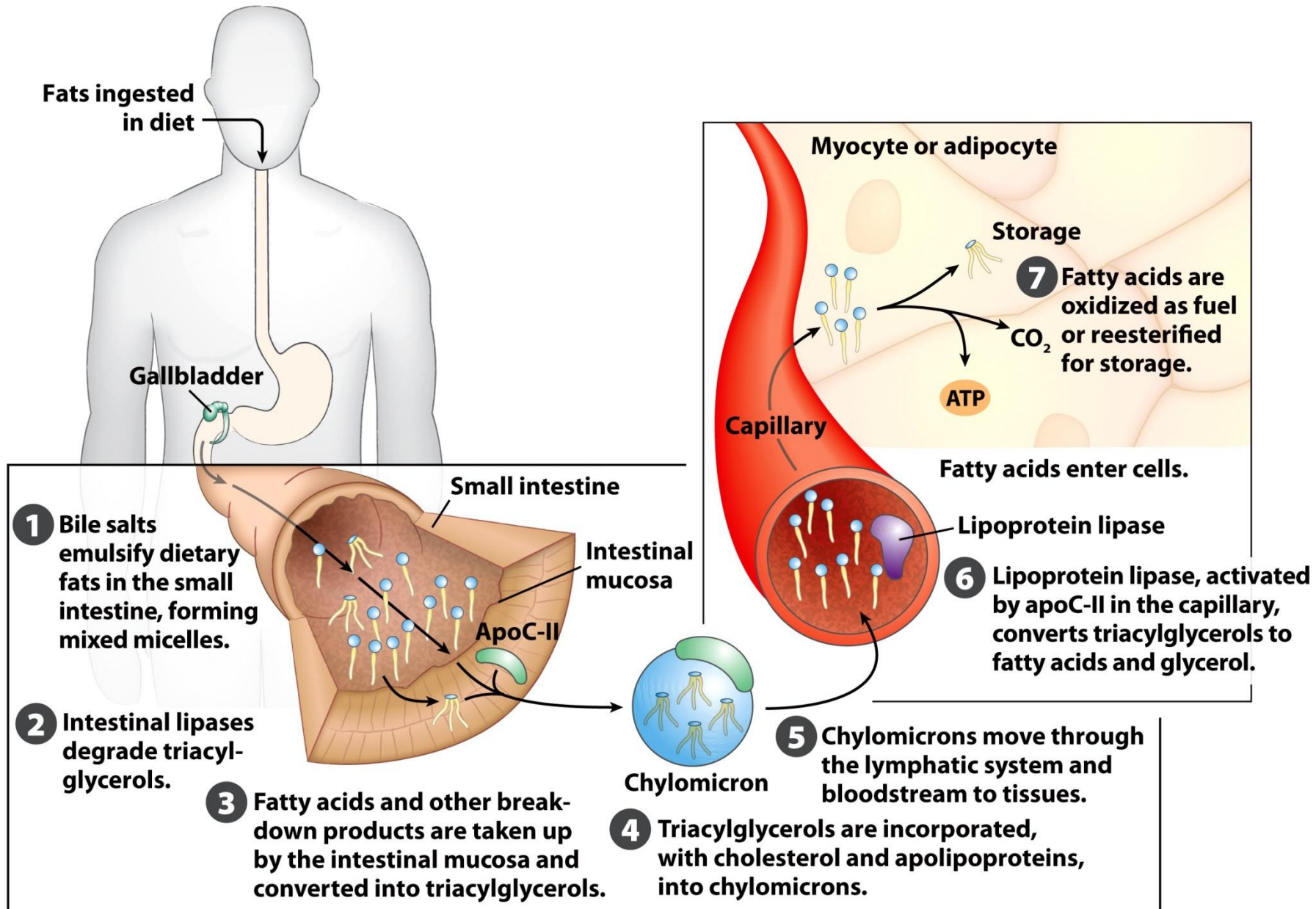
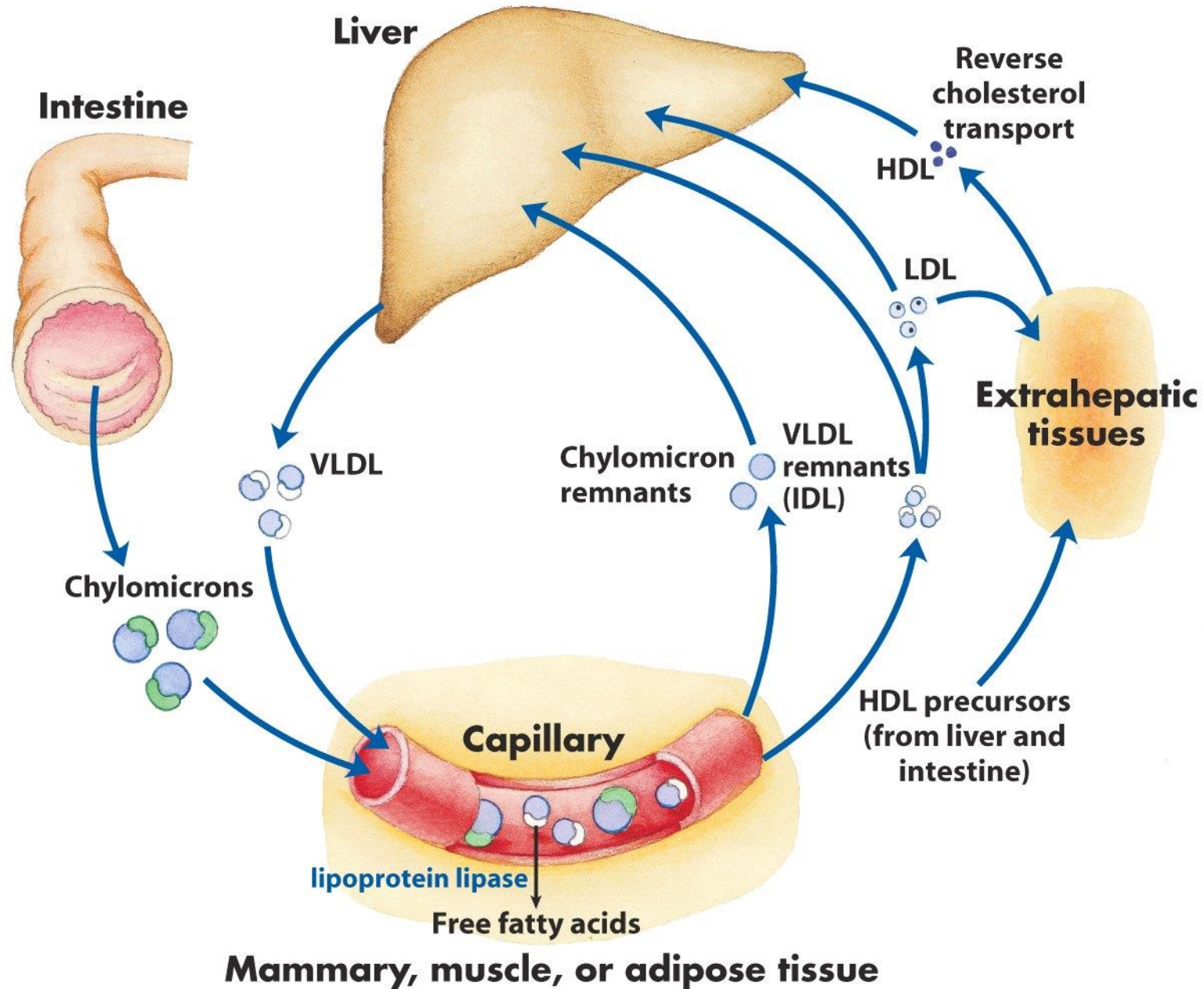


## Lipid metabolism I.

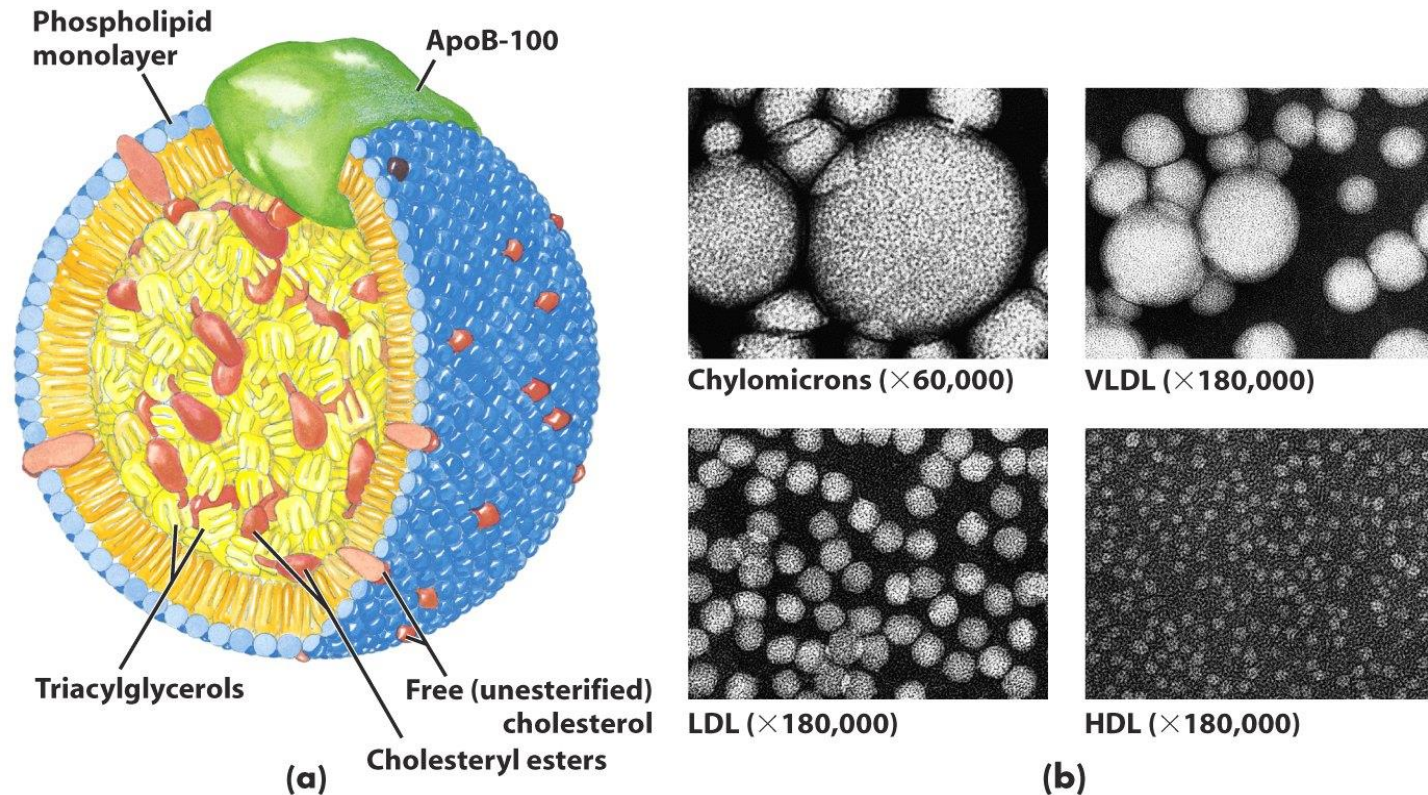
# Processing of dietary lipids



# Lipid and cholesterol transport



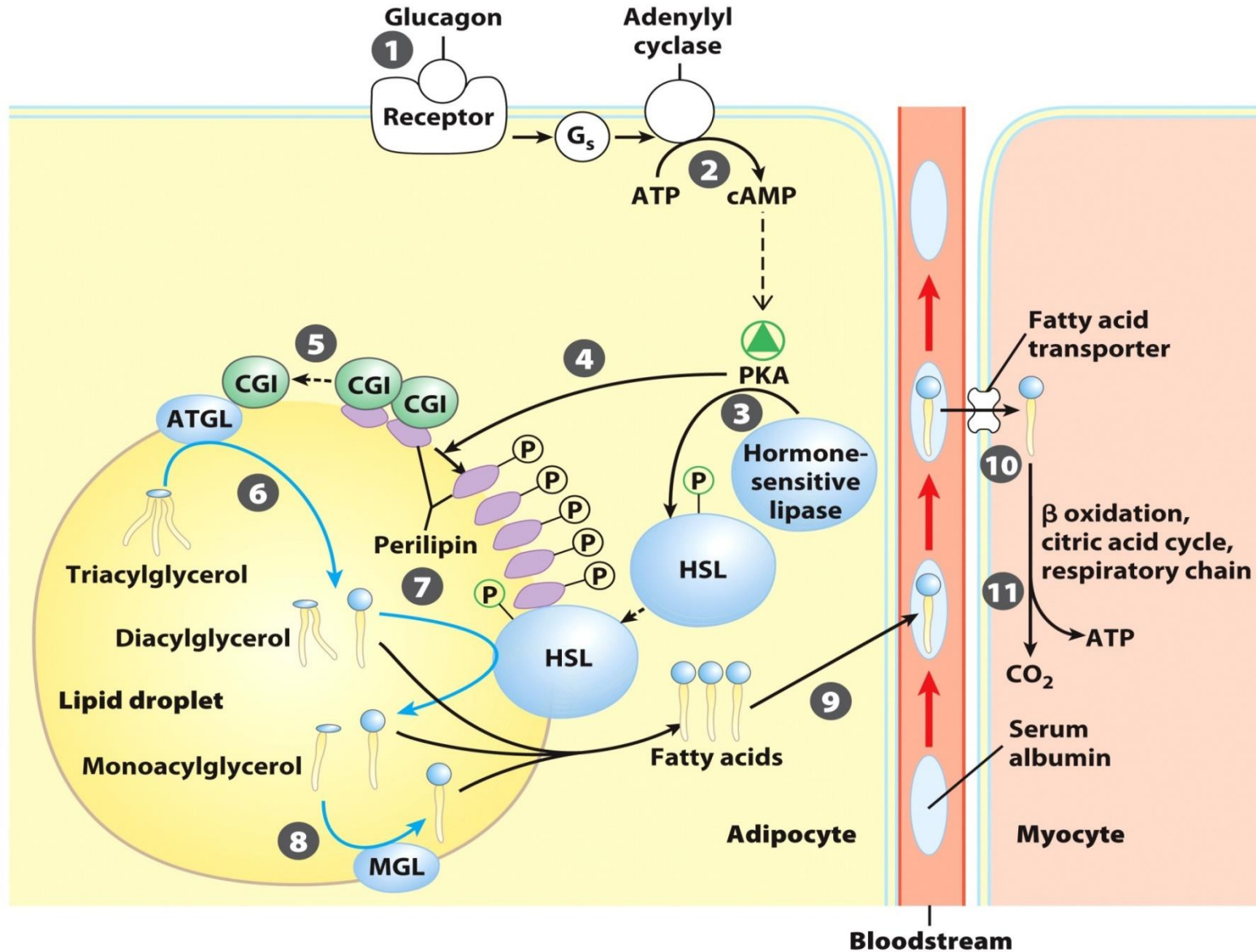
# Major classes of human plasma lipoproteins



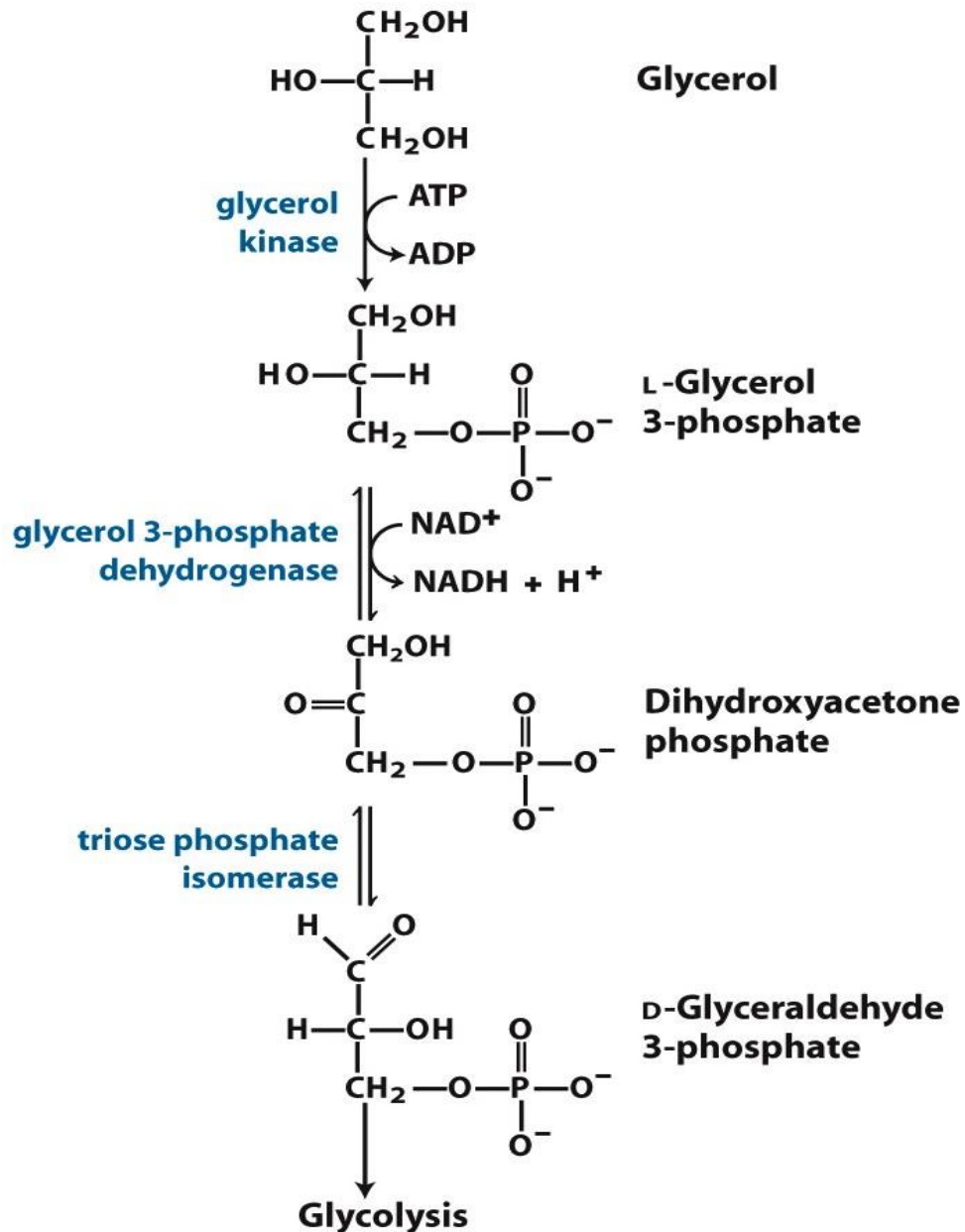
**TABLE 21-2** Major Classes of Human Plasma Lipoproteins: Some Properties

Lipoprotein	Density (g/mL)	Composition (wt %)				
		Protein	Phospholipids	Free cholesterol	Cholesteryl esters	Triacylglycerols
Chylomicrons	<1.006	2	9	1	3	85
VLDL	0.95-1.006	10	18	7	12	50
LDL	1.006-1.063	23	20	8	37	10
HDL	1.063-1.210	55	24	2	15	4

# Mobilization of triacylglycerols

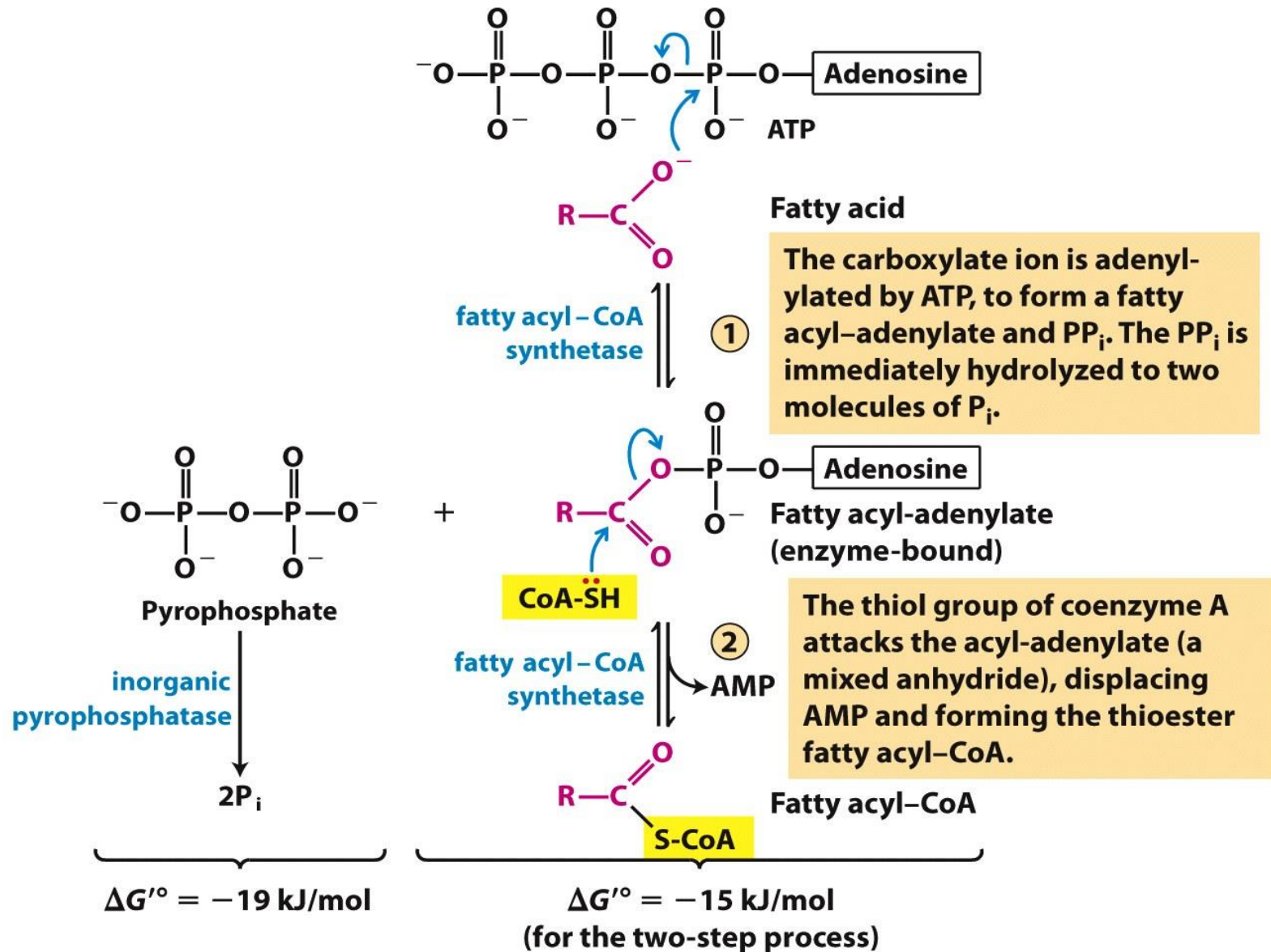


# Entry of glycerol into glycolysis

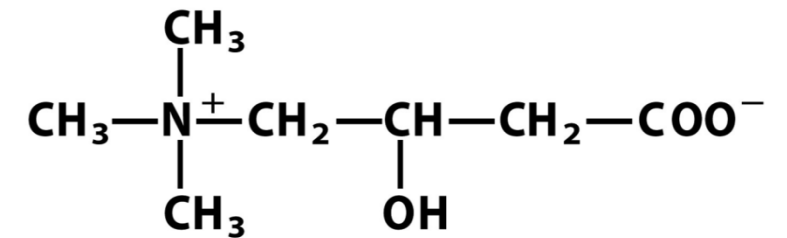
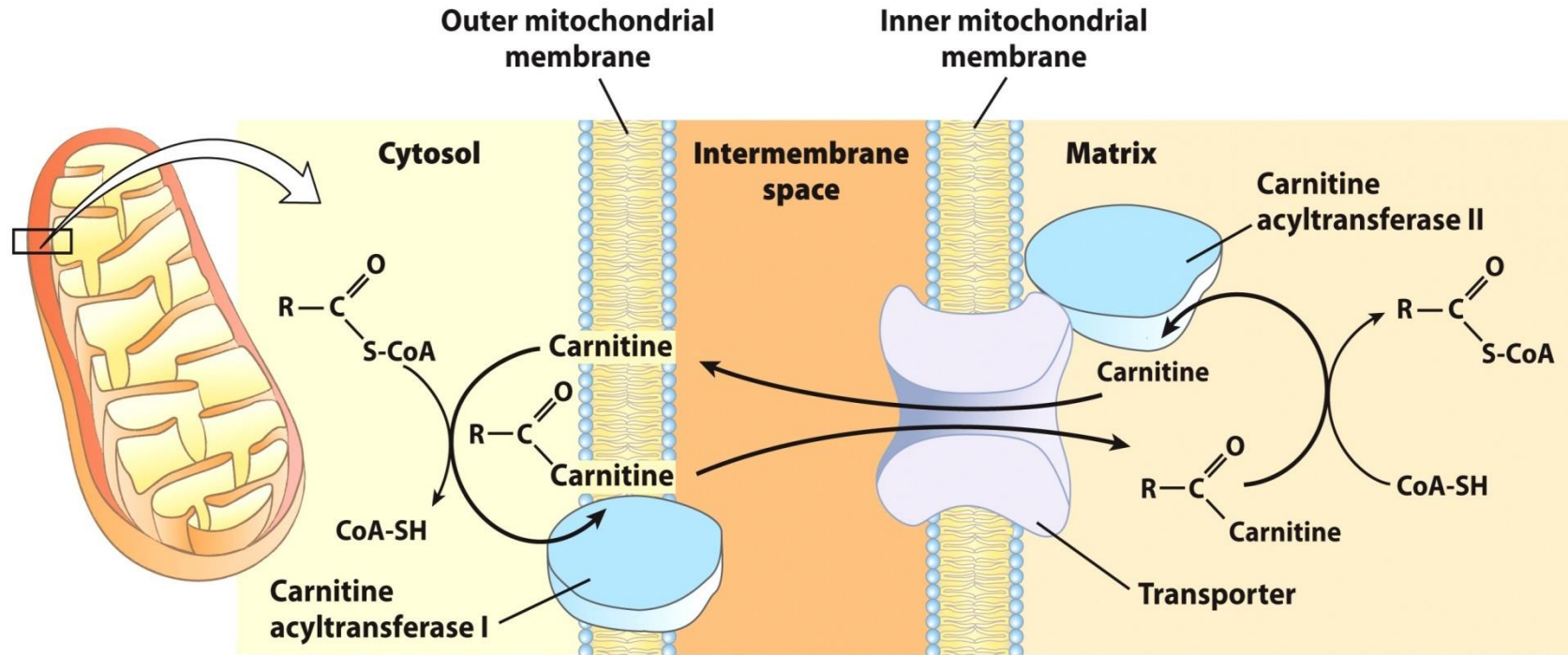


About 95% of the biologically available energy of triacylglycerols resides in their three long-chain fatty acids; only 5% is contributed by the glycerol moiety.

# Activation of fatty acids

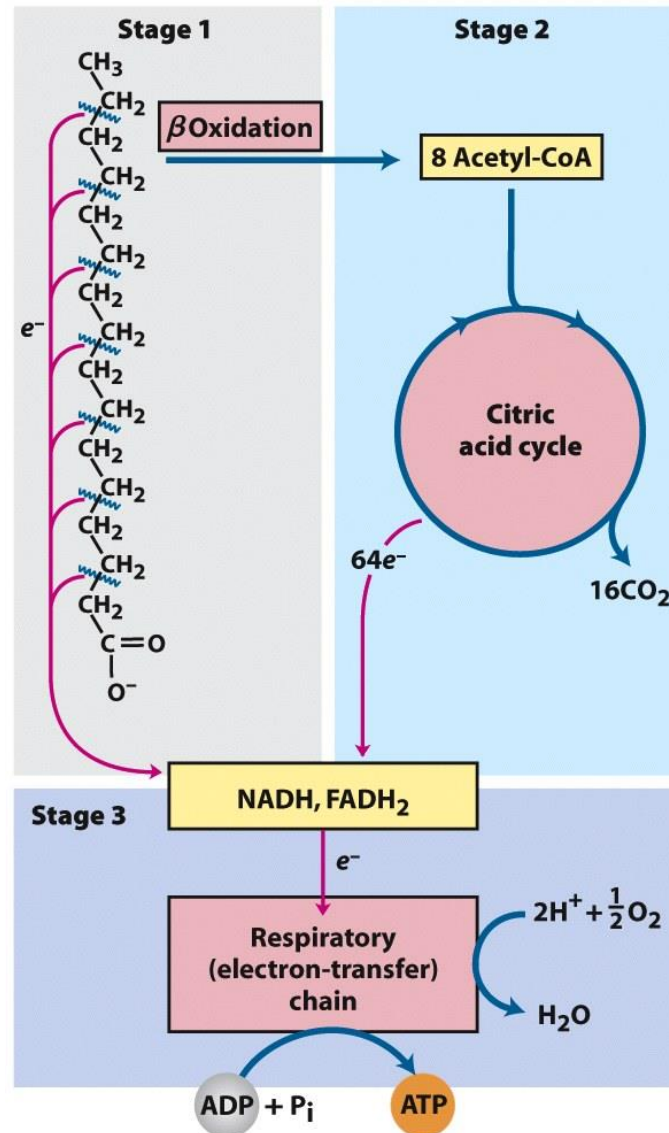


# Fatty acid entry into mitochondrion



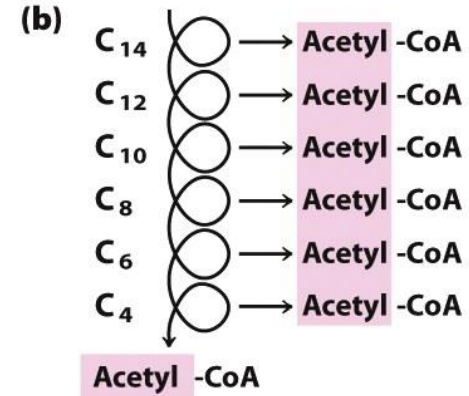
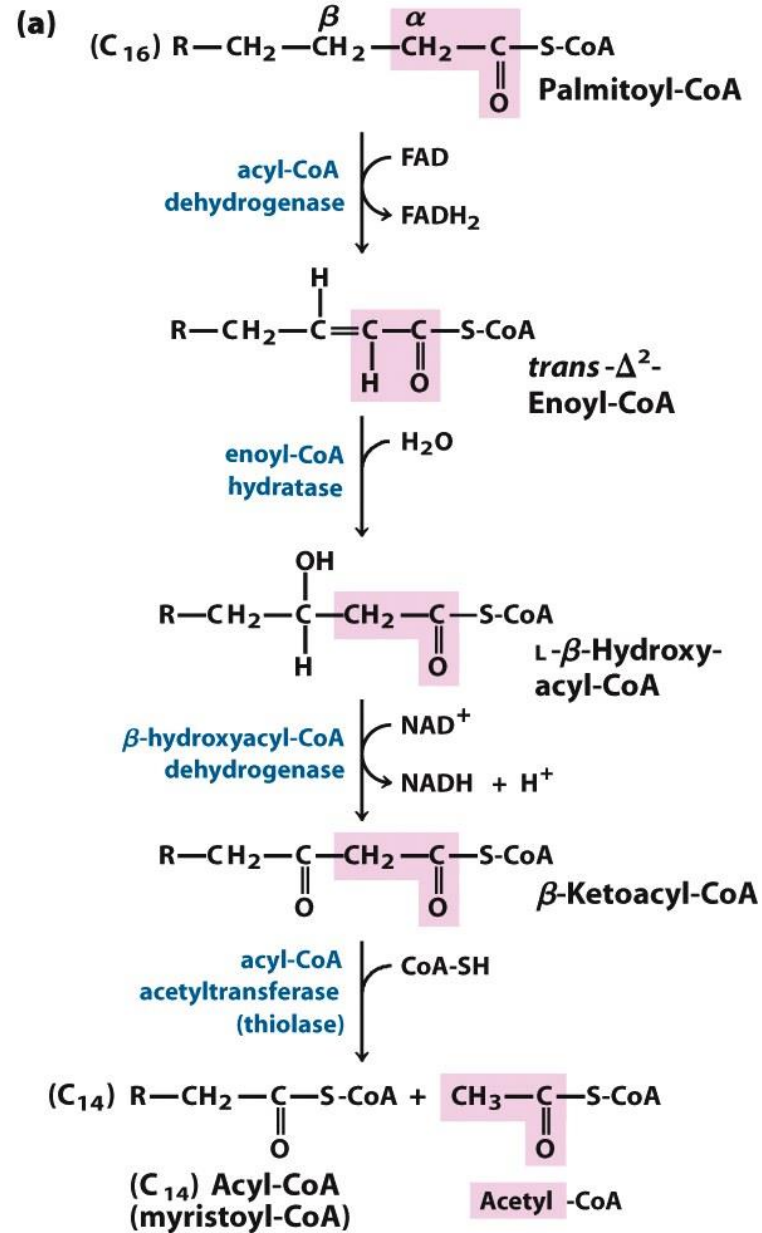
**Carnitine**

# Stages of fatty acid oxidation



**Figure 17-7**  
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# Reactions of $\beta$ -oxidation



# ATP yield of palmitoyl-CoA oxidation



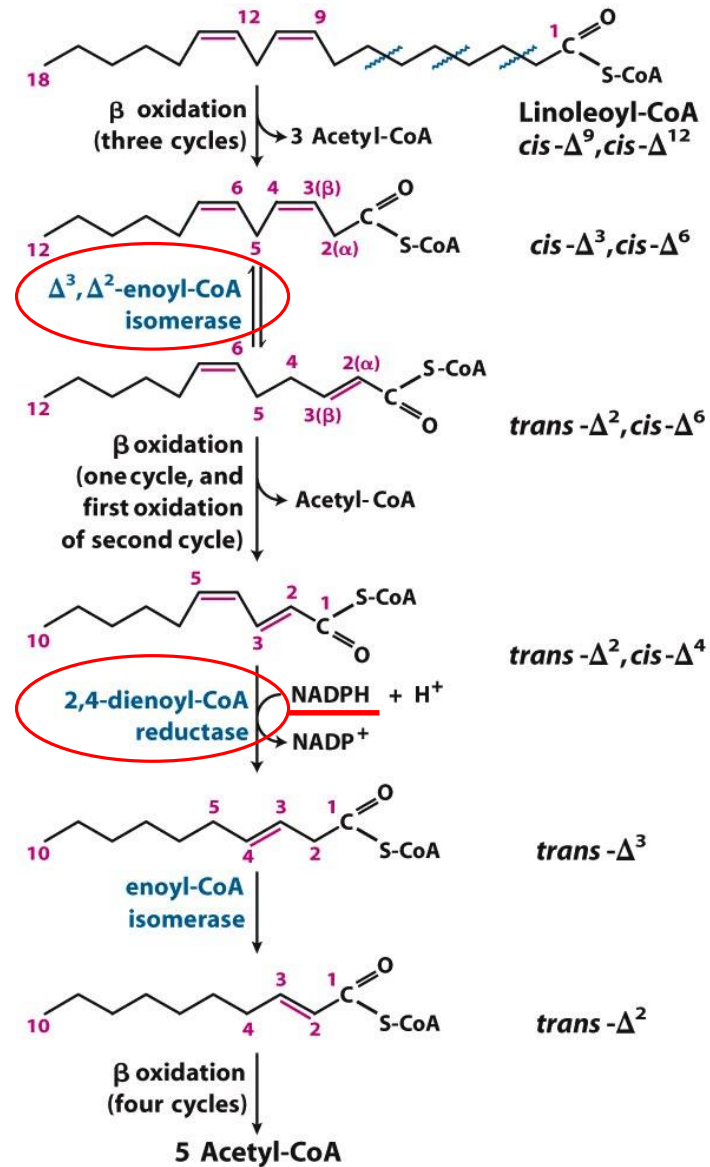
<b>TABLE 17–1    Yield of ATP during Oxidation of One Molecule of Palmitoyl-CoA to CO<sub>2</sub> and H<sub>2</sub>O</b>		
<b>Enzyme catalyzing the oxidation step</b>	<b>Number of NADH or FADH<sub>2</sub> formed</b>	<b>Number of ATP ultimately formed*</b>
Acyl-CoA dehydrogenase	7 FADH <sub>2</sub>	10.5
β-Hydroxyacyl-CoA dehydrogenase	7 NADH	17.5
Isocitrate dehydrogenase	8 NADH	20
α-Ketoglutarate dehydrogenase	8 NADH	20
Succinyl-CoA synthetase		8 <sup>†</sup>
Succinate dehydrogenase	8 FADH <sub>2</sub>	12
Malate dehydrogenase	8 NADH	20
<b>Total</b>		<b>108</b>

\*These calculations assume that mitochondrial oxidative phosphorylation produces 1.5 ATP per FADH<sub>2</sub> oxidized and 2.5 ATP per NADH oxidized.

<sup>†</sup>GTP produced directly in this step yields ATP in the reaction catalyzed by nucleoside diphosphate kinase (p. 510).

The energetic cost of activating a fatty acid is equivalent to two ATP, and the net gain per molecule of palmitate is 106 ATP.

# Oxidation of polyunsaturated fatty acids



# Oxidation of odd-number fatty acids

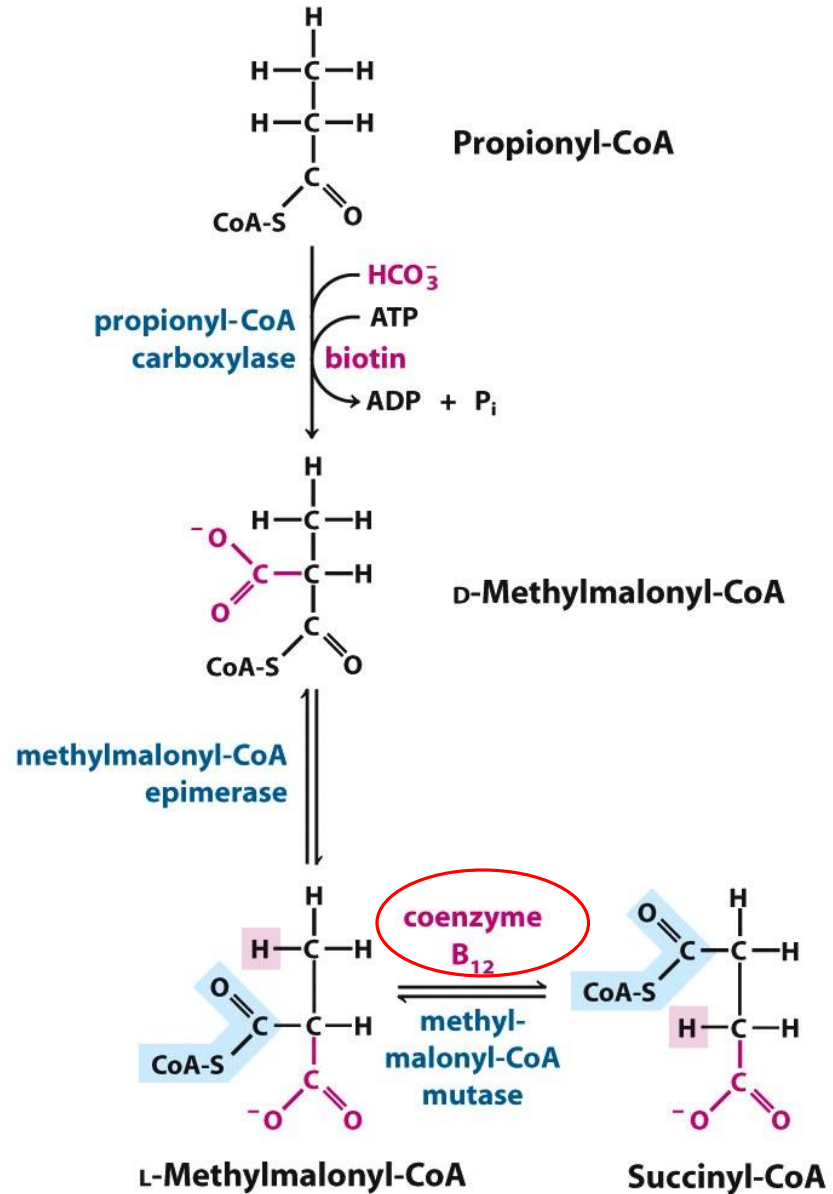


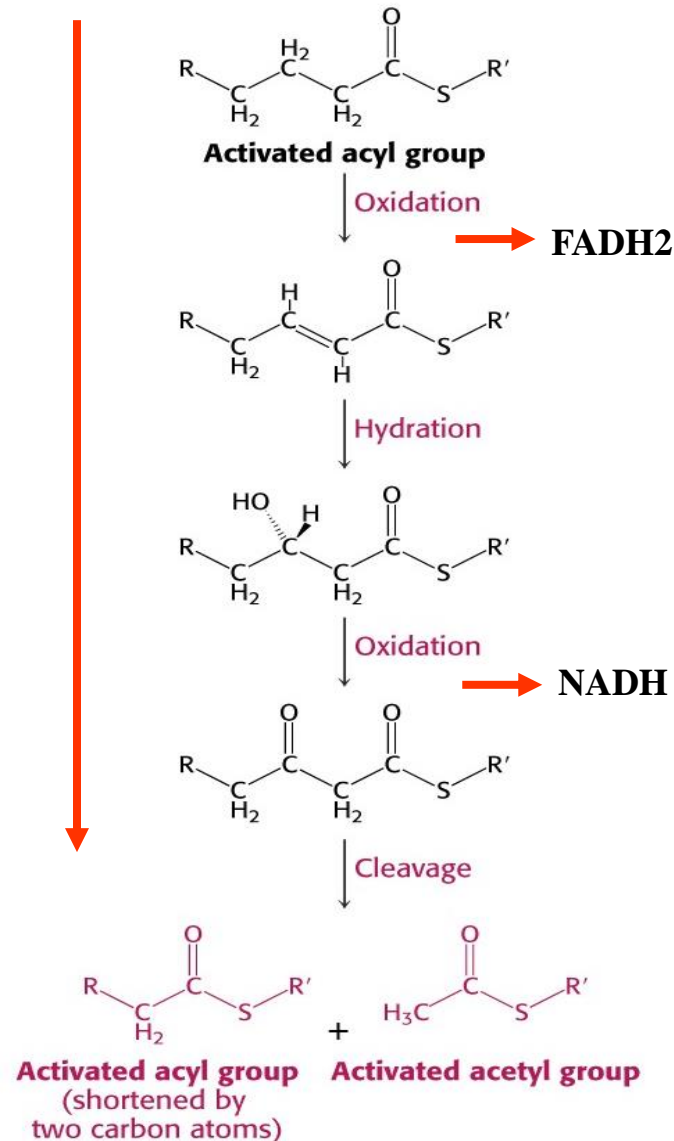
Figure 17-11

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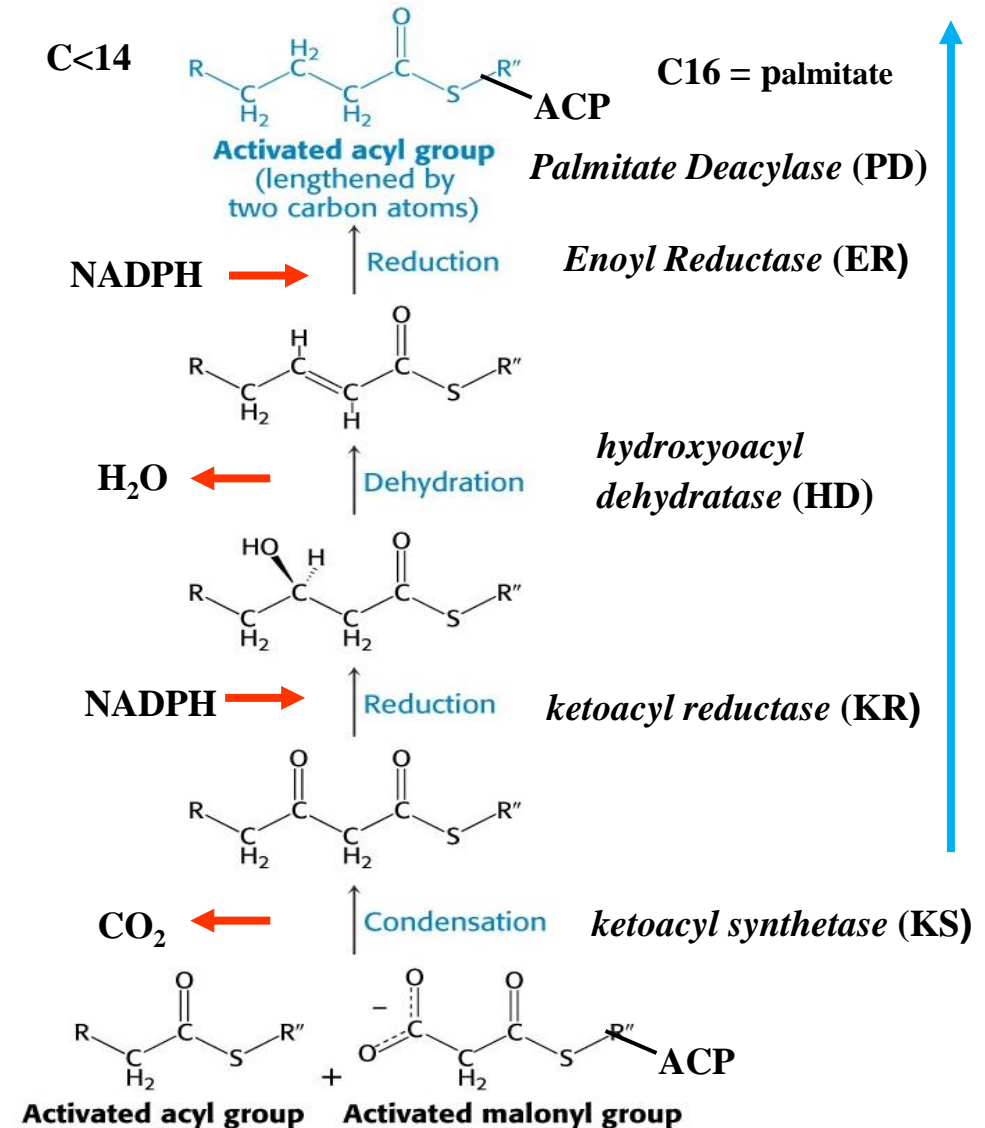
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# Comparison of fatty acid oxidation and synthesis

## FATTY ACID DEGRADATION

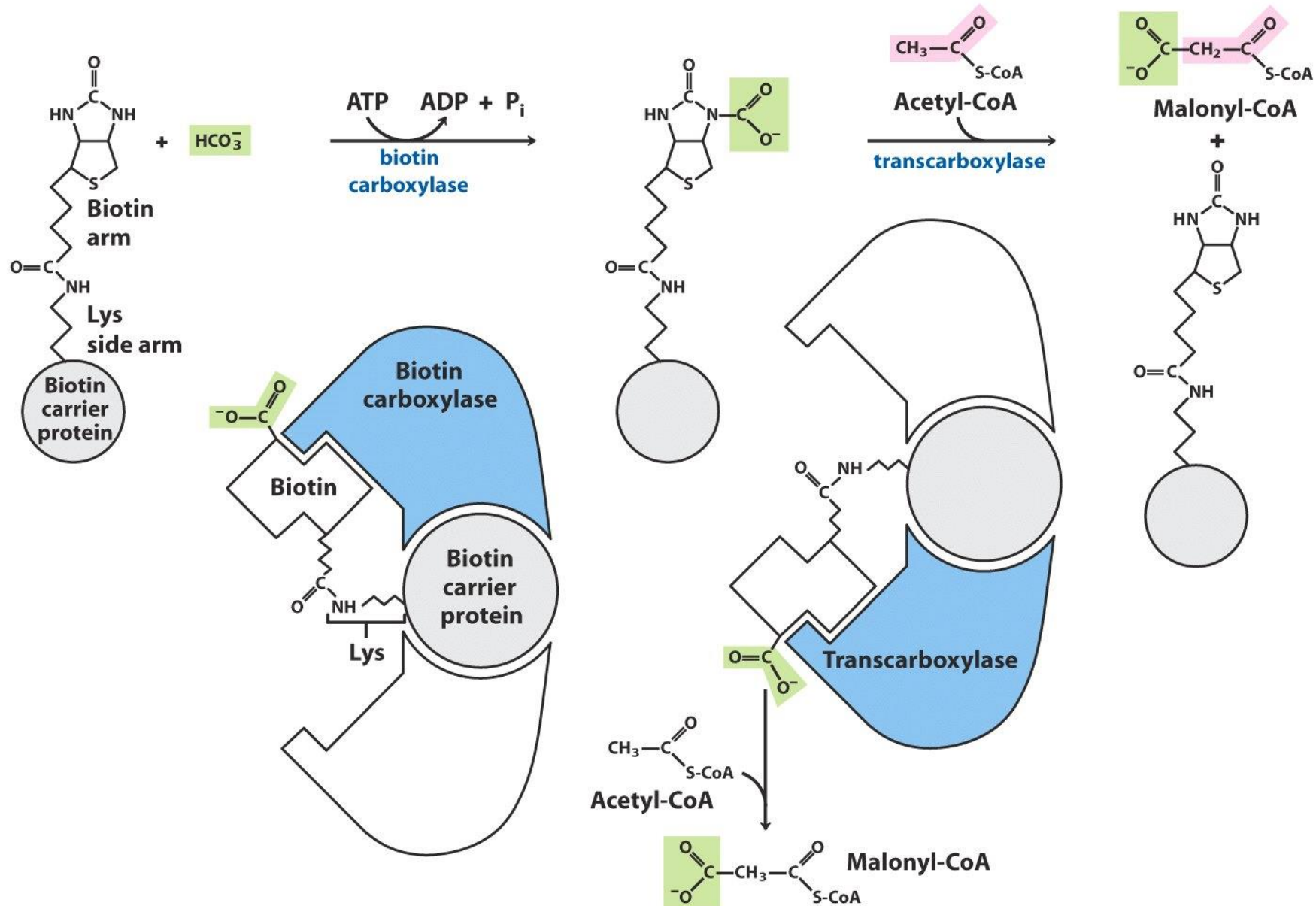


## FATTY ACID SYNTHESIS

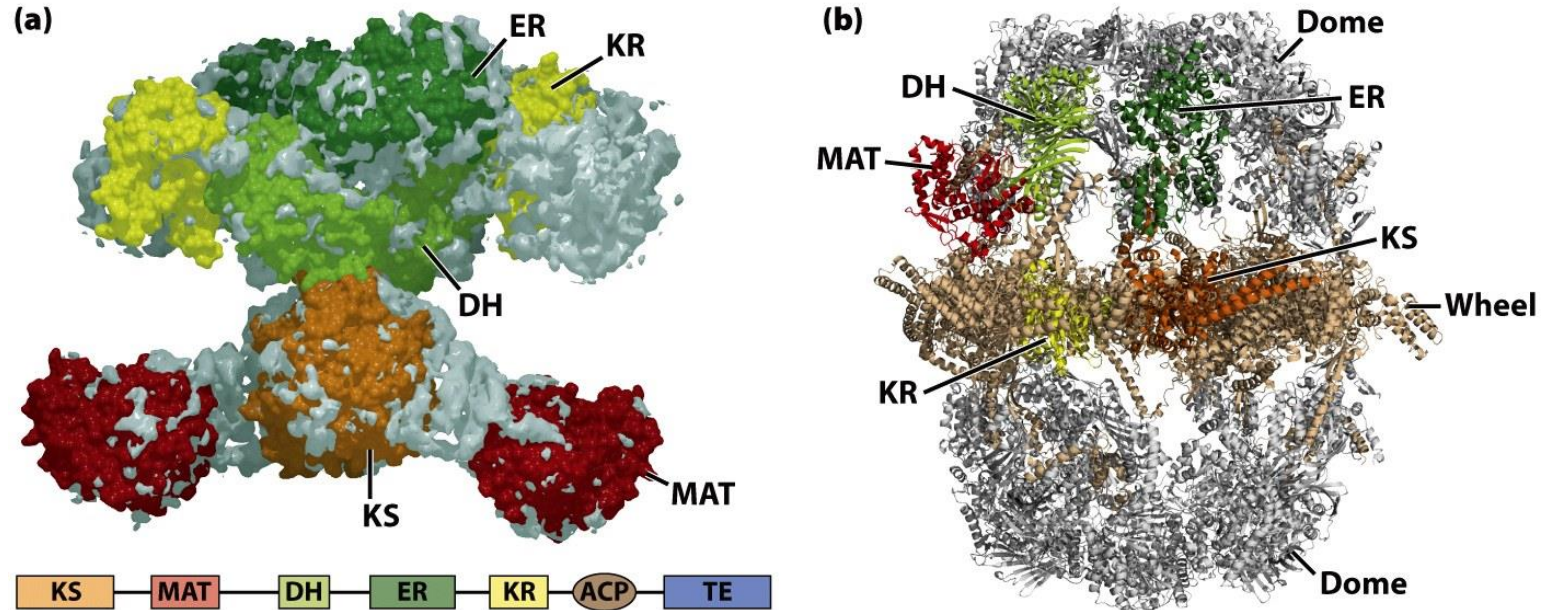


# Synthesis of malonyl-CoA:

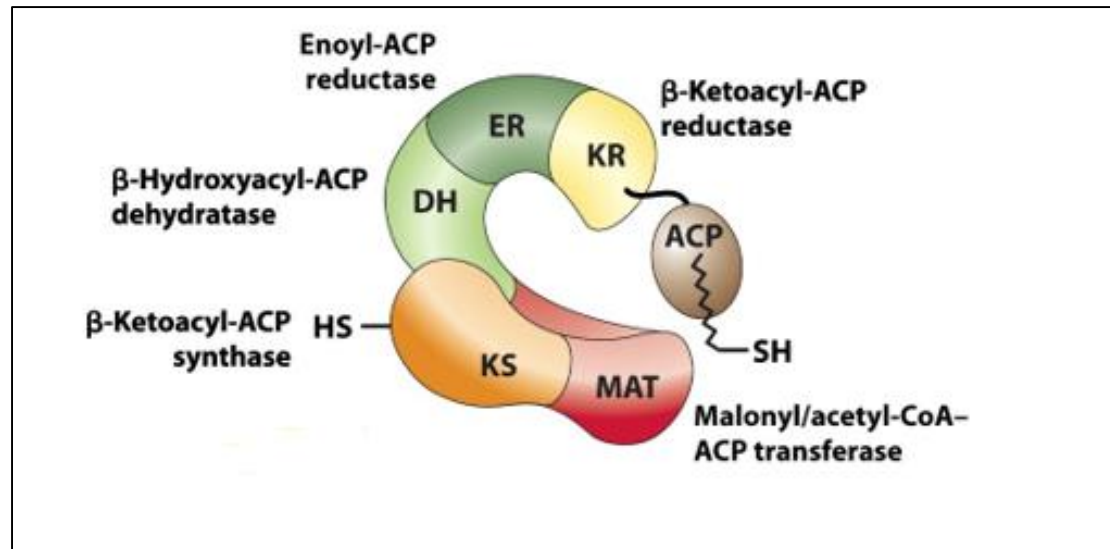
## Acetyl-CoA carboxylase reaction



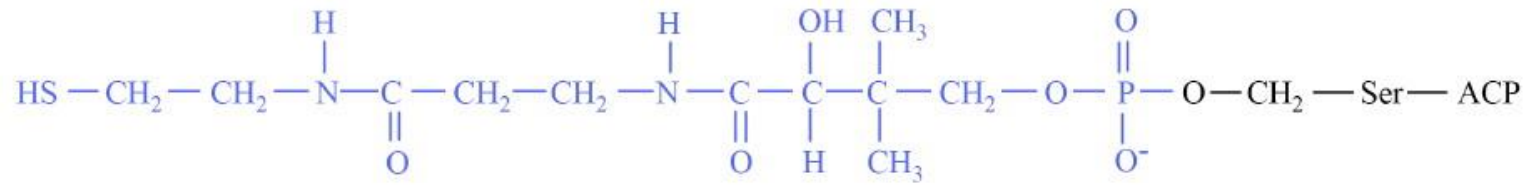
# Fatty acid synthase



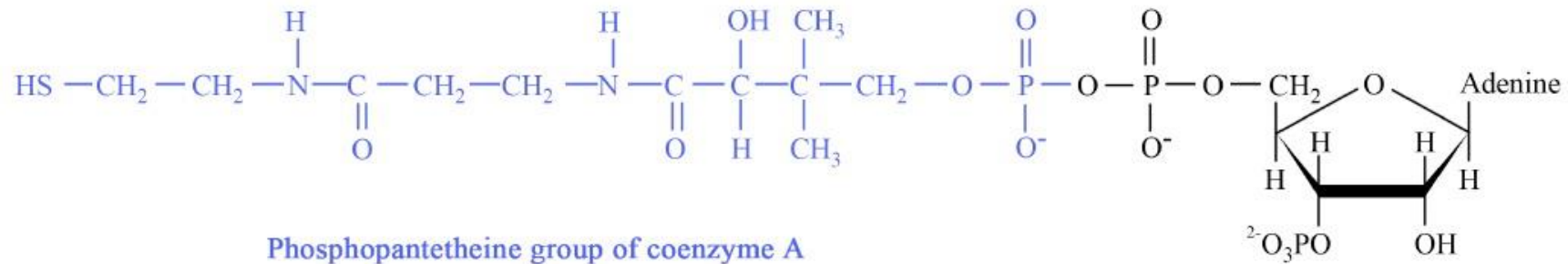
**Figure 21-3**  
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# 4'-phosphopantetheine group of ACP and Co-A

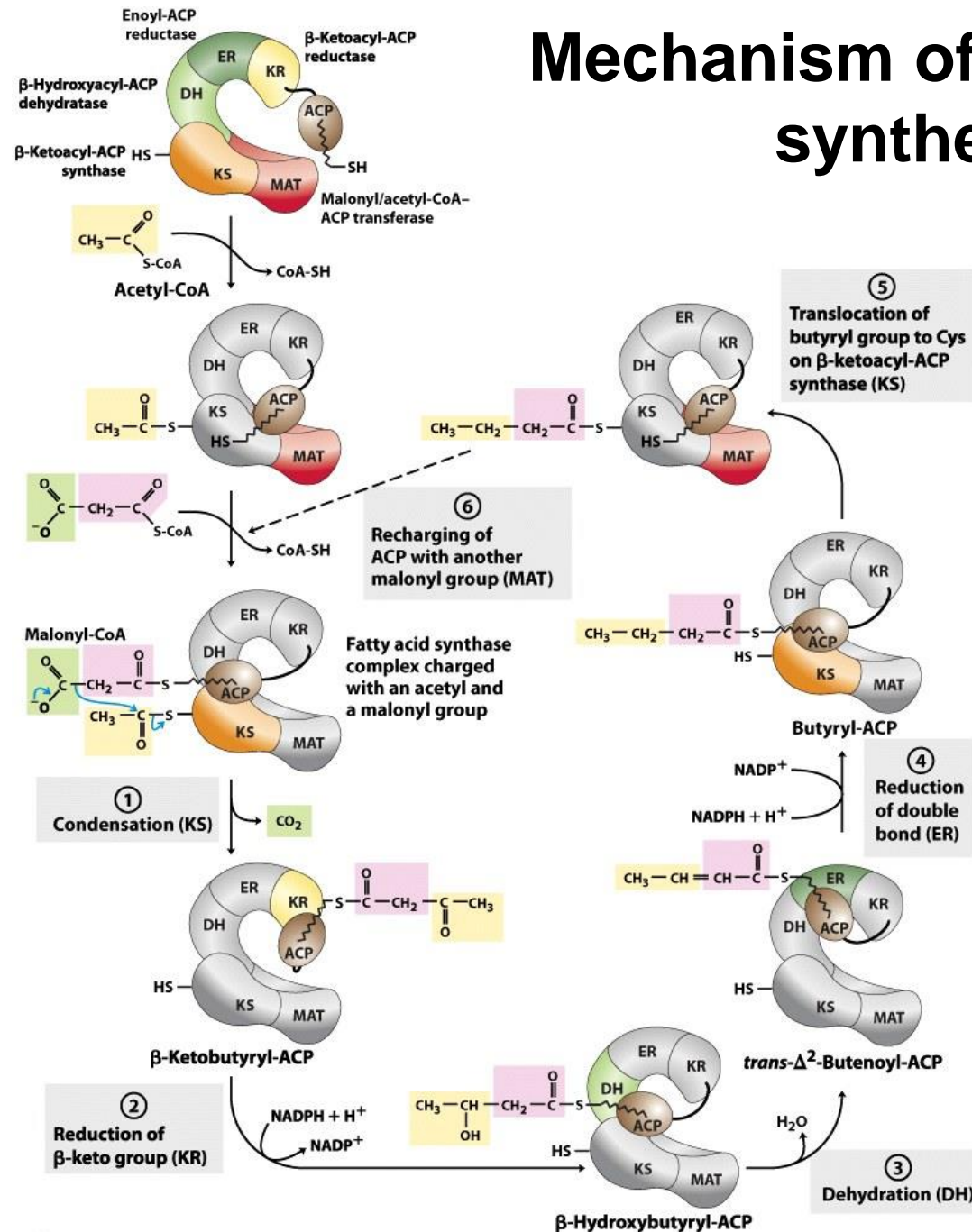


Phosphopantetheine group of ACP

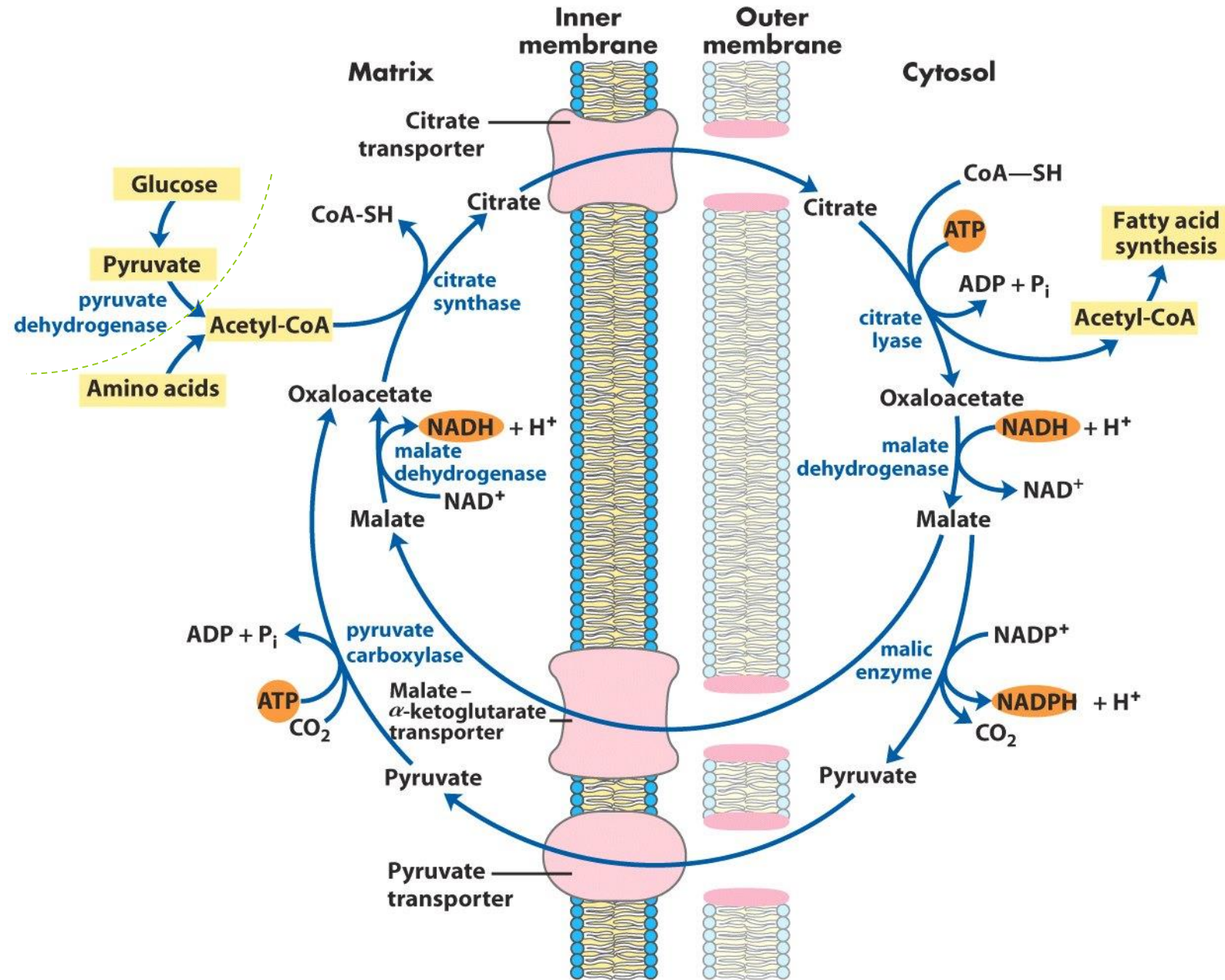


Phosphopantetheine group of coenzyme A

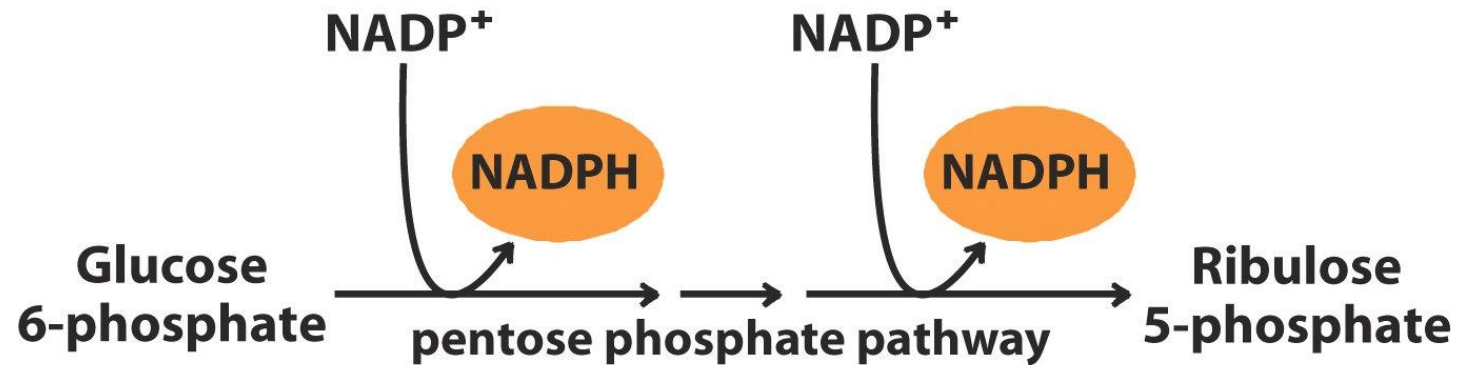
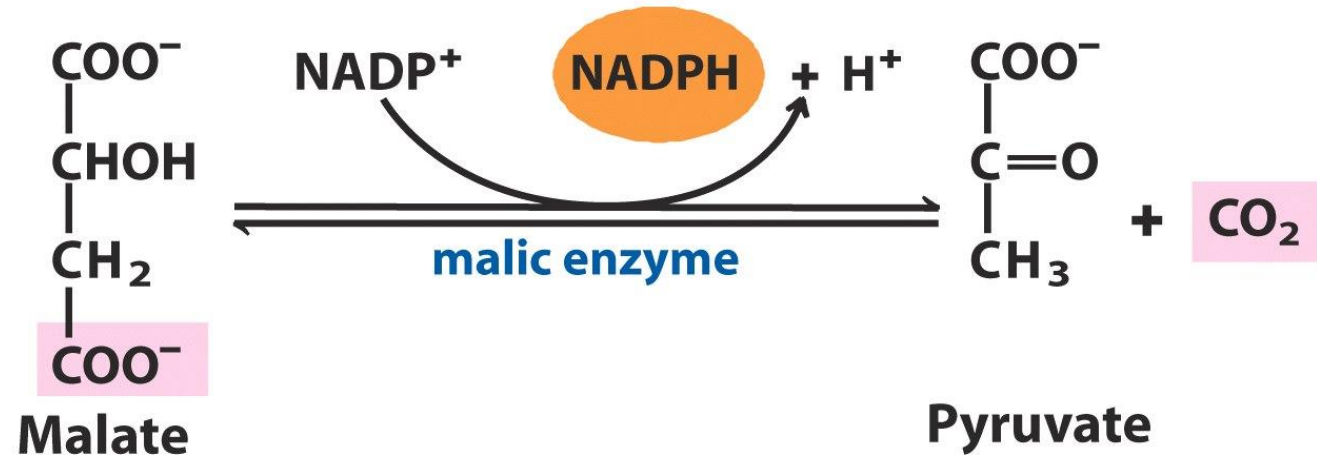
# Mechanism of fatty acids synthesis



# Acetyl-CoA transport to cytosol



# Sources of cytosolic NADPH



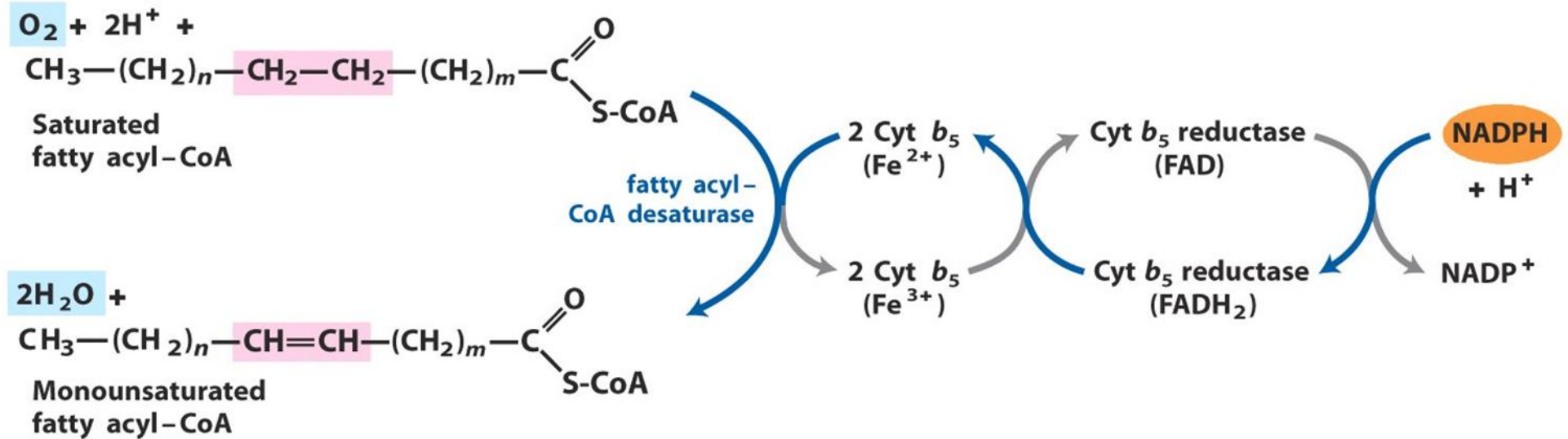
Cytosolic coenzyme

NADPH/NADP<sup>+</sup> ~75

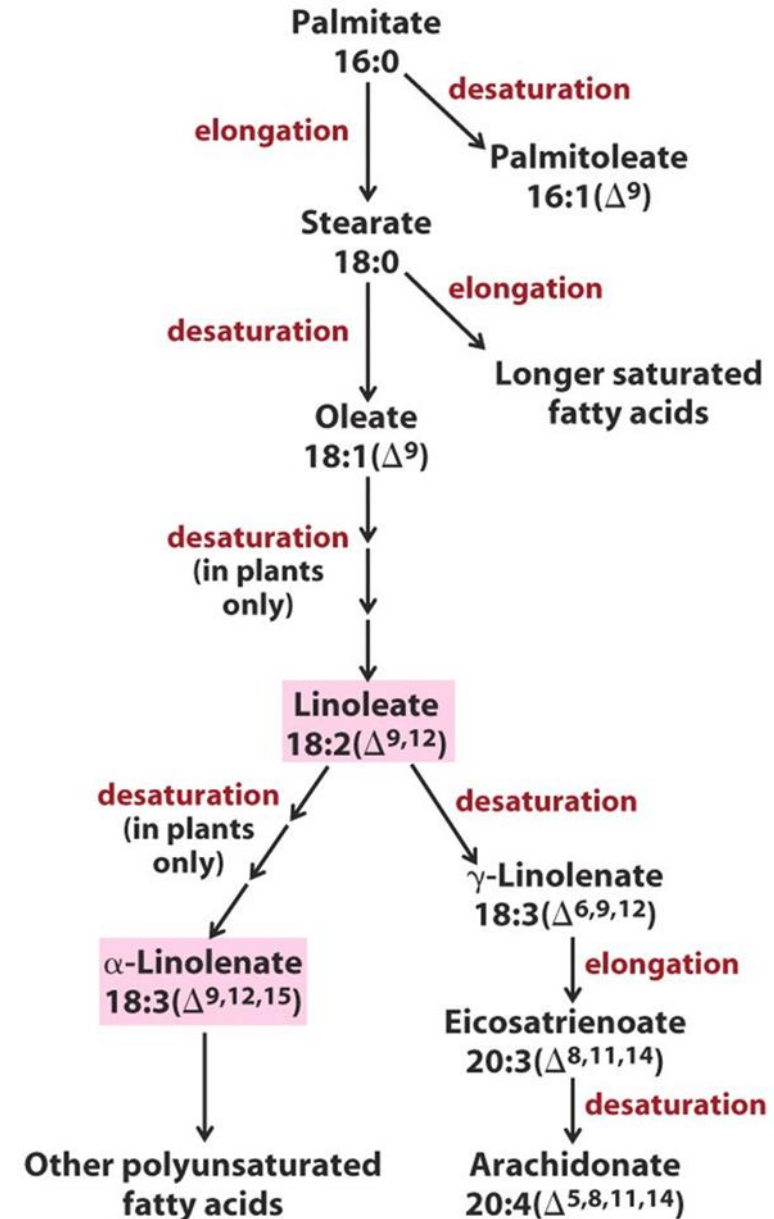
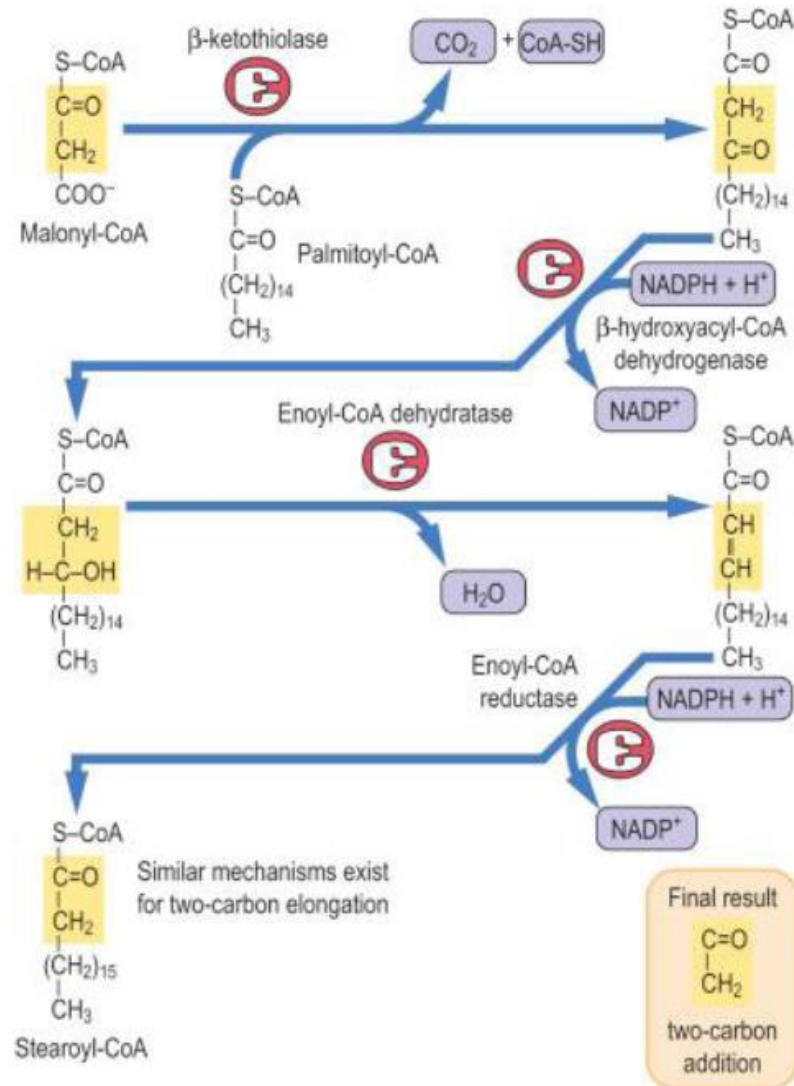
levels in hepatocytes:

NADH/NAD<sup>+</sup> ~8x10<sup>-4</sup>

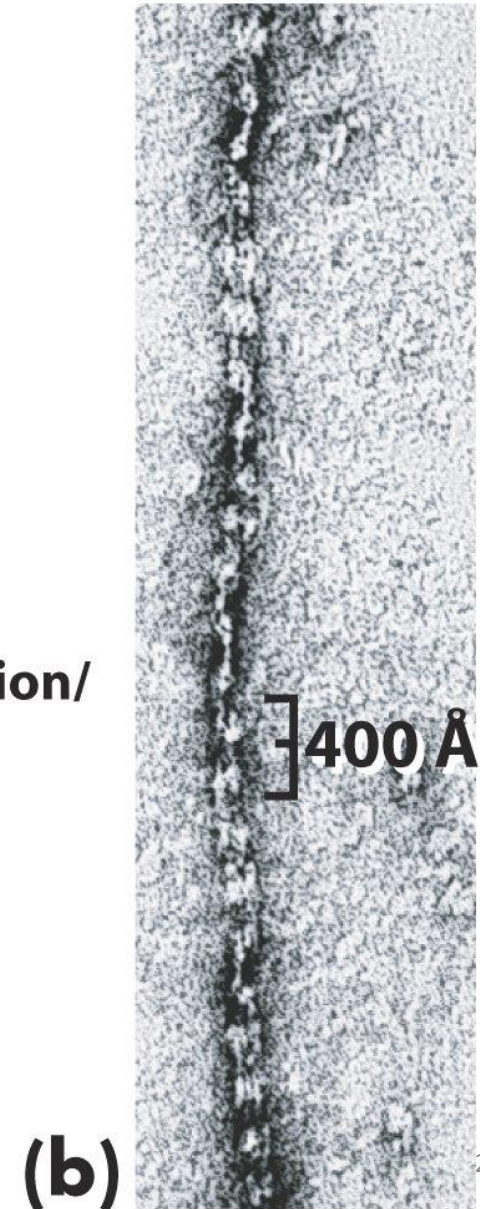
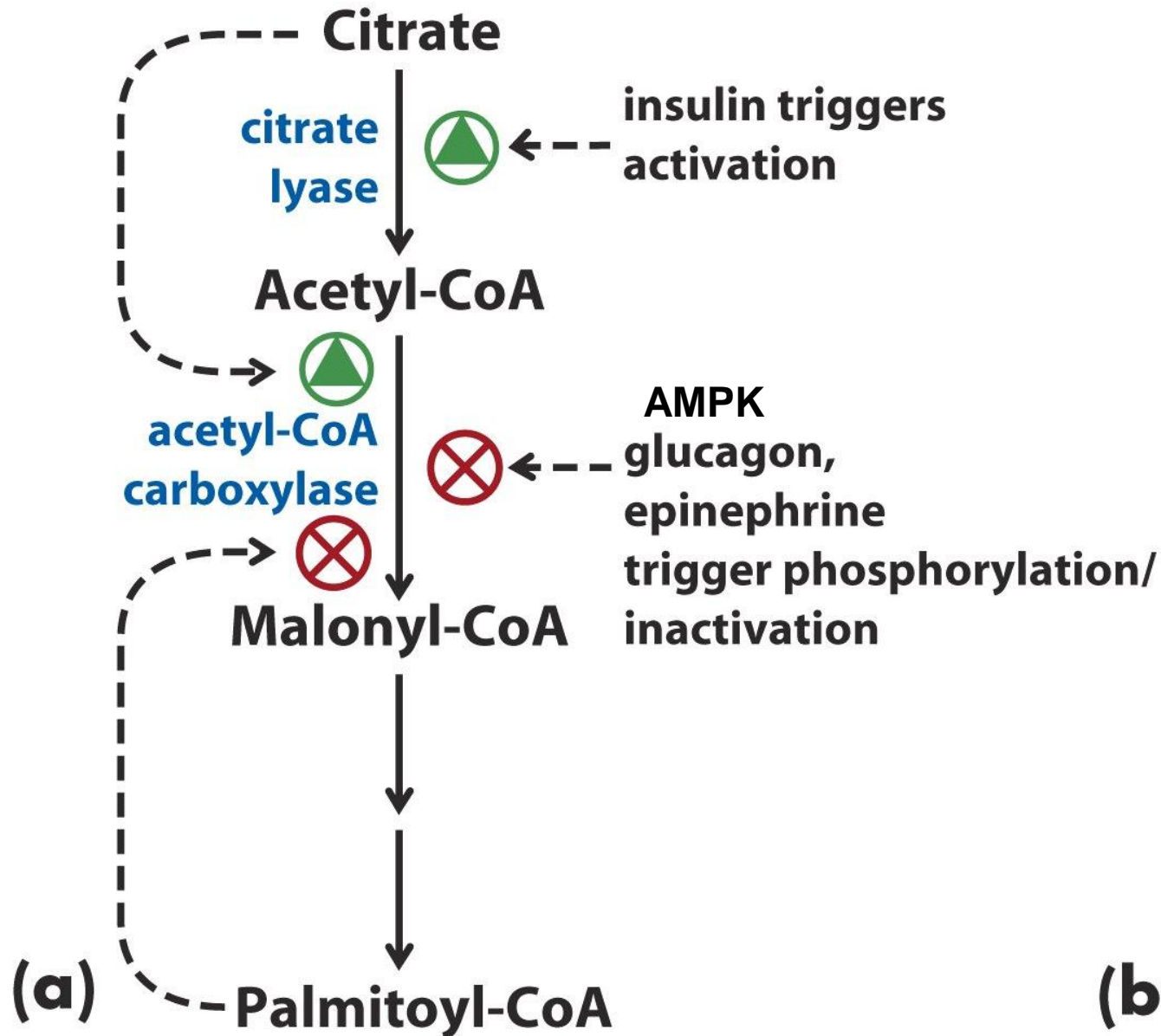
# Synthesis of unsaturated fatty acids



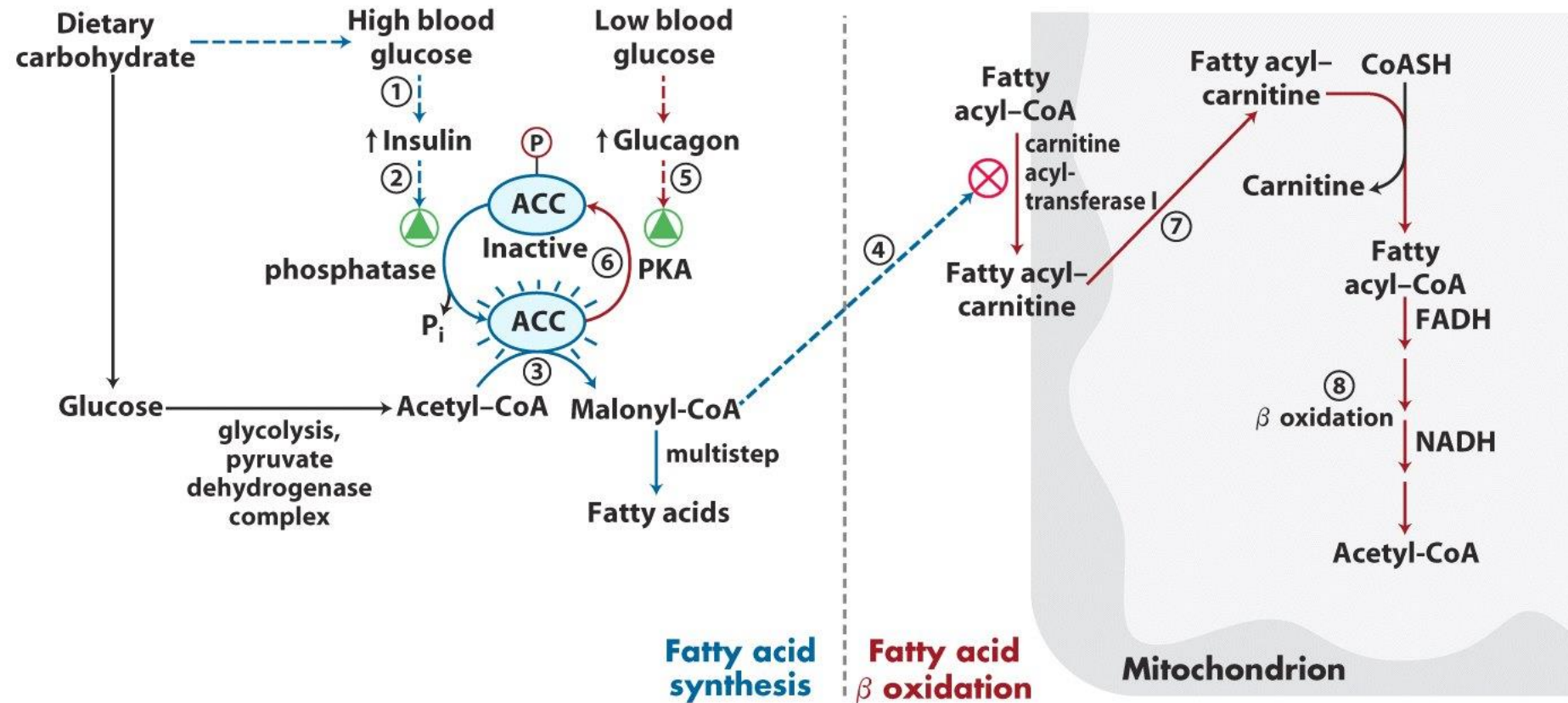
# Elongation of fatty acids



# Regulation of acetyl-CoA carboxylase



# Coordinated regulation of fatty acid synthesis and breakdown

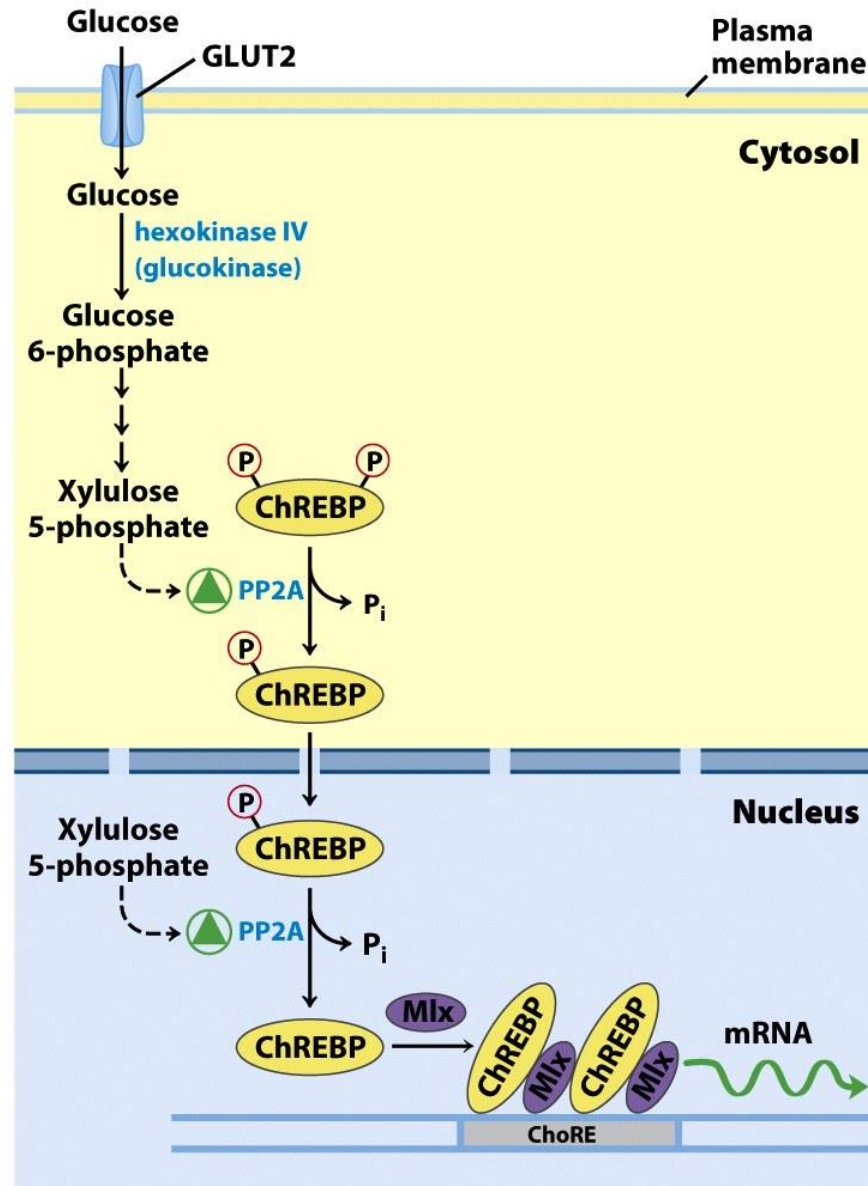


# Transcriptional regulation

<b>TABLE 15–5    Some of the Genes Regulated by Insulin</b>	
<b>Change in gene expression</b>	<b>Pathway</b>
<b>Increased expression</b>	
Hexokinase II	Glycolysis
Hexokinase IV	Glycolysis
Phosphofructokinase-1 (PFK-1)	Glycolysis
Pyruvate kinase	Glycolysis
PFK-2/FBPase-2	Regulation of glycolysis/gluconeogenesis
Glucose 6-phosphate dehydrogenase	Pentose phosphate pathway (NADPH)
6-Phosphogluconate dehydrogenase	Pentose phosphate pathway (NADPH)
Pyruvate dehydrogenase	Fatty acid synthesis
Acetyl-CoA carboxylase	Fatty acid synthesis
Malic enzyme	Fatty acid synthesis (NADPH)
ATP-citrate lyase	Fatty acid synthesis (provides acetyl-CoA)
Fatty acid synthase complex	Fatty acid synthesis
Stearoyl-CoA dehydrogenase	Fatty acid desaturation
Acyl-CoA–glycerol transferases	Triacylglycerol synthesis
<b>Decreased expression</b>	
PEP carboxykinase	Gluconeogenesis
Glucose 6-phosphatase (catalytic subunit)	Glucose release to blood

**Table 15-5**  
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# Transcriptional regulation

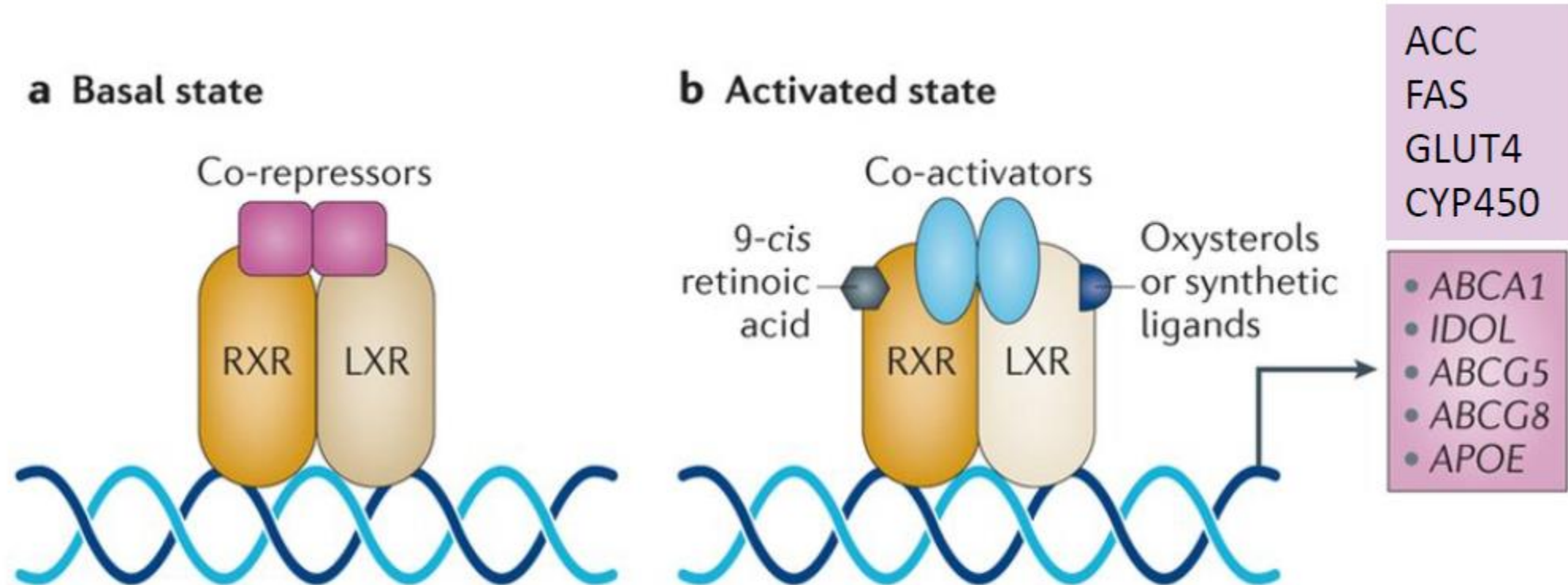


**Figure 15-21**

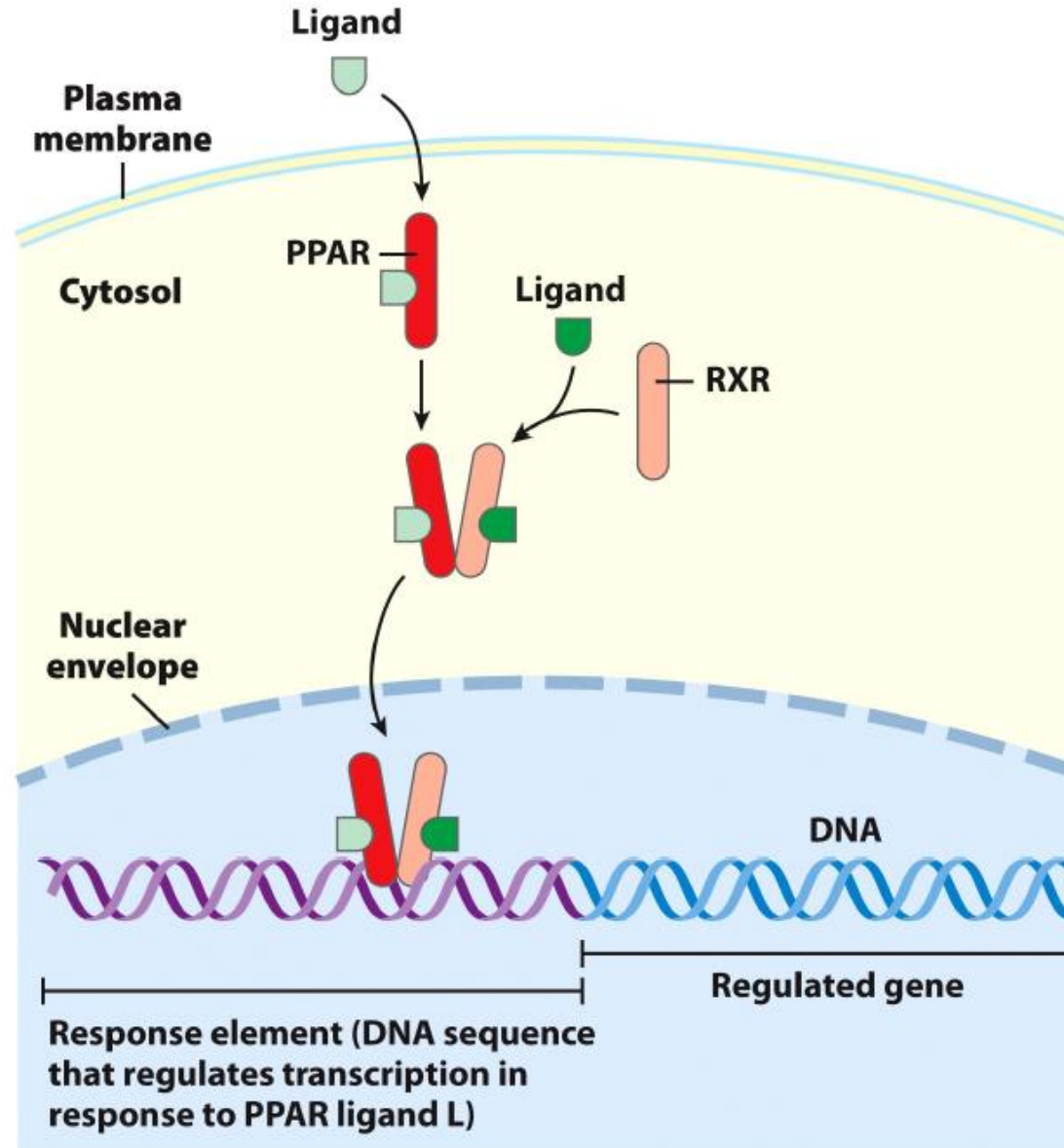
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# Transcriptional regulation

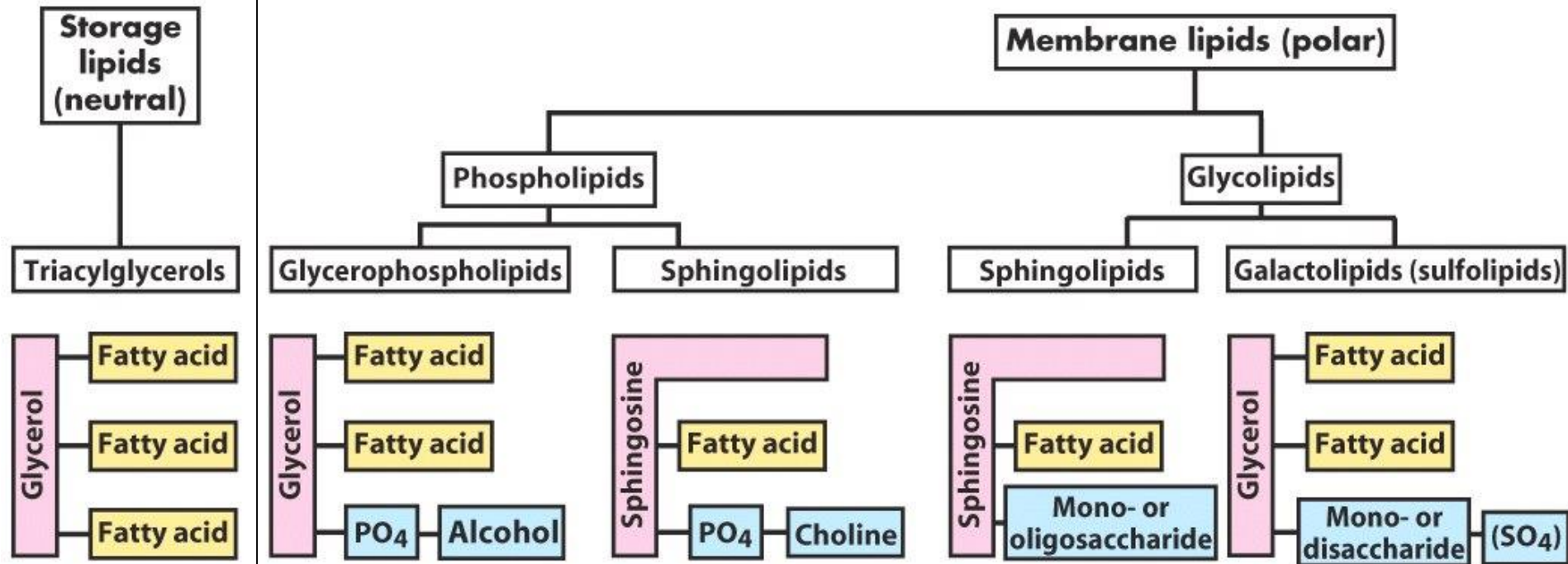


# Transcriptional regulation



PPAR  $\alpha$   
PPAR  $\beta/\delta$   
PPAR  $\gamma$

# Complex lipids



# Synthesis of phosphatidic acid and triacylglycerols

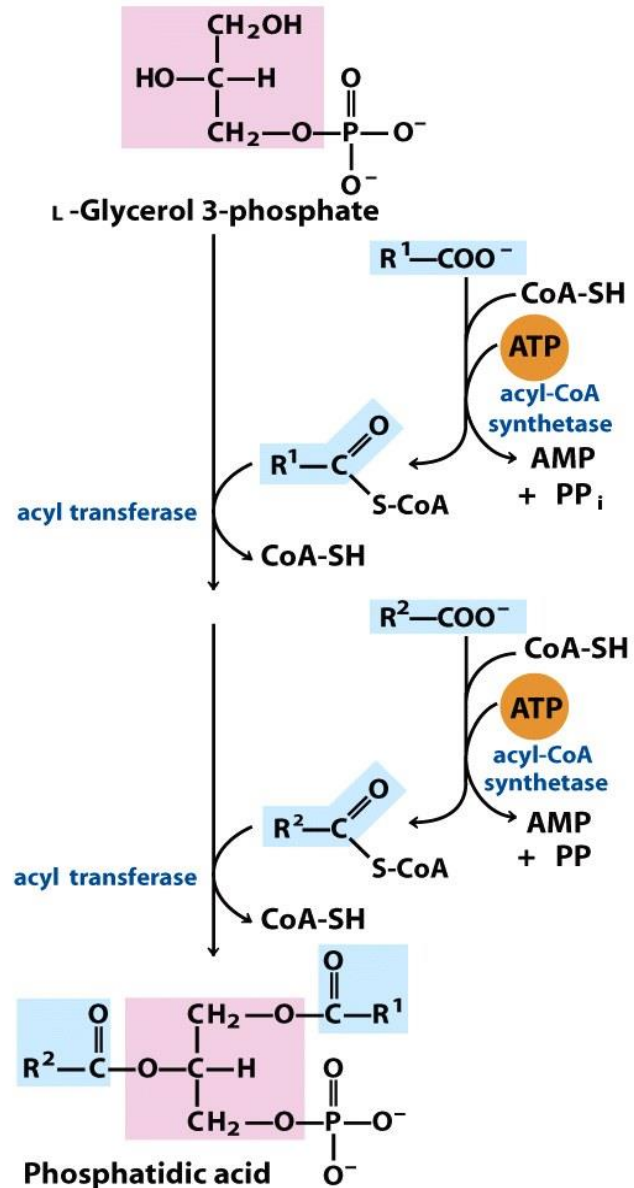


Figure 21-17 part 2

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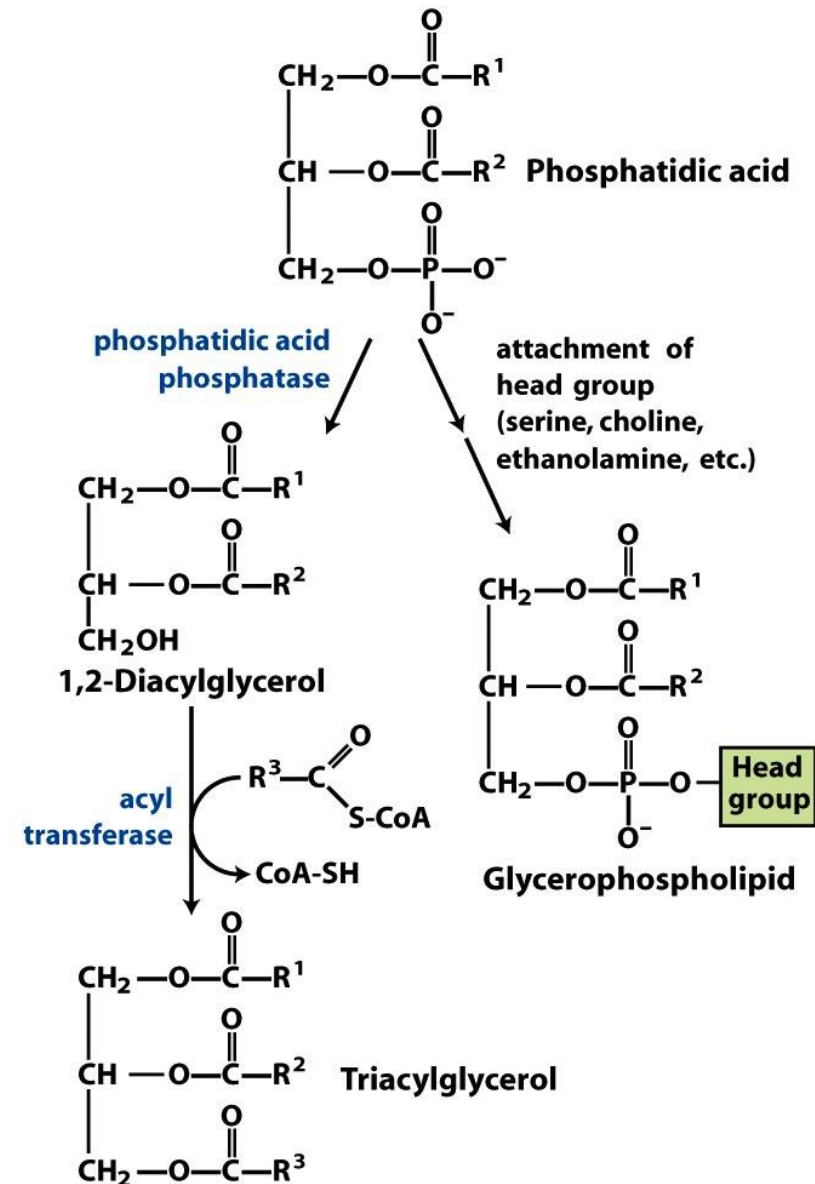
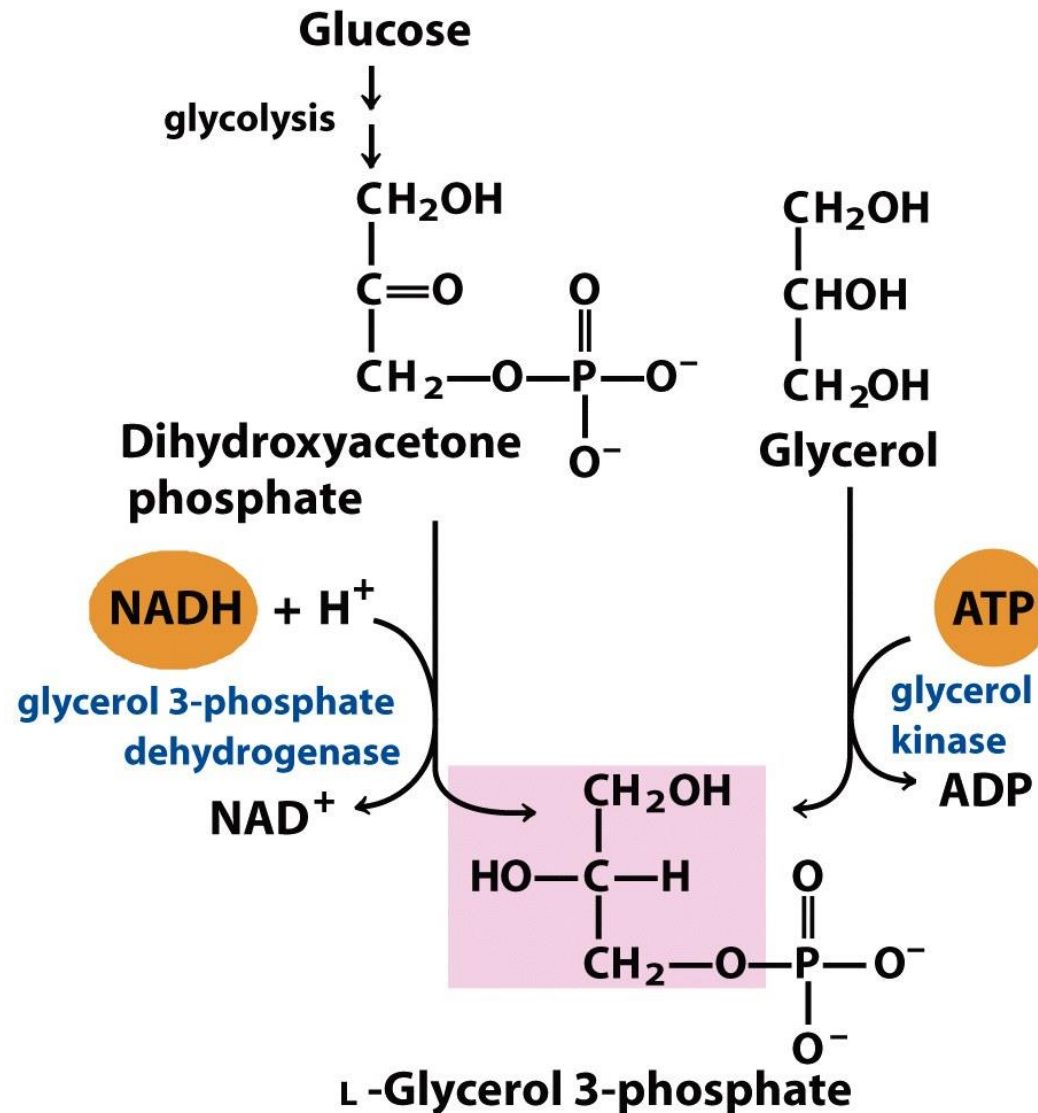


Figure 21-18

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# Production of glycerol-3-phosphate



**Figure 21-17 part 1**  
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# Glyceroneogenesis

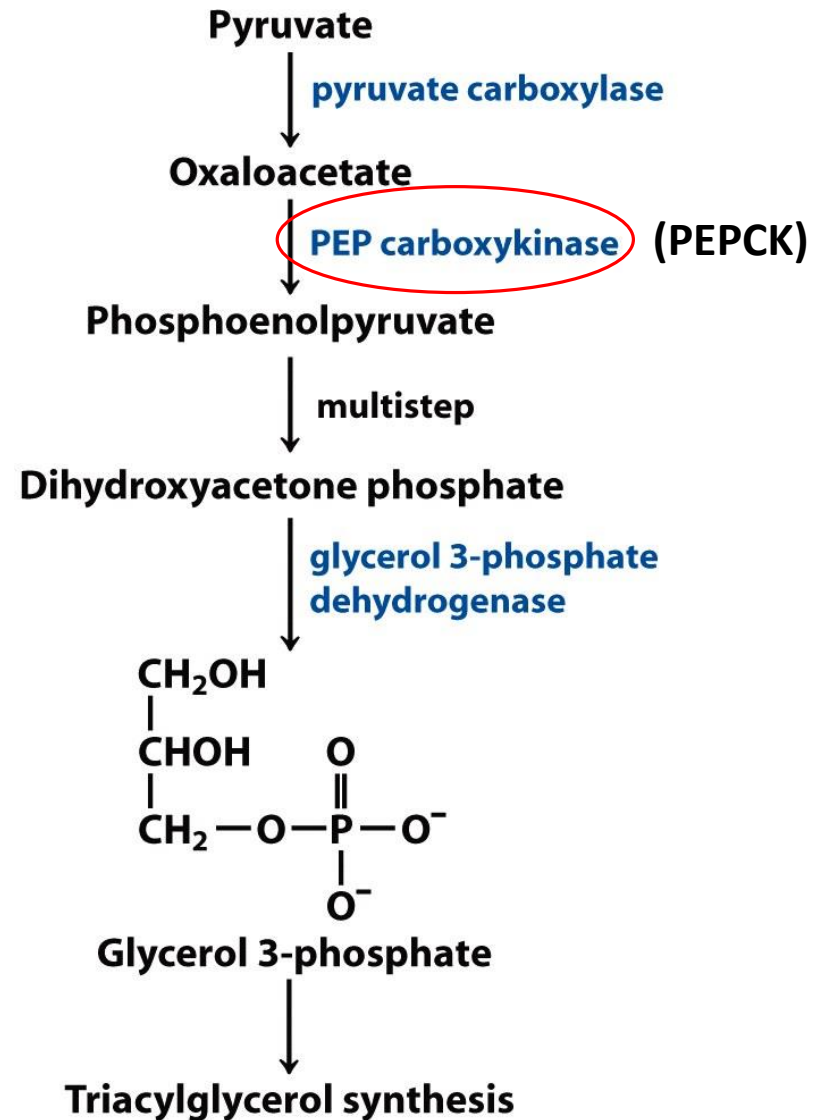
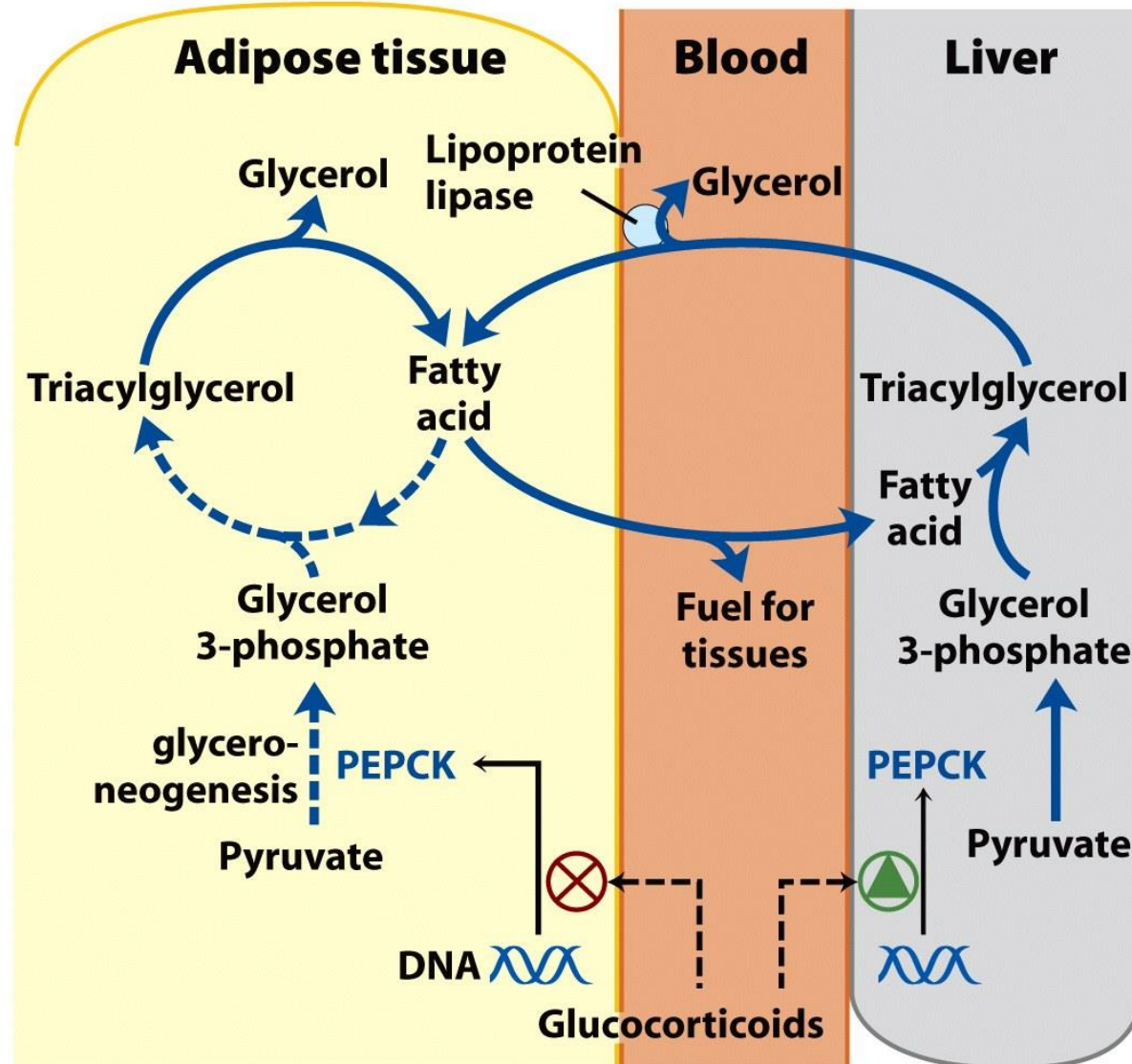


Figure 21-21

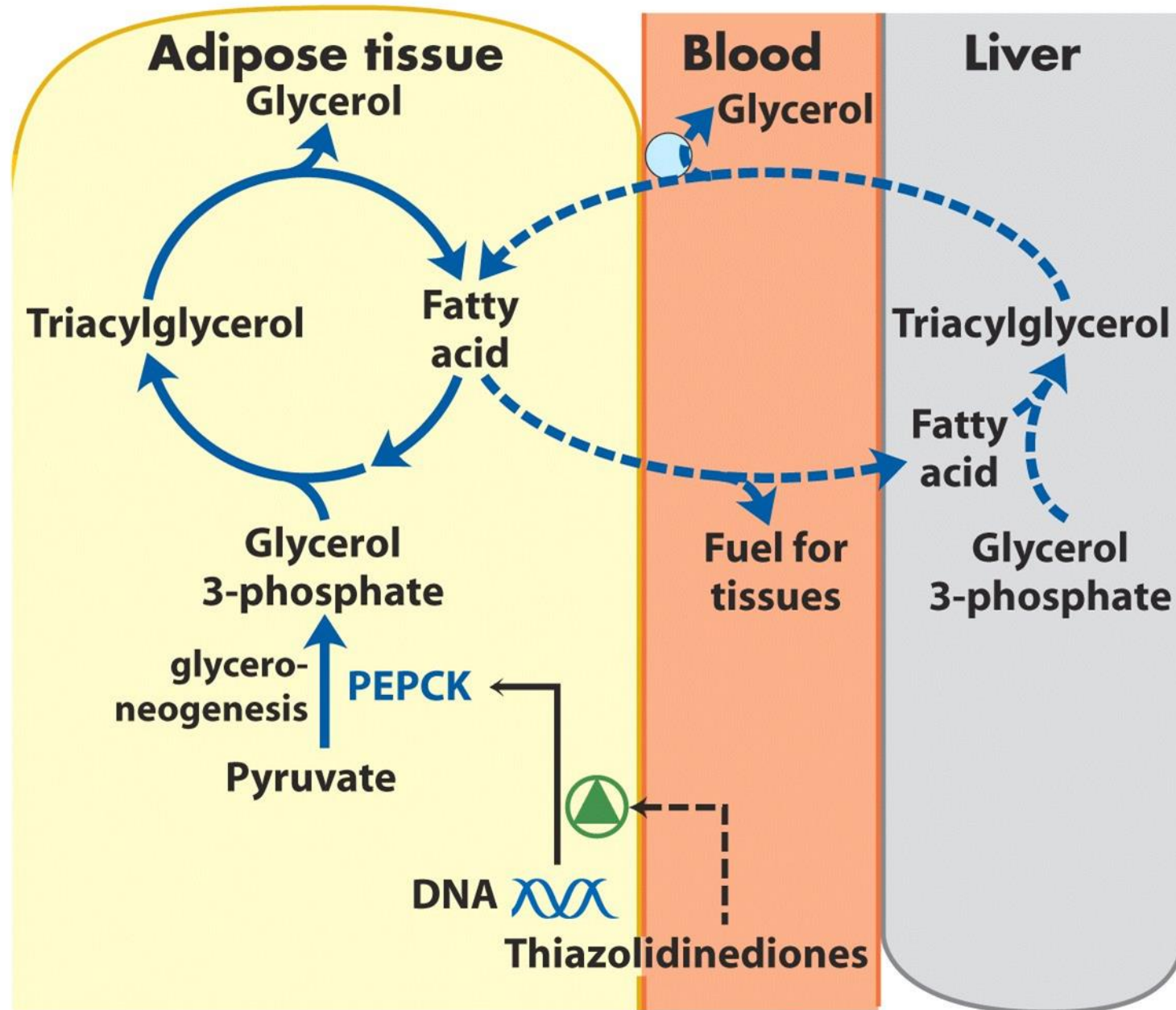
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# Effect of glucocorticoids on glyceroneogenesis

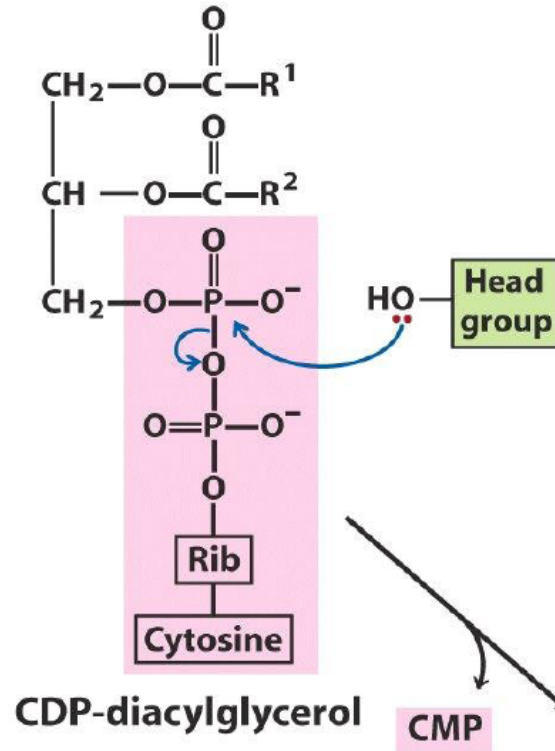


# Effect of thiazolidinediones on glyceroneogenesis

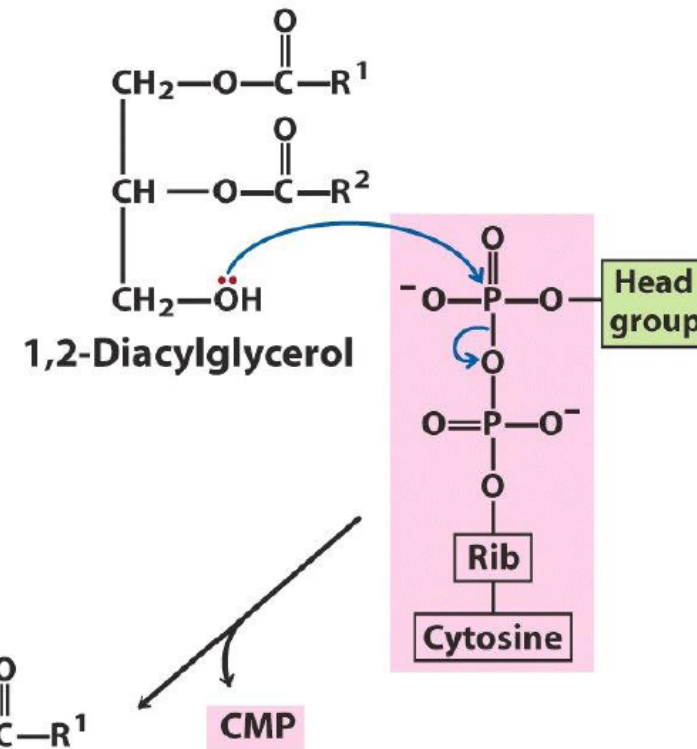


# Complex lipids

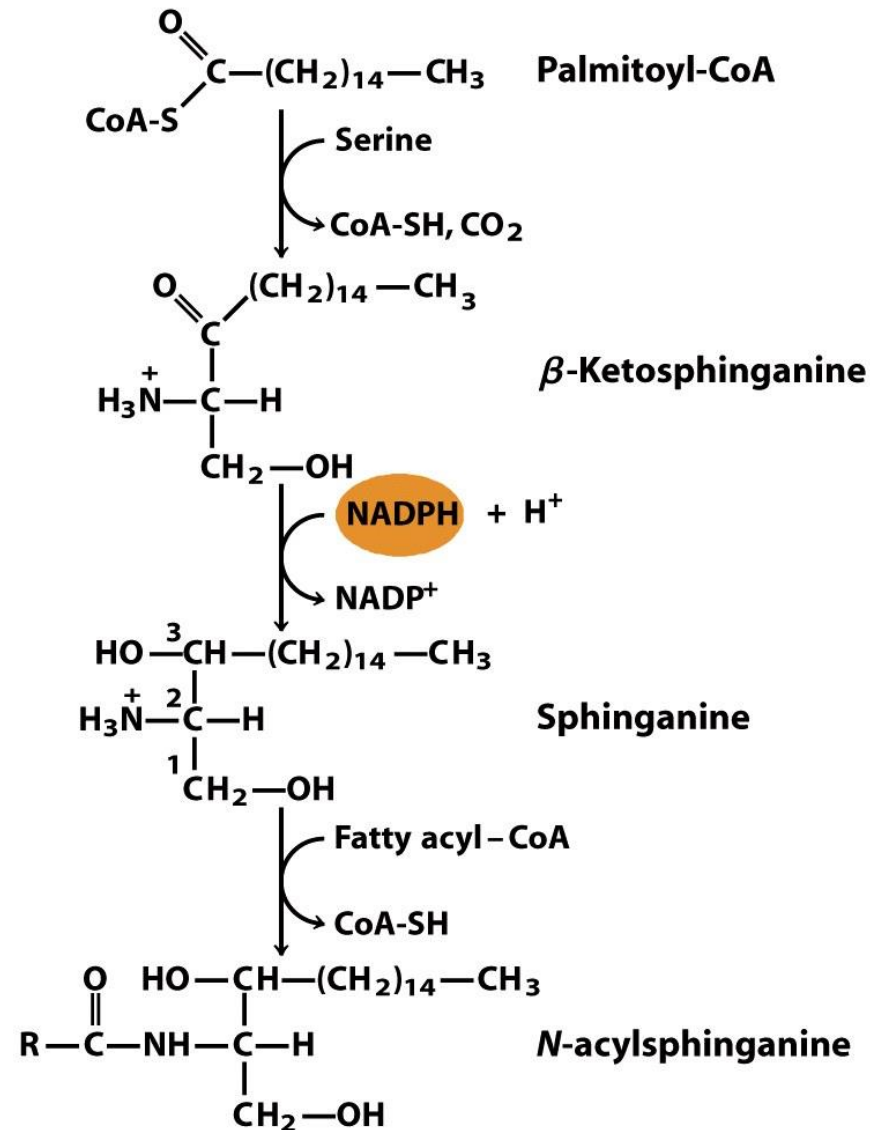
## Strategy 1 Diacylglycerol activated with CDP



## Strategy 2 Head group activated with CDP

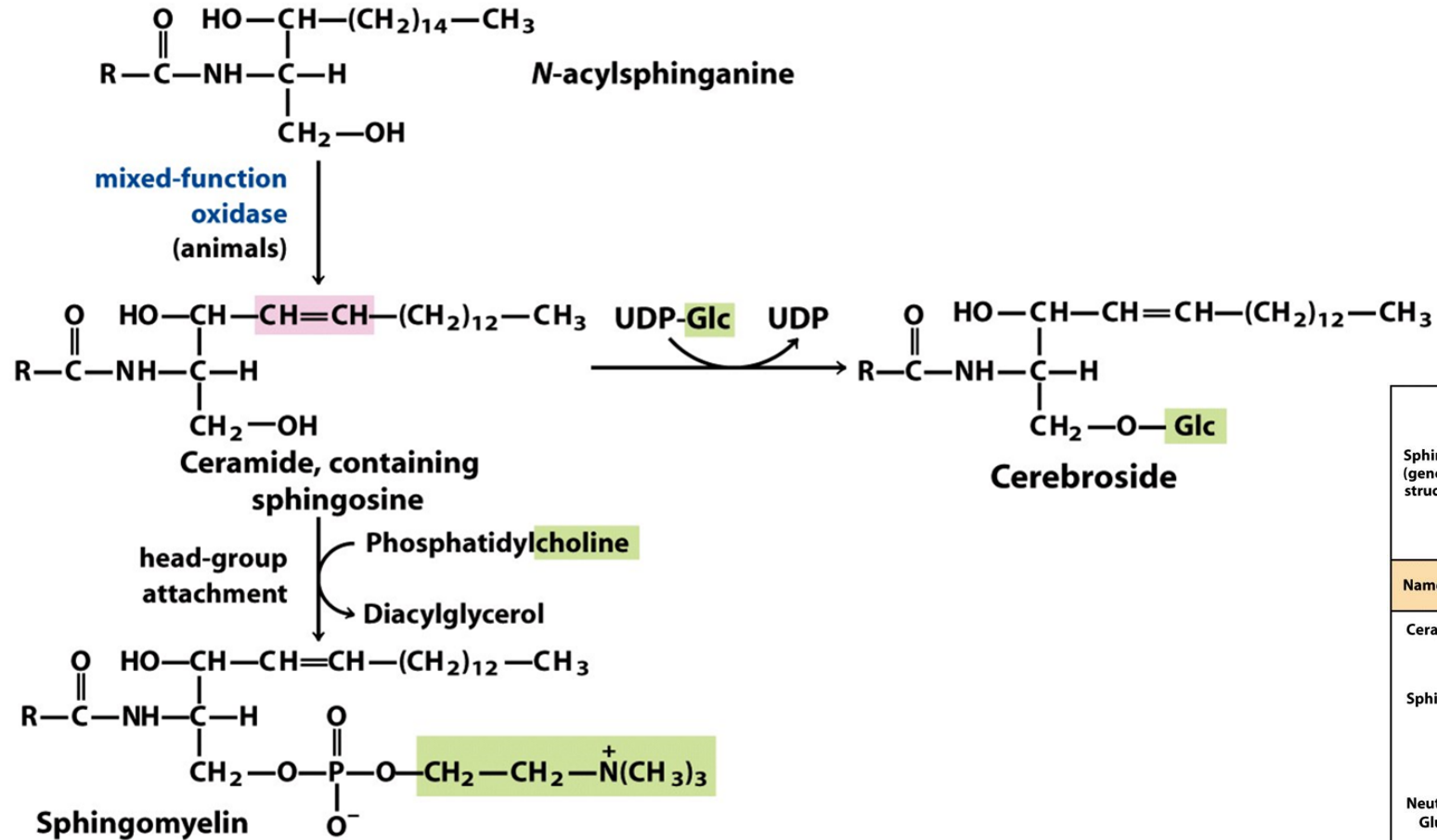


# Sphingolipids

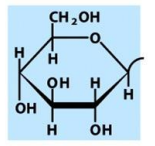
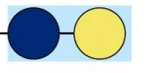
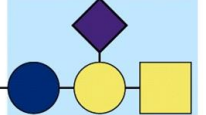


**Figure 21-31 part 1**  
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# Sphingolipids



**Figure 21-31 part 2**  
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<div> <div> <div>Sphingosine</div> <div>HO-<sup>3</sup>CH-CH=CH-(CH<sub>2</sub>)<sub>12</sub>-CH<sub>3</sub></div> </div> <div> <div>Fatty acid</div> <div> <math>\text{C}(=\text{O})-\text{CH}_2-\text{CH}_2-\dots-\text{CH}_2-\text{CH}_2-\text{CH}_3</math> </div> </div> </div>		
Name of sphingolipid	Name of X—O	Formula of X
Ceramide	—	—H
Sphingomyelin	Phosphocholine	$\begin{array}{c} \text{O} \\ \parallel \\ \text{P}-\text{O}-\text{CH}_2-\text{CH}_2-\text{N}^+(\text{CH}_3)_3 \\   \\ \text{O}^- \end{array}$
Neutral glycolipids Glucosylcerebroside	Glucose	
Lactosylceramide (a globoside)	Di-, tri-, or tetrasaccharide	
Ganglioside GM2	Complex oligosaccharide	

**Figure 10-13**  
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