Chapter 7-I:

Lipid Metabolism

Lipid: a major storage form of metabolic energy

Chapter 19 Opener Fundamentals of Biochemistry, 2/e

Fatty acids

1. 지방산의 주요 생리적 기능
   (1) 인지질 (phospholipid)과 당지질 (glycolipid)들의 구성성분
   (2) 유도체들은 호르몬들이나 세포 내 전령 (intracellular messenger)로 작용
   (3) triacylglycerol과 같은 에너지 저장물질

2. 구조
   일반적인 구조식: $CH_3(CH_2)nCOOH$
   포화지방산: no C-C double bonds
   불포화지방산: double bonds

명명법; common name (http://www.cyberlipid.org/fa/acid0001.htm)
systematic name: n-octadecan**oic** acid(stearic acid)
octade**cenoic** acid (oleate)
octadeca**dienoic** acid
octadeca**trienoic** acid
numbering: carboxyl 말단부터 시작

생물계에 존재하는 지방산들은 전형적으로는 14와 24개 사이의 짝수로 존재
그 중에서도 16과 18개의 탄소를 가진 것들이 가장 많다.

Fatty acids: carboxylic acids with long-chain hydrocarbon side groups
<14 or >20 are uncommon

Table 9-1 The Common Biological Fatty Acids

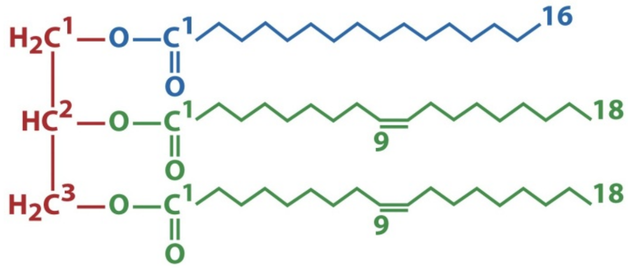
Symbol[a]	Common Name	Systematic Name	Structure	mp (°C)
Saturated fatty acids				
12:0	Lauric acid	Dodecanoic acid	$CH_3(CH_2)_{10}COOH$	44.2
14:0	Myristic acid	Tetradecanoic acid	$CH_3(CH_2)_{12}COOH$	52
16:0	Palmitic acid	Hexadecanoic acid	$CH_3(CH_2)_{14}COOH$	63.1
18:0	Stearic acid	Octadecanoic acid	$CH_3(CH_2)_{16}COOH$	69.1
20:0	Arachidic acid	Eicosanoic acid	$CH_3(CH_2)_{18}COOH$	75.4
22:0	Behenic acid	Docosanoic acid	$CH_3(CH_2)_{20}COOH$	81
24:0	Lignoceric acid	Tetracosanoic acid	$CH_3(CH_2)_{22}COOH$	84.2
Unsaturated fatty acids (all double bonds are cis)				
16:1*n*−7	Palmitoleic acid	9-Hexadecenoic acid	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$	−0.5
18:1*n*−9	Oleic acid	9-Octadecenoic acid	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$	13.2
18:2*n*−6	Linoleic acid	9,12-Octadecadienoic acid	$CH_3(CH_2)_4(CH{=}CHCH_2)_2(CH_2)_6COOH$	−9
18:3*n*−3	α-Linolenic acid	9,12,15-Octadecatrienoic acid	$CH_3CH_2(CH{=}CHCH_2)_3(CH_2)_6COOH$	−17
18:3*n*−6	γ-Linolenic acid	6,9,12-Octadecatrienoic acid	$CH_3(CH_2)_4(CH{=}CHCH_2)_3(CH_2)_3COOH$	
20:4*n*−6	Arachidonic acid	5,8,11,14-Eicosatetraenoic acid	$CH_3(CH_2)_4(CH{=}CHCH_2)_4(CH_2)_2COOH$	−49.5
20:5*n*−3	EPA	5,8,11,14,17-Eicosapentaenoic acid	$CH_3CH_2(CH{=}CHCH_2)_5(CH_2)_2COOH$	−54
22:6*n*−3	DHA	4,7,10,13,16,19-Docosohexenoic acid	$CH_3CH_2(CH{=}CHCH_2)_6CH_2COOH$	
24:1*n*−9	Nervonic acid	15-Tetracosenoic acid	$CH_3(CH_2)_7CH{=}CH(CH_2)_{13}COOH$	39

[a]Number of carbon atoms: Number of double bonds. For unsaturated fatty acids, the quantity "*n*−*x*" indicates the position of the last double bond in the fatty acid, where *n* is its number of C atoms, and *x* is the position of the last double-bonded C atom counting from the methyl terminal (ω) end.

Source: Dawson, R.M.C., Elliott, D.C., Elliott, W.H., and Jones, K.M., *Data for Biochemical Research* (3rd ed.), Chapter 8, Clarendon Press (1986).

Table 9-1 Fundamentals of Biochemistry, 2/e

<u>Lipid digestion, absorption, and transport</u>

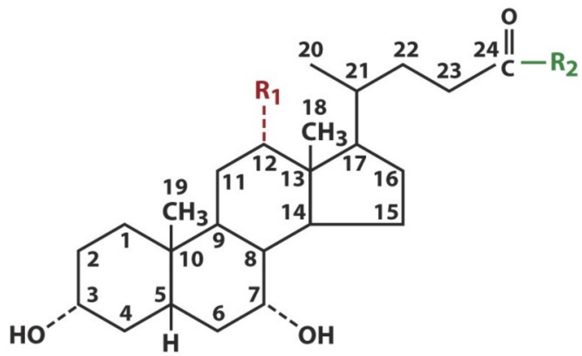


1-Palmitoyl-2,3-dioleoyl-glycerol

Unnumbered figure pg 628 Fundamentals of Biochemistry, 2/e

Triacylglycerol: long term *E* storage
reduced, nonpolar, anhydrous

Digestion & absorption in small intestine
Bile acids (syn by liver, stored in gall bladder, secreted into small intestine)
Increase lipid-water interface



	$R_1 = OH$	$R_1 = H$
$R_2 = OH$	**Cholic acid**	**Chenodeoxycholic acid**
$R_2 = NH—CH_2—COOH$	**Glycocholic acid**	**Glycochenodeoxycholic acid**
$R_2 = NH—CH_2—CH_2—SO_3H$	**Taurocholic acid**	**Taurochenodeoxycholic acid**

Figure 19-1 Fundamentals of Biochemistry, 2/e

Pancreatic lipase

Hydrolysis at 1 and 3 positions of TG
Interfacial activation:
Mixed micelles of
  phosphatidylcholine, bile acids, and colipase

Activated by adrenaline, glucagon, ACTH

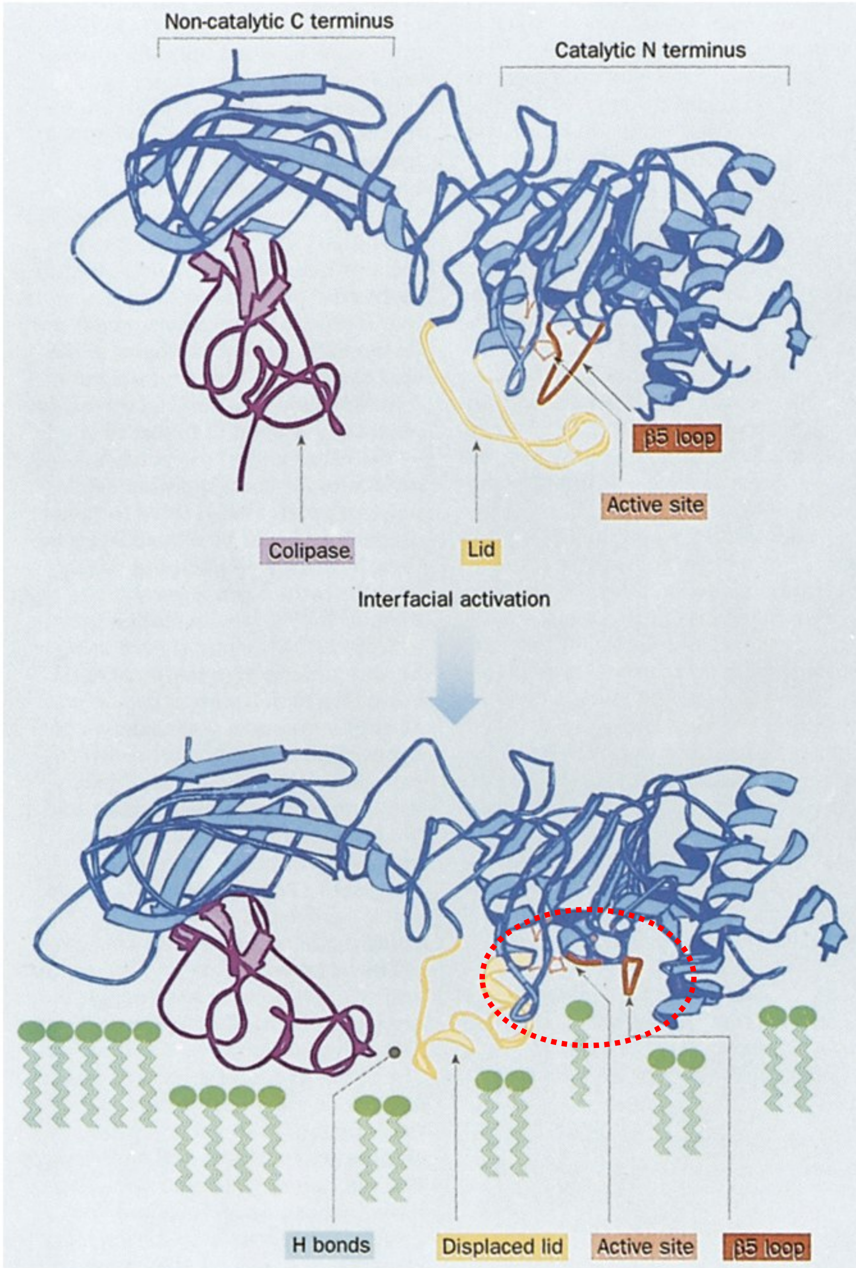
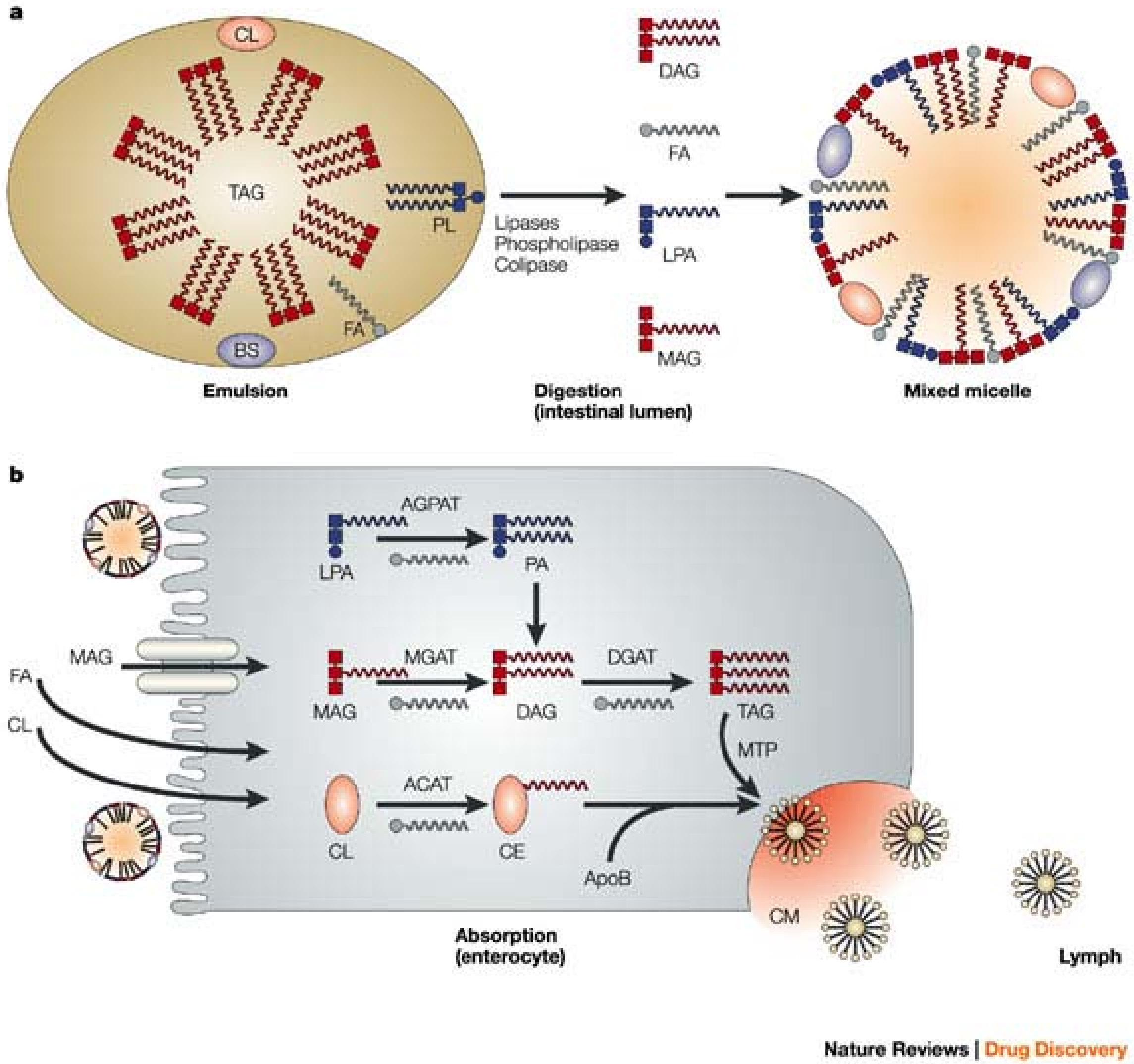


Figure 19-2 Fundamentals of Biochemistry, 2/e

The process of dietary lipid digestion and absorption



a | Dietary lipid digestion begins in the stomach, where lipids are subjected to partial digestion by gastric lipase and form large fat globules with hydrophobic triacylglycerol (TAG) cores surrounded by polar molecules, including phospholipids (PLs), cholesterol (CL), fatty acids (FAs) and ionized proteins. The digestive processes are completed in the intestinal lumen, where large emulsions of fat globules are mixed with bile salts (BS) and pancreatic juice containing lipid digestive enzymes to form an aqueous suspension of small fatty droplets to maximize exposure to the pancreatic lipases for lipid hydrolysis. Monoacylglycerol (MAG), diacylglycerol (DAG) and free FAs that are released by lipid hydrolysis join BS, CL, lysophosphatidic acid (LPA) and fat-soluble vitamins to form mixed micelles that provide a continuous source of digested dietary products for absorption at the brush-border membranes of the enterocytes. b | FAs and MAG enter the enterocytes by passive diffusion and are facilitated by transporters, such as intestinal FA-binding protein (IFABP), CD36 and FA-transport protein-4 (FATP4). They are then re-esterified sequentially inside the endoplasmic reticulum by MAG acyltransferase (MGAT) and diacylglycerol acyltransferase (DGAT) to form TAG. Phospholipids from the diet as well as bile — mainly LPA — are acylated by 1-acyl-glycerol-3-phosphate acyltransferase (AGPAT) to form phosphatidic acid (PA), which is also converted into TAG. Dietary CL is acylated by acyl-CoA:cholesterol acyltransferase (ACAT) to cholesterol esters (CE). Facilitated by microsomal triglyceride transfer protein (MTP), TAG joins CE and apolipoprotein B (ApoB) to form chylomicrons (CM) that enter circulation through the lymph.

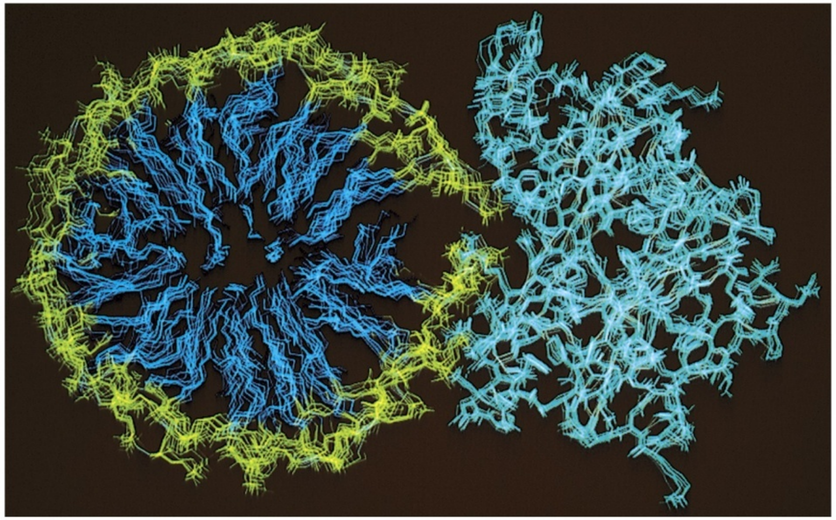


Figure 19-3a Fundamentals of Biochemistry, 2/e

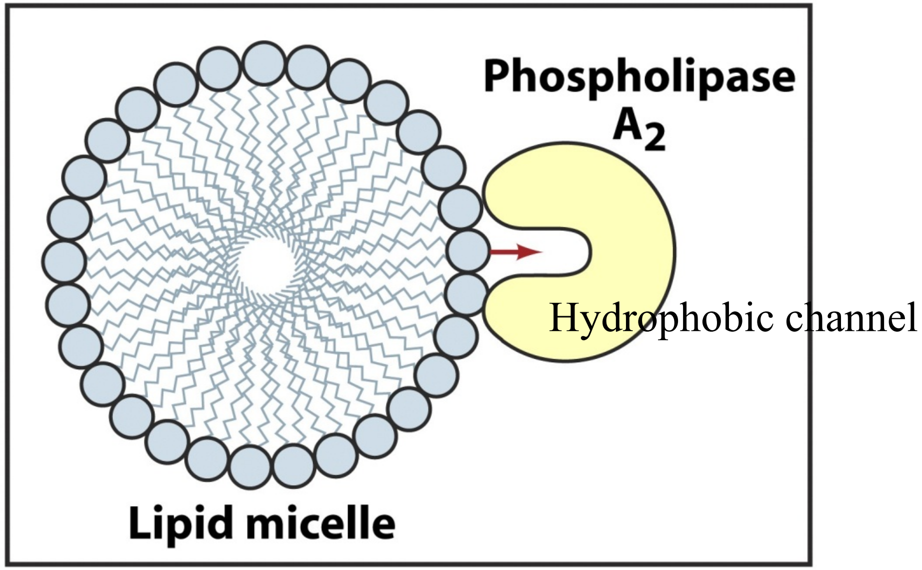


Figure 19-3b Fundamentals of Biochemistry, 2/e

I-FABP

(intestinal fatty acid-binding protein)
participate in the uptake, intracellular metabolism and/or transport of long chain fatty acids

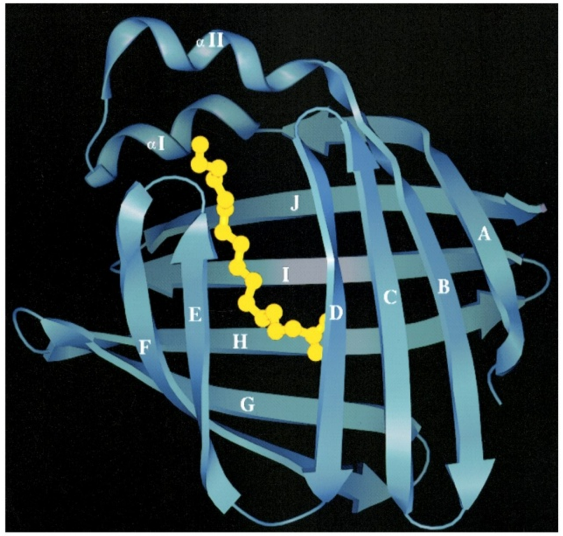


Figure 19-4 Fundamentals of Biochemistry, 2/e

Lipid transport

in complex with proteins: lipoproteins

globular micelle-like particles

nonpolar core of triacylglycerols and cholesteryl esters
surrounded by an amphiphilic coating of protein, phospholipid, and cholesterol

Table 19-1 Characteristics of the Major Classes of Lipoproteins in Human Plasma.

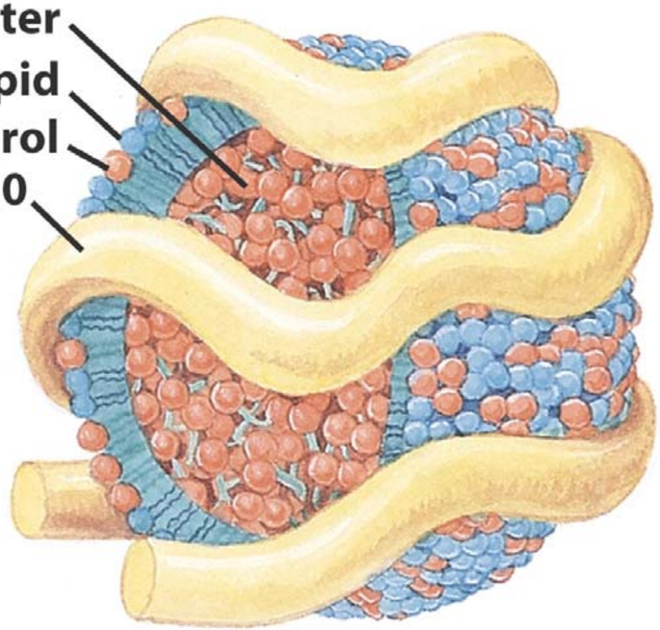
	Chylomicrons	VLDL	IDL	LDL	HDL
Density ($g \cdot cm^{-3}$)	<0.95	<1.006	1.006–1.019	1.019–1.063	1.063–1.210
Particle diameter (Å)	750–12,000	300–800	250–350	180–250	50–120
Particle mass (kD)	400,000	10,000–80,000	5000–10,000	2300	175–360
% Protein[a]	1.5–2.5	5–10	15–20	20–25	40–55
% Phospholipids[a]	7–9	15–20	22	15–20	20–35
% Free cholesterol[a]	1–3	5–10	8	7–10	3–4
% Triacylglycerols[b]	84–89	50–65	22	7–10	3–5
% Cholesteryl esters[b]	3–5	10–15	30	35–40	12
Major apolipoproteins	A-I, A-II, B-48, C-I, C-II, C-III, E	B-100, C-I, C-II, C-III, E	B-100, C-I, C-II, C-III, E	B-100	A-I, A-II, C-I, C-II, C-III, D, E

[a]Surface components.

[b]Core lipids.

Table 19-1 Fundamentals of Biochemistry, 2/e

Apolipoproteins: at least nine are known



LDL

Figure 19-5 Fundamentals of Biochemistry, 2/e

Human apoA-1

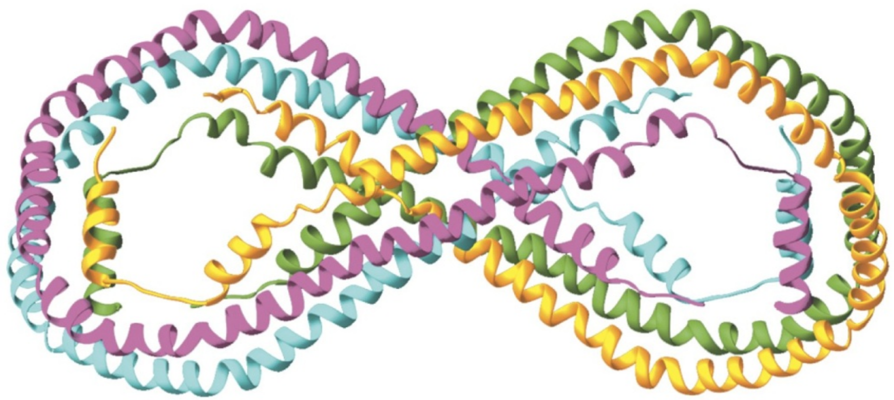


Figure 19-6a Fundamentals of Biochemistry, 2/e

tetramer

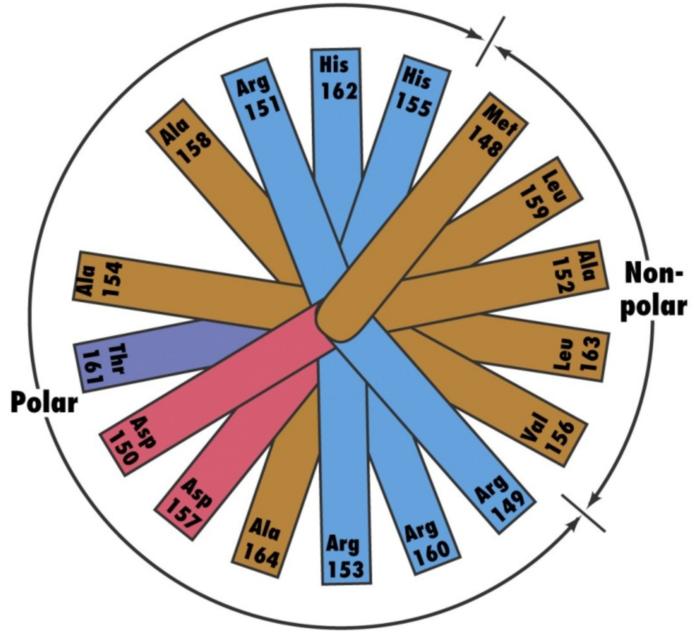


Figure 19-6b Fundamentals of Biochemistry, 2/e

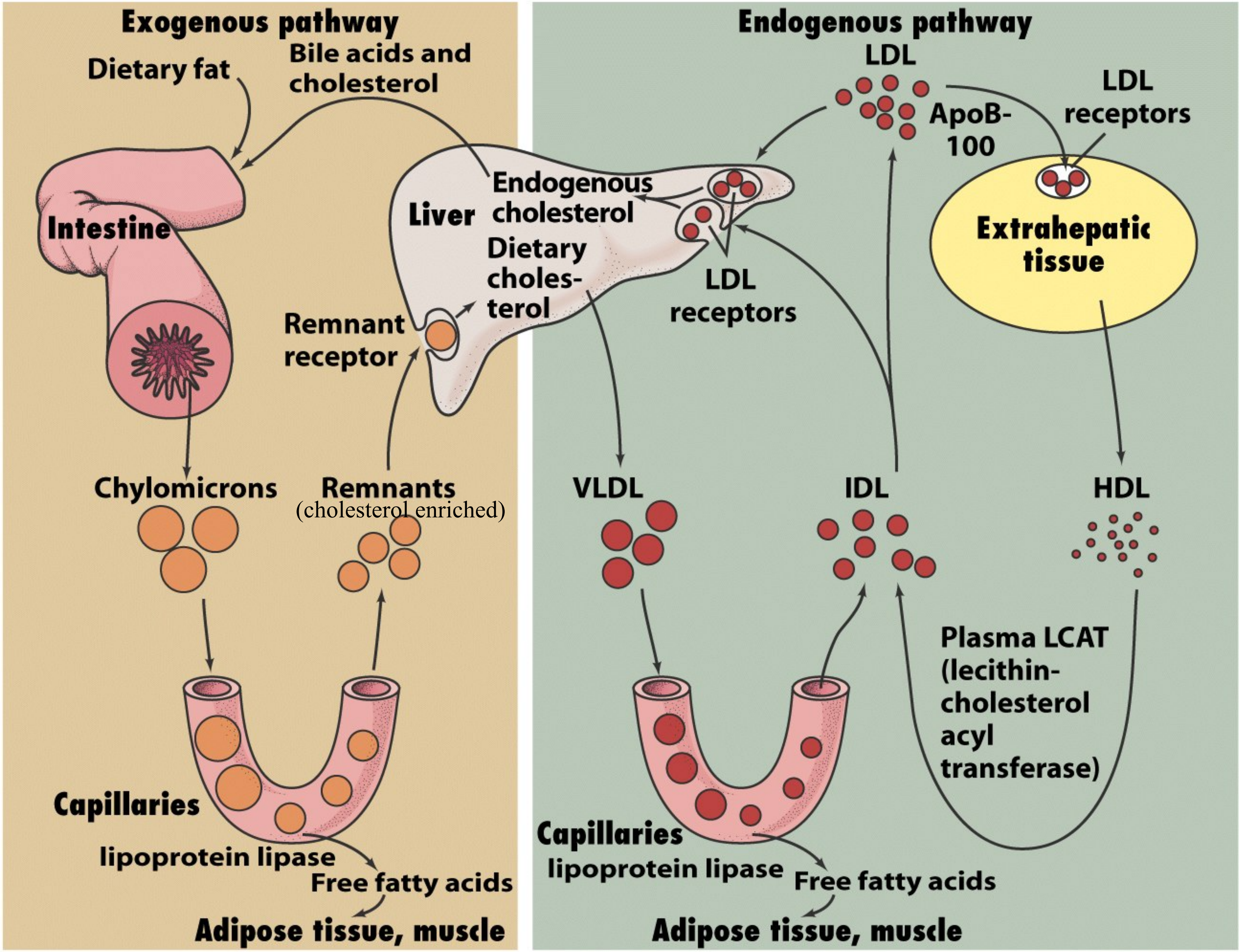
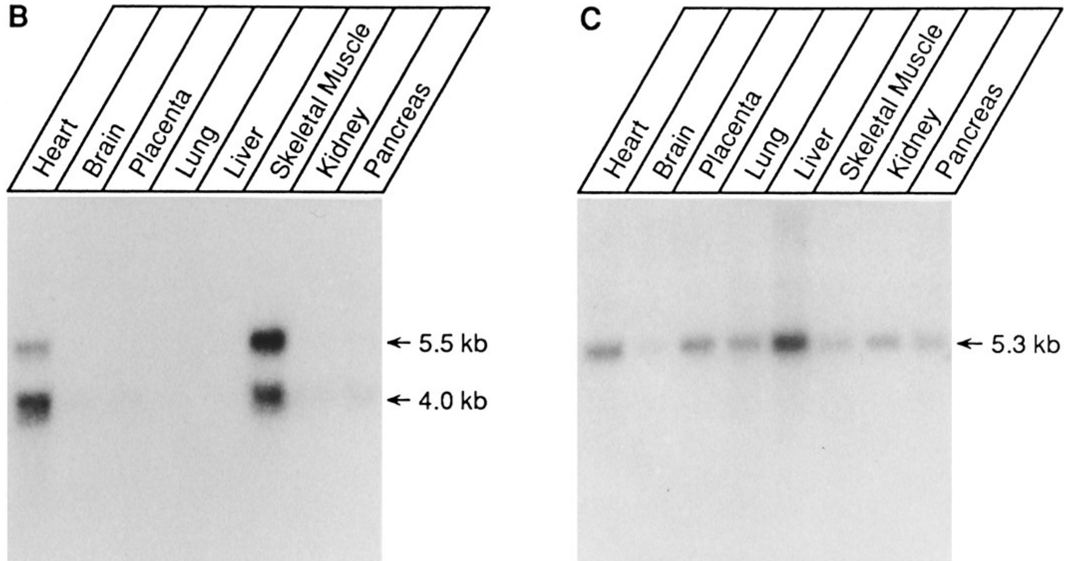


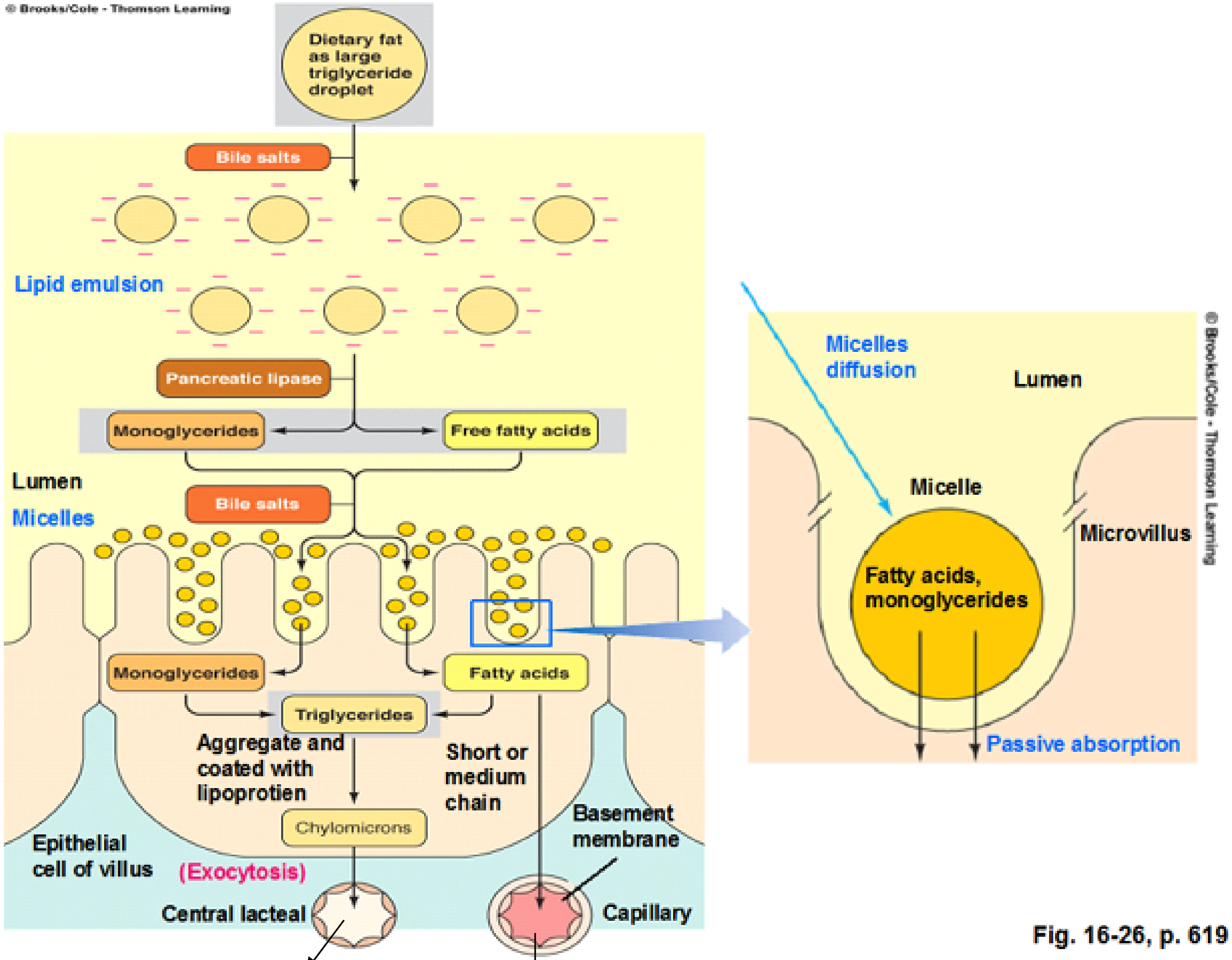
Figure 19-7 Fundamentals of Biochemistry, 2/e

VLDL receptor

LDL receptor



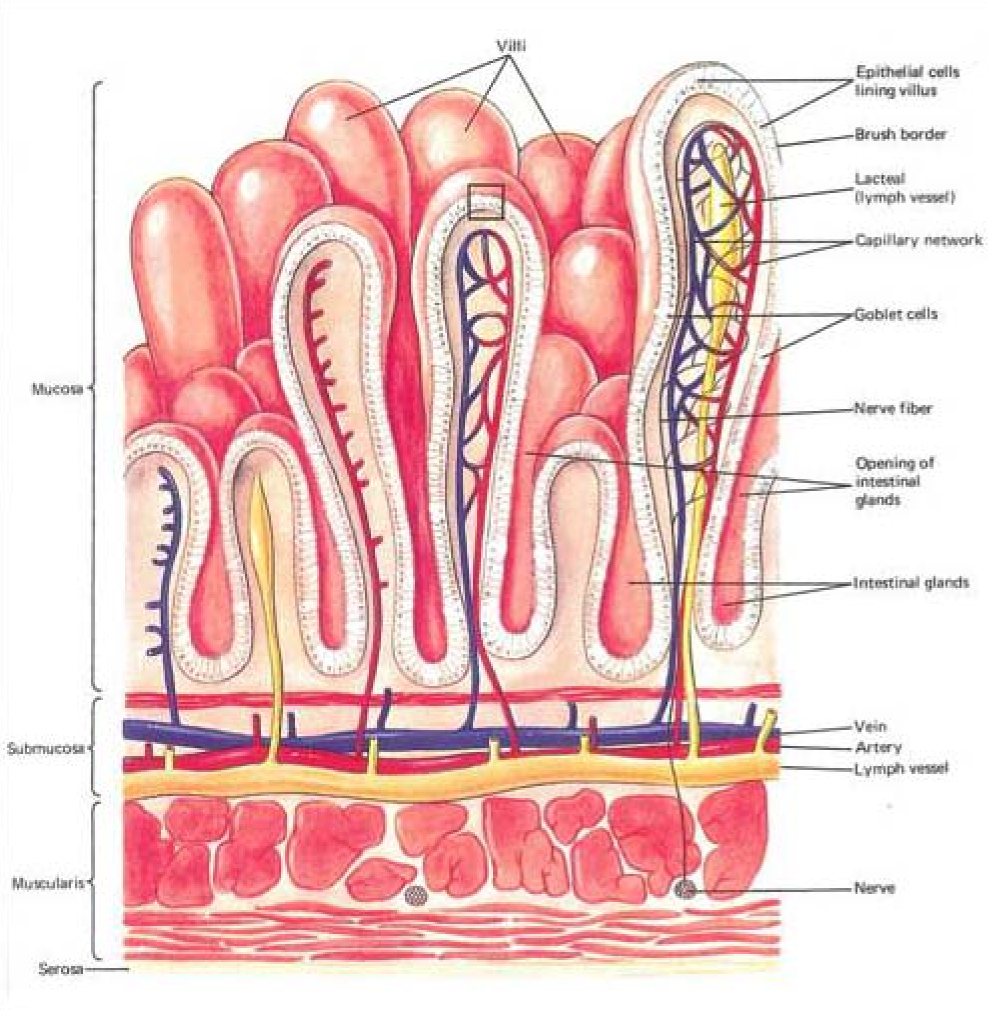
JBC (1996) 271,8373-8380



thoracic duct and left jugular vein

Portal vein to liver

Fig. 16-26, p. 619



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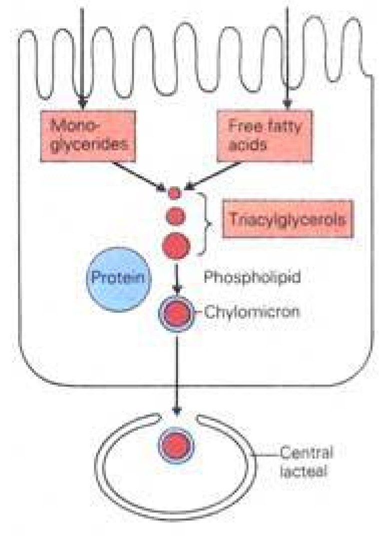
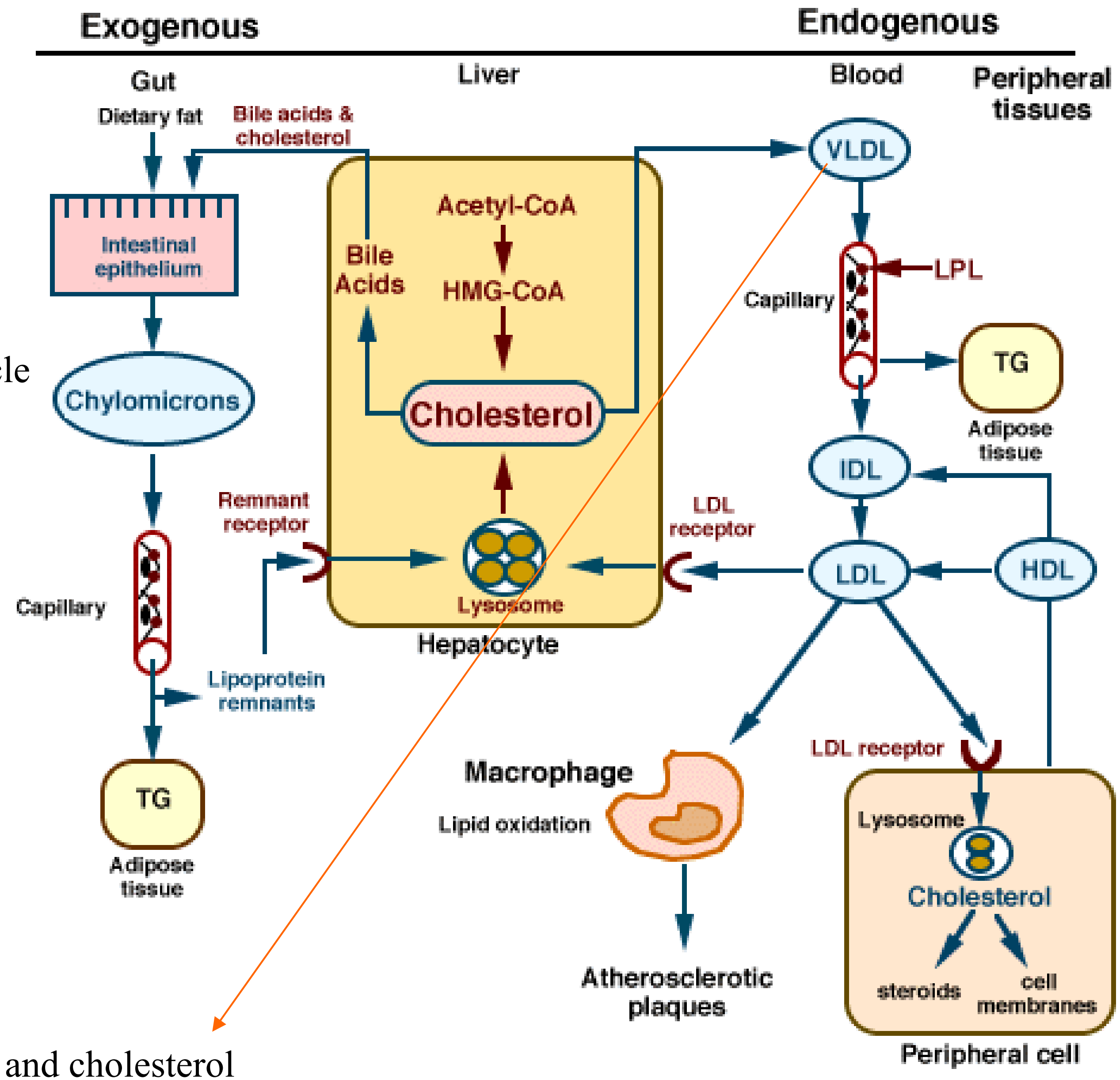
r phase of triacylglycerol absorption.



Deliver dietary TG to muscle and adipose tissue



Transport endogenous TG and cholesterol

Receptor-mediated endocytosis of LDL

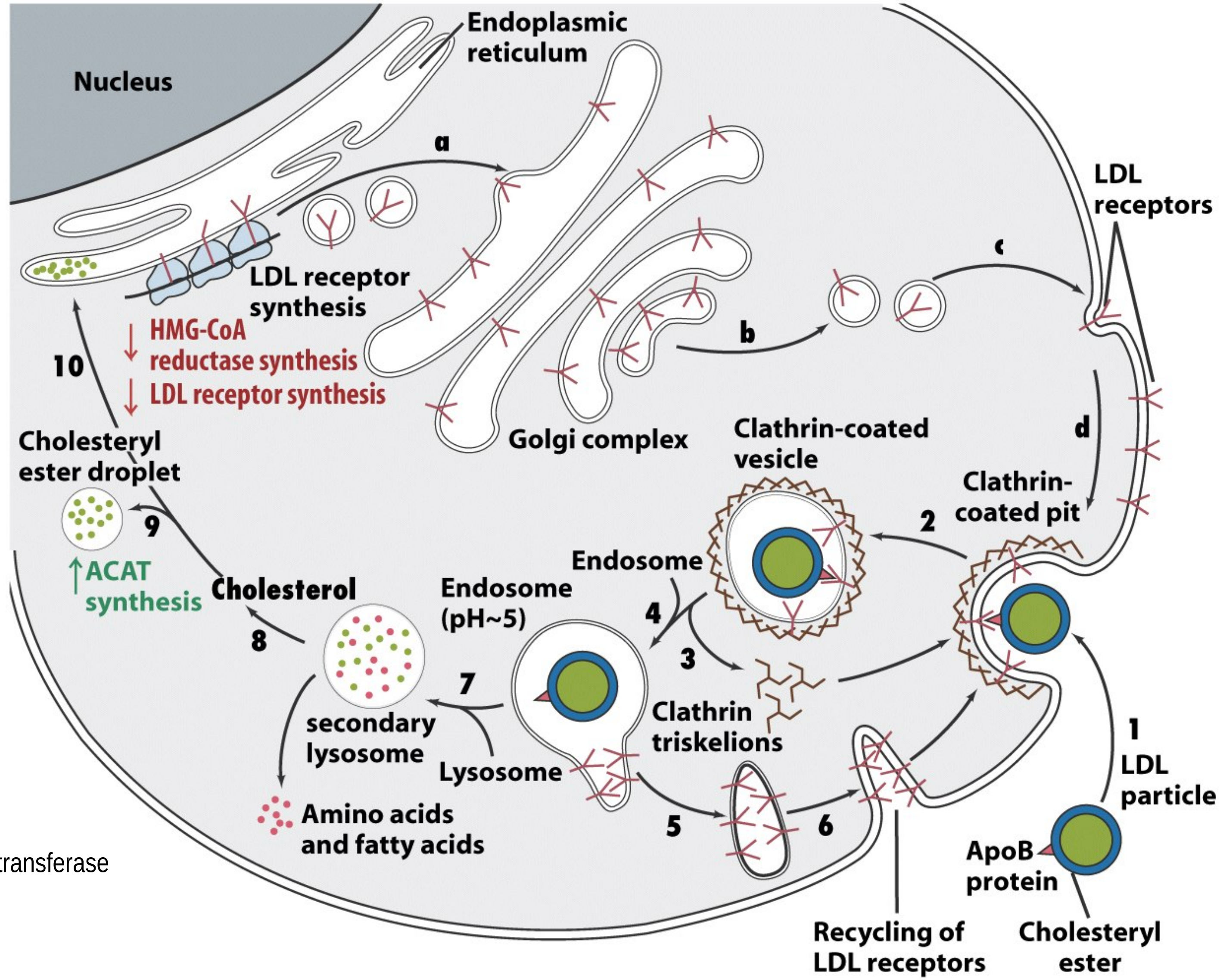


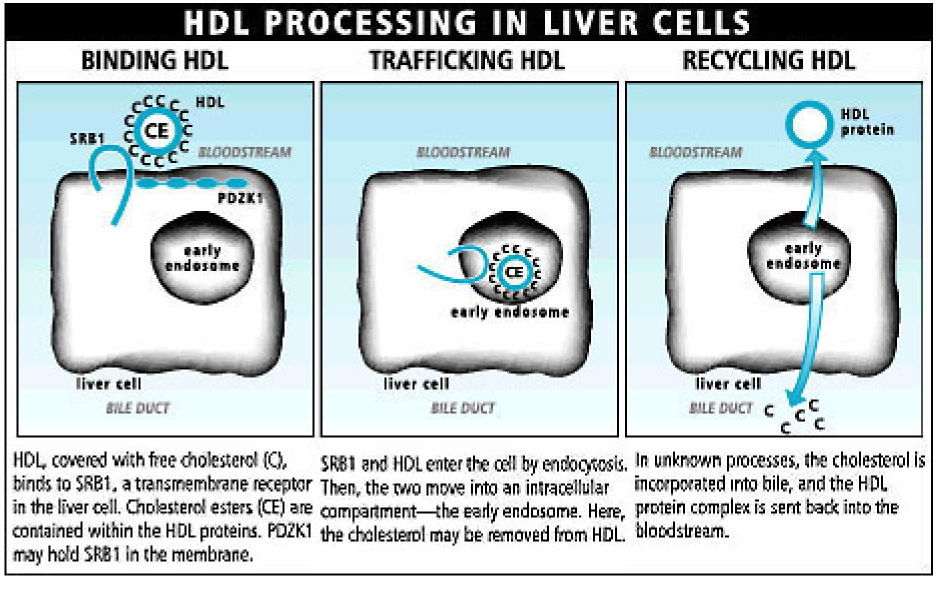
Figure 19-8 Fundamentals of Biochemistry, 2/e

ACAT: acyl-CoA:cholesterol acyltransferase

HDL transports cholesterol from the tissue to the liver

The liver is the only organ capable of disposing of significant quantities of cholesterol (by its conversion to bile acids)

LDL: receptor-mediated endocytosis
HDL: SR-BI (cell-surface receptor)-mediated



http://www.cumc.columbia.edu/publications/in-vivo/Vol1_Iss5_mar11_02/cholesterol.html

Fatty acid oxidation

occur in mitochondria

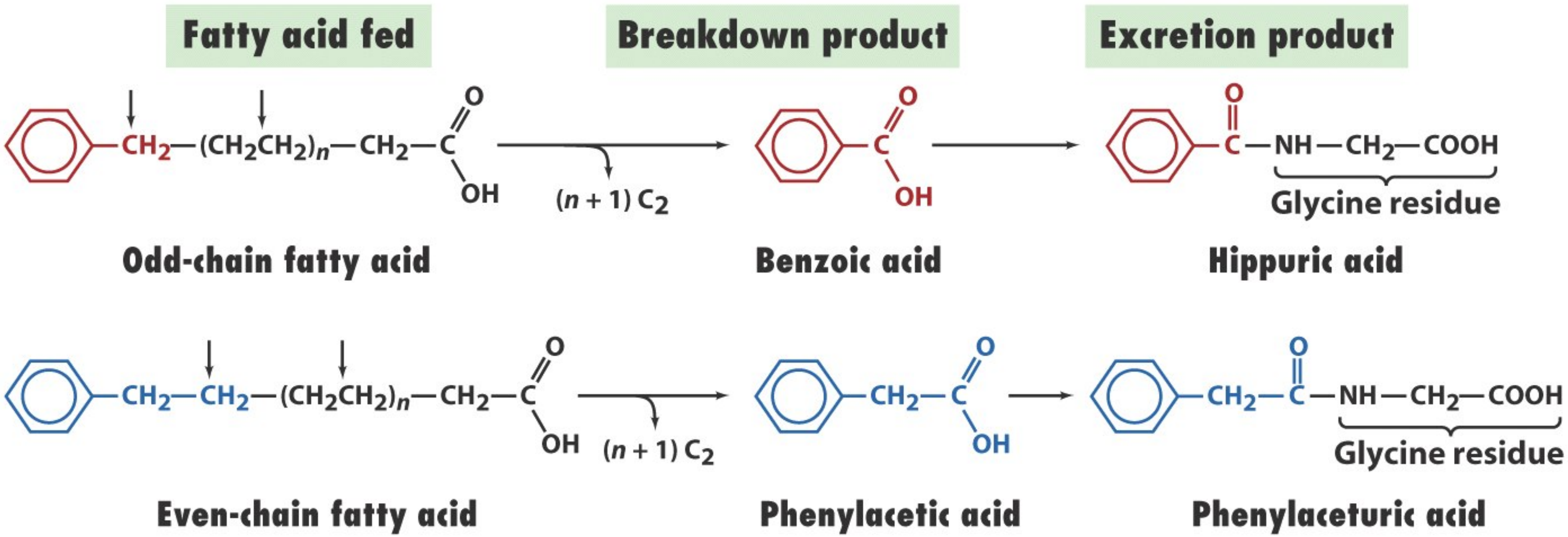


Figure 19-9 Fundamentals of Biochemistry, 2/e

Fatty acid activation

by Acyl-CoA synthetases (thiokinases): ER or outer mito membrane bound
at least 3 families specific to varying chain length

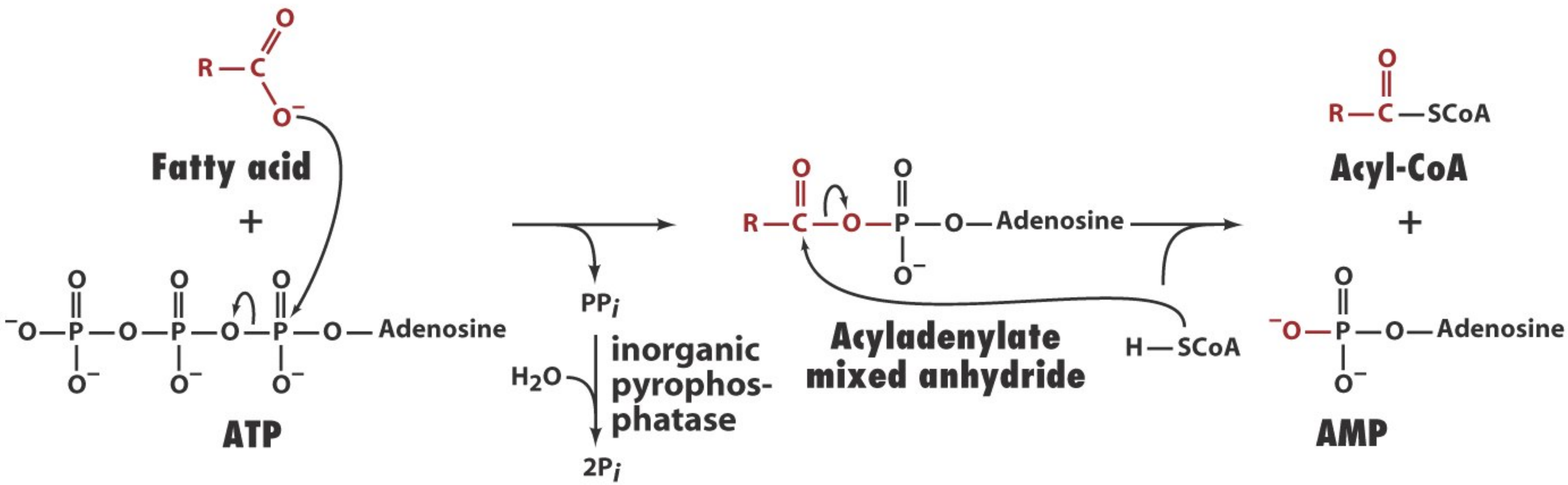
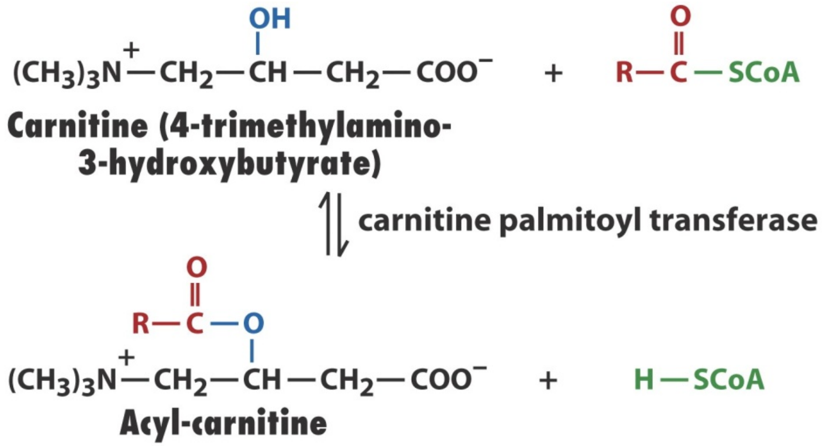


Figure 19-10 Fundamentals of Biochemistry, 2/e

Transport across mito membrane

Medium chain: direct transfer & activation to acyl-CoA
Long chain: carnitine mediated



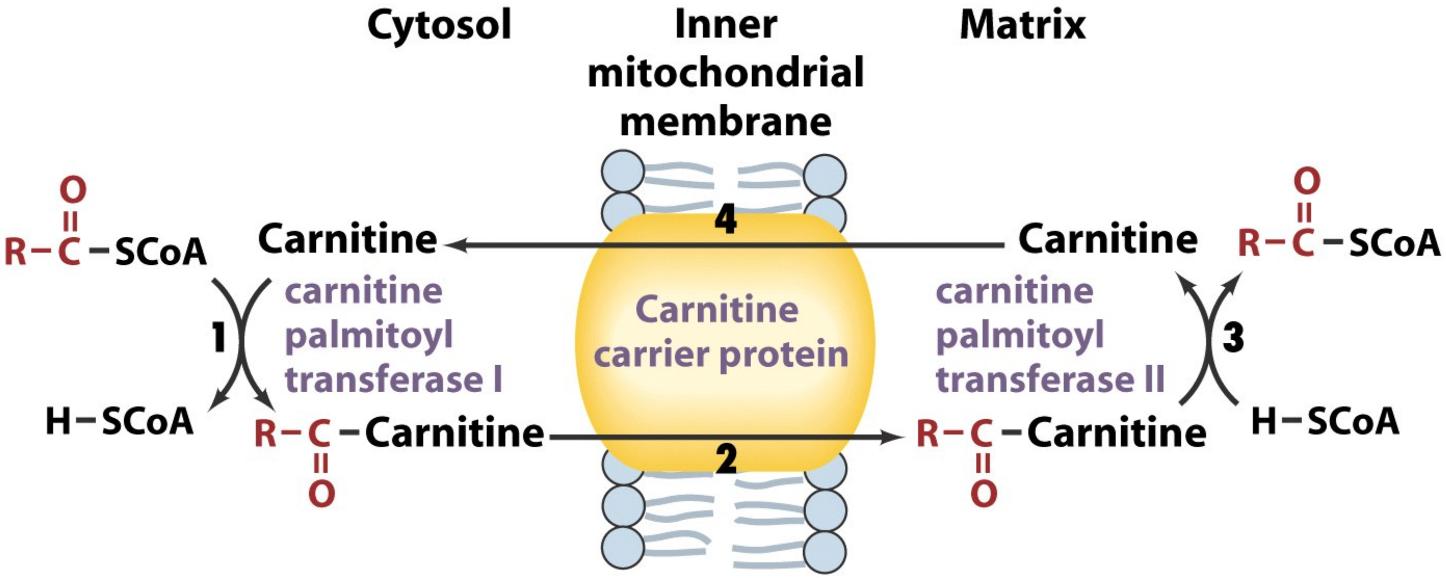


Figure 19-11 Fundamentals of Biochemistry, 2/e

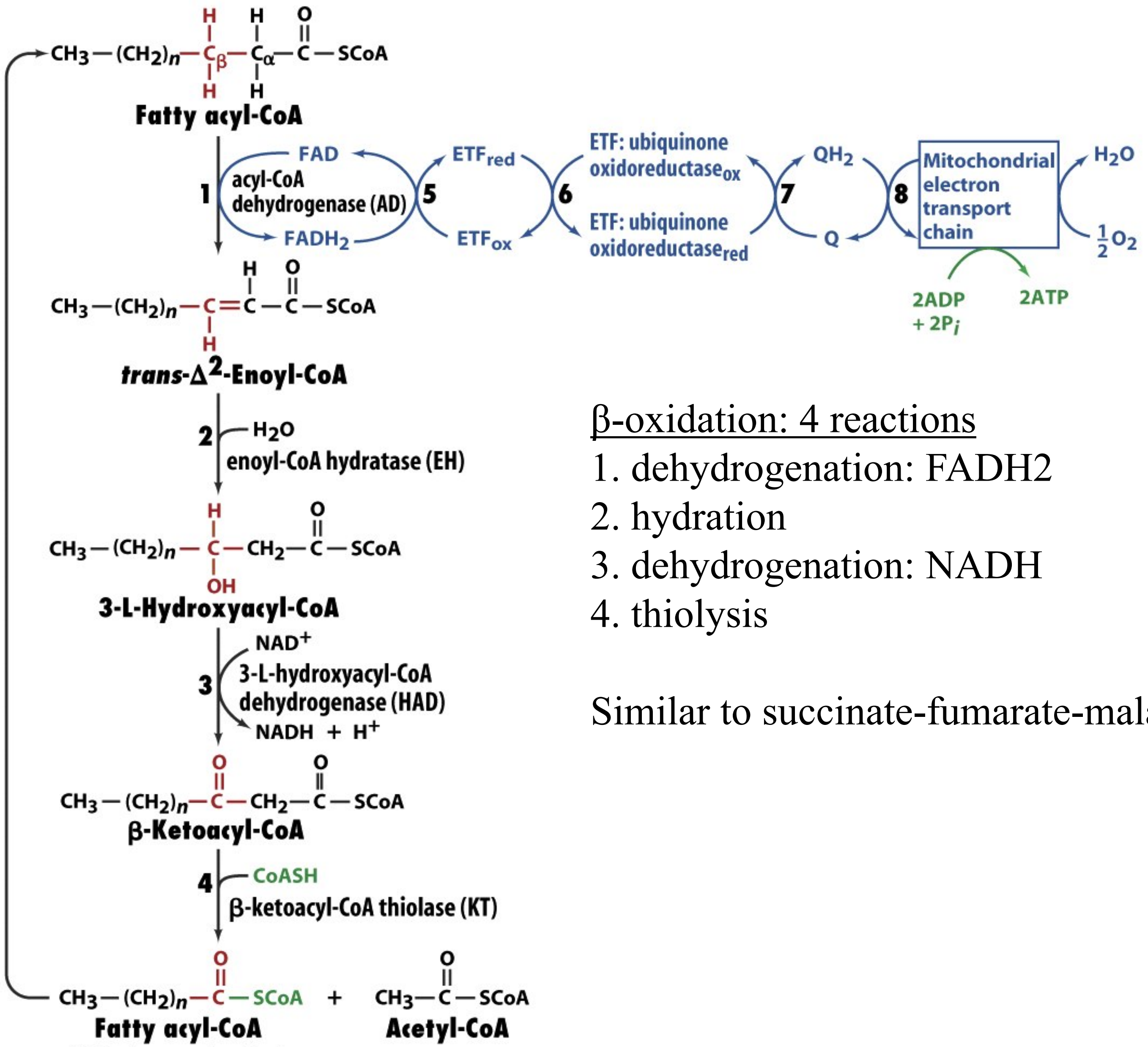


Figure 19-12 Fundamentals of Biochemistry, 2/e

<u>β-oxidation: 4 reactions</u>

1. dehydrogenation: FADH2
2. hydration
3. dehydrogenation: NADH
4. thiolysis

Similar to succinate-fumarate-malate-oxaloacetate