

Metabolism of Lipid (1)

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Outline

- **Introduction**
- **Lipids catabolism**
 - **Mobilization of fats (TG) from dietary intake and adipose tissues**
 - **Fatty acids oxidation**
 - **Ketone bodies**
 - **Regulation of FAs metabolism**
- **Lipids biosynthesis**
 - **FAs biosynthesis**
 - **Biosynthesis of TG, complex lipids and cholesterol**
 - **Lipid transport**



1. Introduction



A grizzly bear prepares its hibernation nest, near the McNeil River in Canada.

expending about 25,000 kJ/day (6,000 kcal/day)



FIGURE 24.1 • Scanning electron micrograph of an adipose cell (fat cell). Globules of triacylglycerols occupy most of the volume of such cells. (Prof. P. Motta, Dept. of Anatomy, University "La Sapienza," Rome/Science Photo Library/Photo Researchers, Inc.)

- **Lipids** : insolubility or lower solubility in water.
- Highly soluble in **non-polar** (非极性) solvents.
- Their water-insolubility contributes to much of the complexity in their digestion, transport, and metabolism.

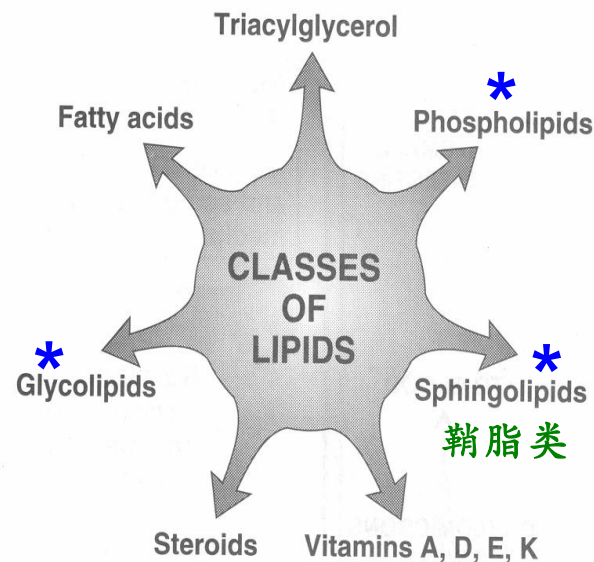


Figure 16.1
Classes of lipids.

* polar, more amphipathic lipids 4

lipid Categories (Chemical Composing) :

➤ Simple lipid (单纯脂质) :

-- glyceride (甘油酯), wax (蜡)

➤ Compound lipid (复合脂质) :

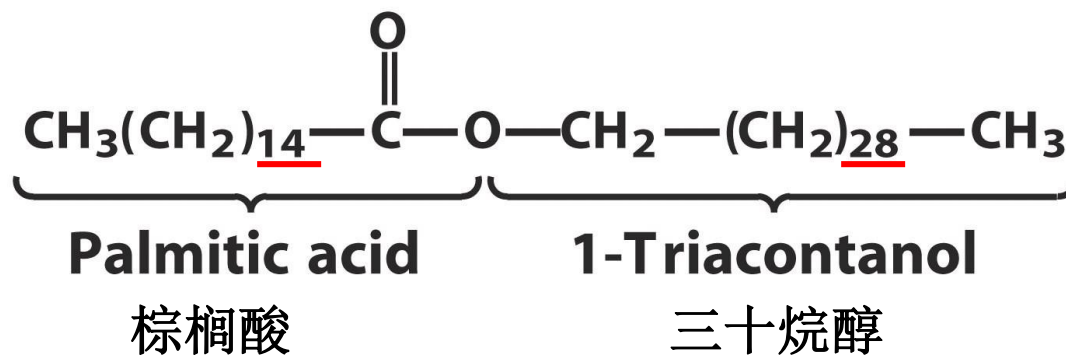
-- phosphatidate (磷脂), glycolipid (糖脂)

➤ Derived lipid (衍生脂质) :

-- sterol (固醇类), terpene (萜)

➤ Biological waxes

- high melting points
- energy stores
- water-impermeable (不透水) coatings.



Triacontanyl-palmitate is the major component of bees wax.

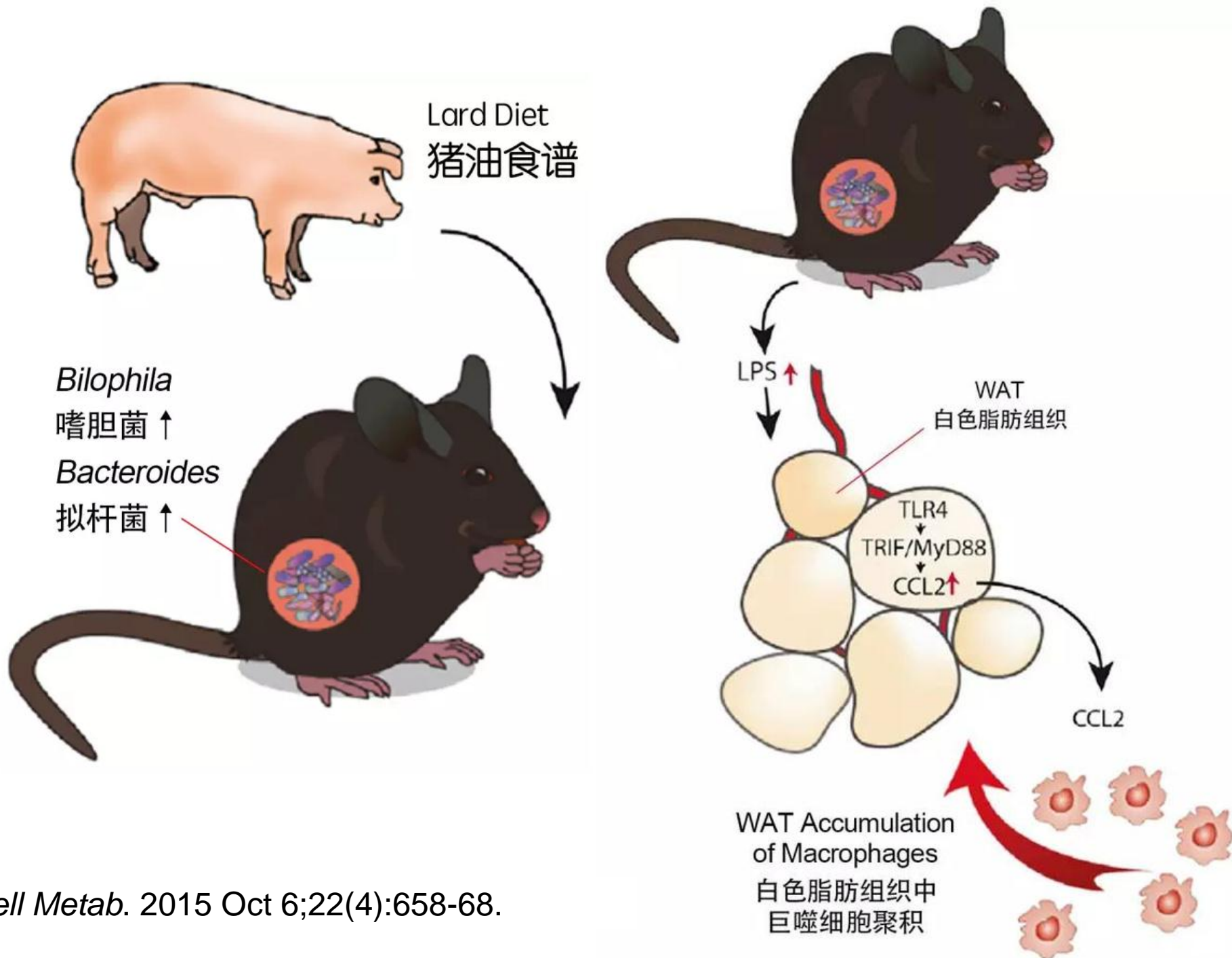
Simple lipid (单纯脂质)

➤ Natural oils mainly contain triacylglycerols with **unsaturated** fatty acids



➤ Solid fats contain primarily **saturated** fatty acids
-- high melting temperature.





lipid biological roles

- **Storage lipid**
- **Structural lipid**
- **Active lipid**

FATTY ACID CATABOLISM

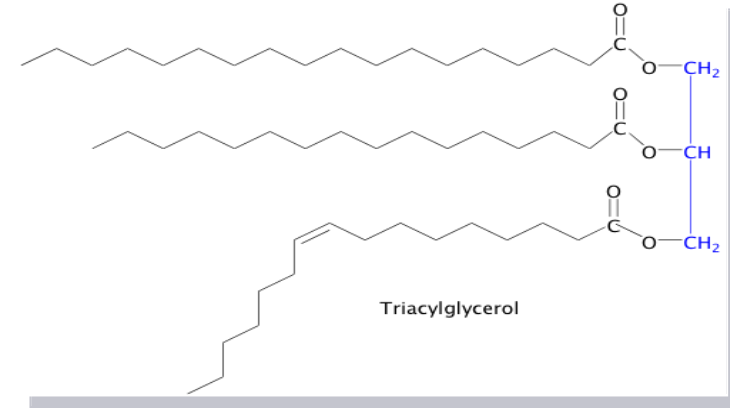
outline

- **Introduction to FA**
- **Mobilization of fats (TG) from dietary intake and adipose tissues**
- **fatty acids oxidation**
- **Ketone bodies (酮体)**
- **FA metabolism regulation and control**

1. Introduction to fatty acids (FAs)

Fatty acids play important roles:

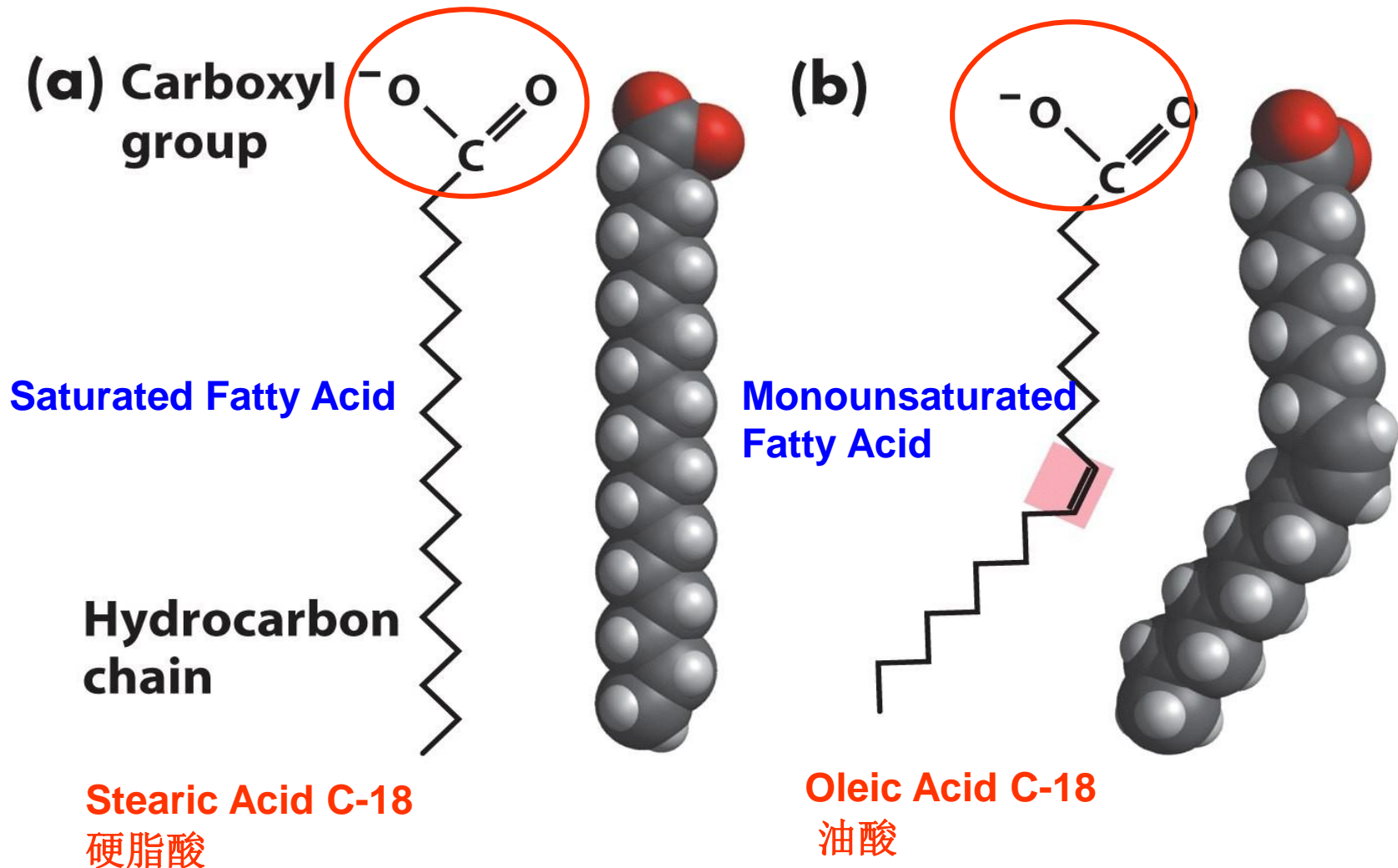
- 1) Building blocks for phospholipids(磷脂) & glycolipids(糖脂)**
- 2) Target proteins to membranes**
- 3) High energy source of fuel**
- 4) Hormones or messengers**



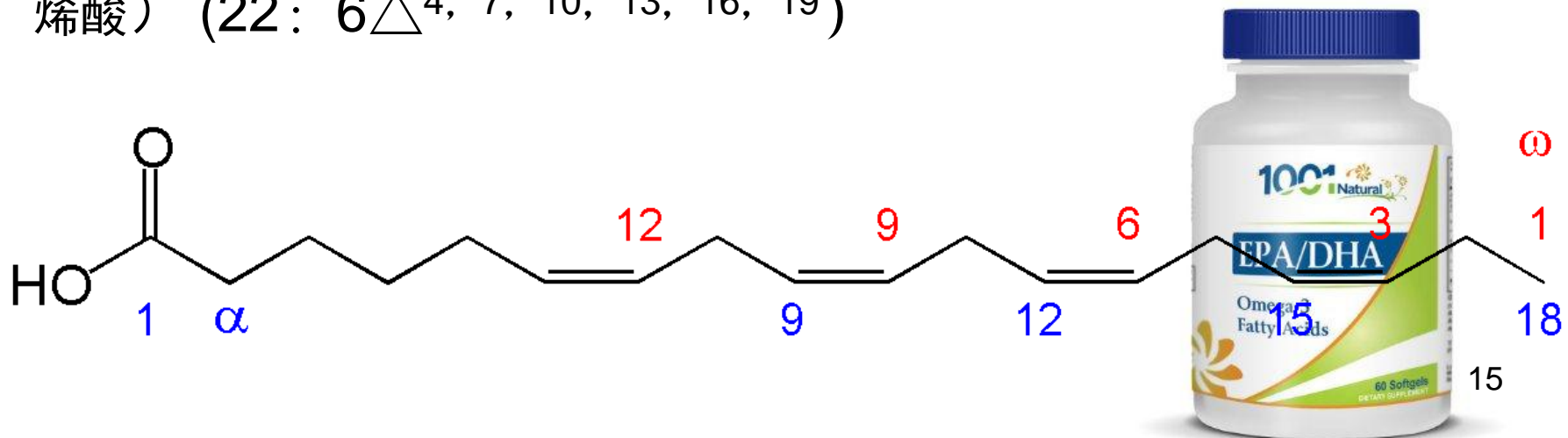
- Two **sources** of FA: **stored** and **dietary fats**
- FAs represent the principal form of stored energy in TG
(**triacylglycerols**/ **triglycerides**, 甘油三酯) (**brown and white fat**)
- The carbon in fatty acids ($-\text{CH}_2$) is **completely reduced**
- Fatty acids are **not hydrated**, so can pack more closely in storage tissues

fatty acid class

Saturated FA ; unsaturated FA ; polyunsaturated FA



- palmitic (软脂酸) (16: 0)、stearic (硬脂酸) (18: 0)
- Palmitoleic (棕榈油酸) (16: 1 \triangle^9)、oleic (18: 1 \triangle^9)
- Linoleic(亚油酸) (18: 2 $\triangle^{9, 12}$)、 α -linolenic (α -亚麻酸) (18: 3 $\triangle^{9, 12, 15}$)、 γ -liolenic (γ -亚麻酸) (18: 3 $\triangle^{6, 9, 12}$)、arachidonic (花生四烯酸) (18: 3 $\triangle^{5, 8, 11, 14}$)、**EPA** (20碳五烯酸) (20: 5 $\triangle^{5, 8, 11, 14, 17}$)、**DHA** (22碳六烯酸) (22: 6 $\triangle^{4, 7, 10, 13, 16, 19}$)



FA structure characteristics

- **even** carbon numbers
- the first twin bond – the **9th**,
the second, third -
the **12th** , **15th** ;
- most double bond is **cis**

坏油 富含反式脂肪酸



中性油 富含饱和脂肪酸



好油 富含单不饱和脂肪酸

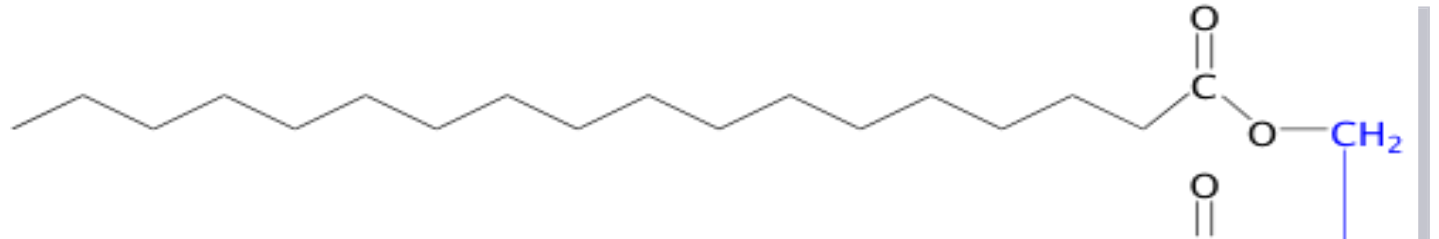


好油 富含多不饱和脂肪酸

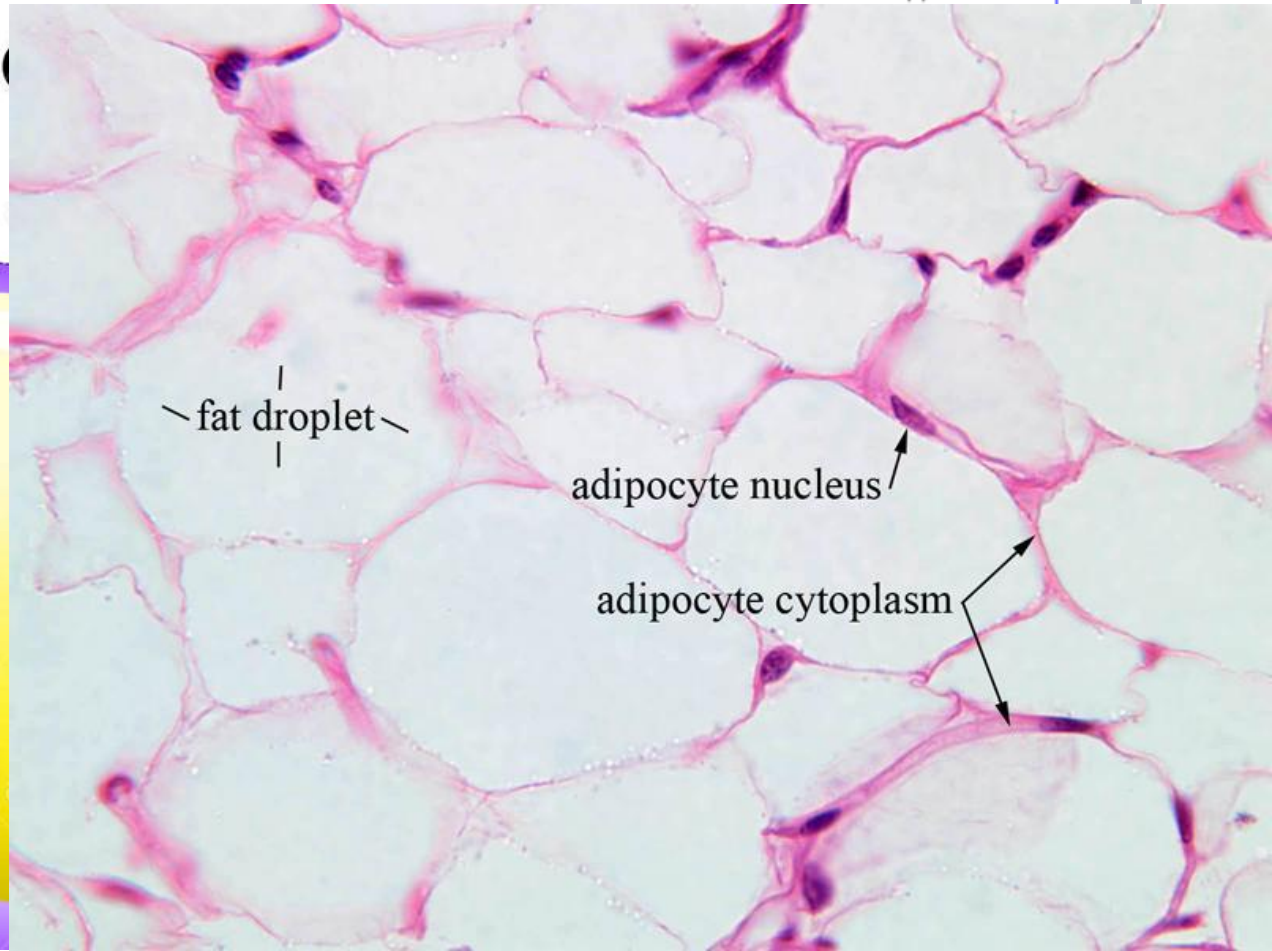
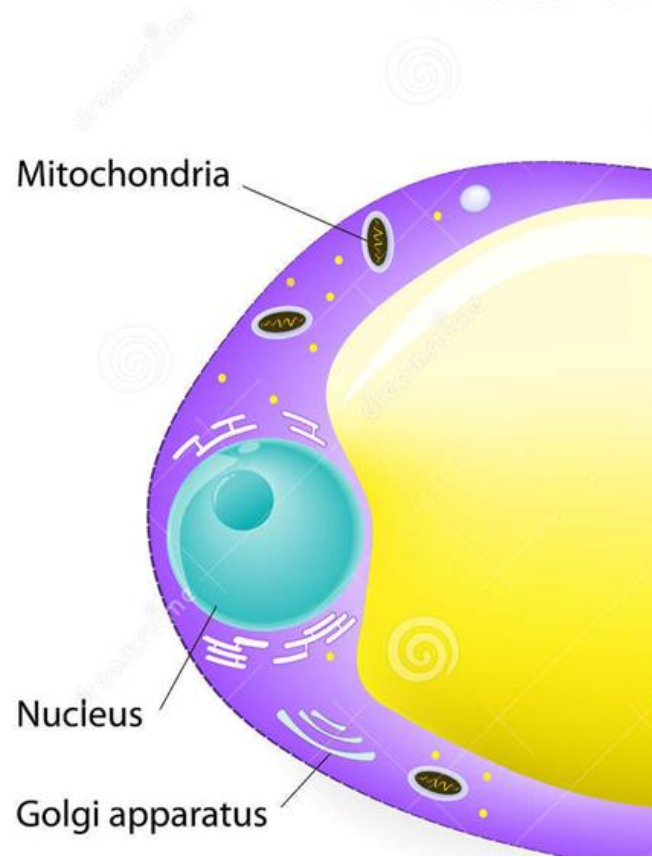


Triglycerides(甘油三酯, TG)

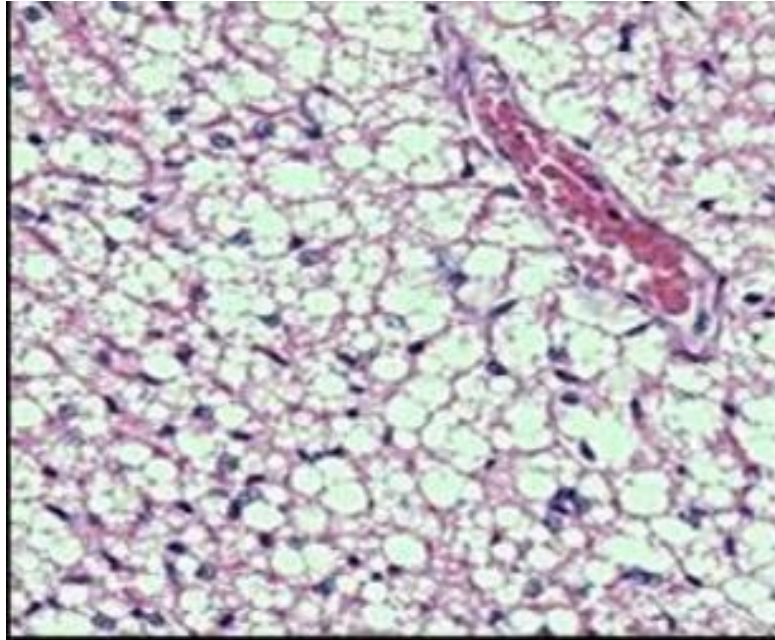
9 kcal/g vs 4 kcal/g for glycogen



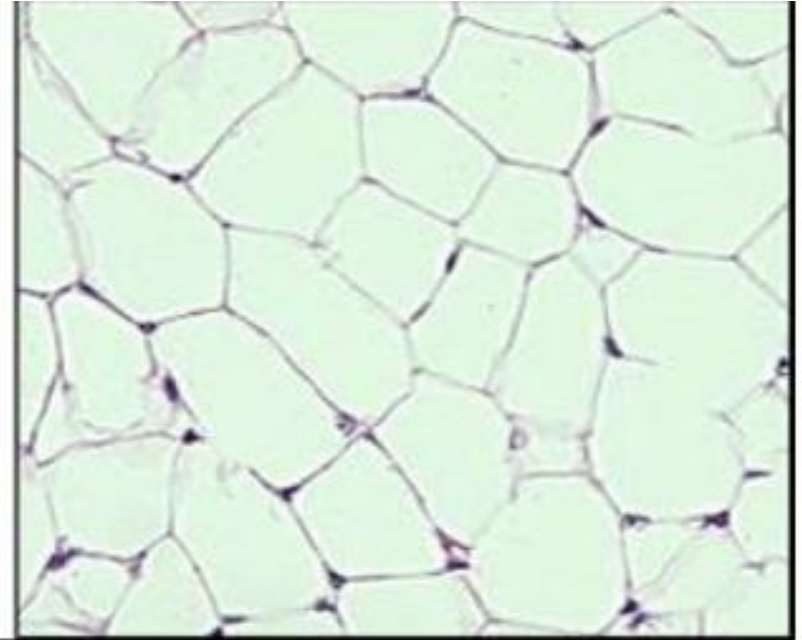
ADIPO



Brown and white fat

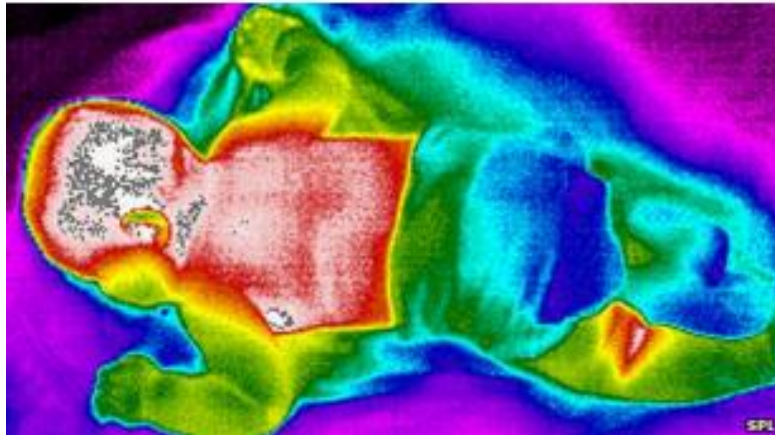


GOOD BROWN FAT



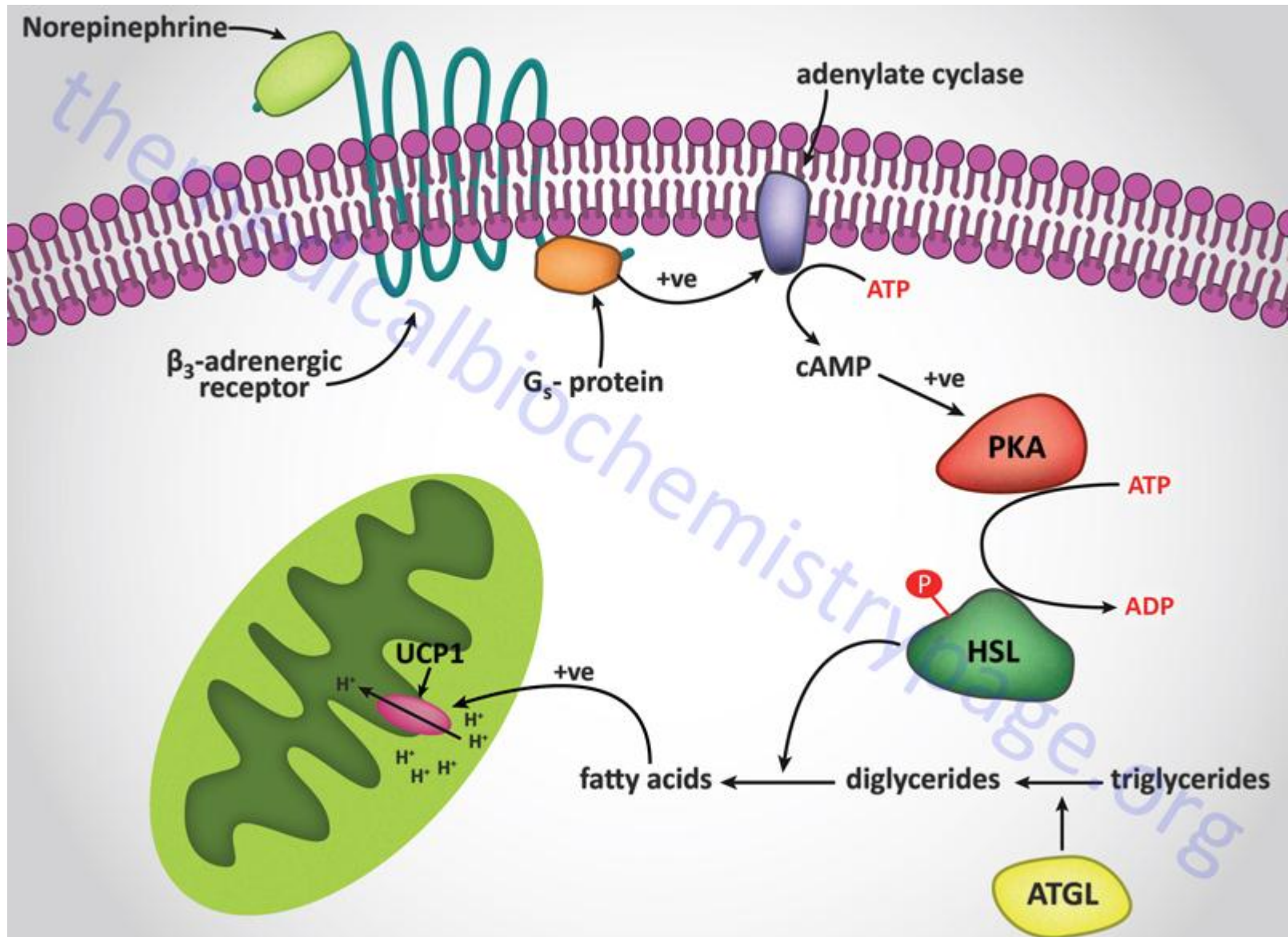
BAD WHITE FAT

**20% of body weight in man and
25% in woman**

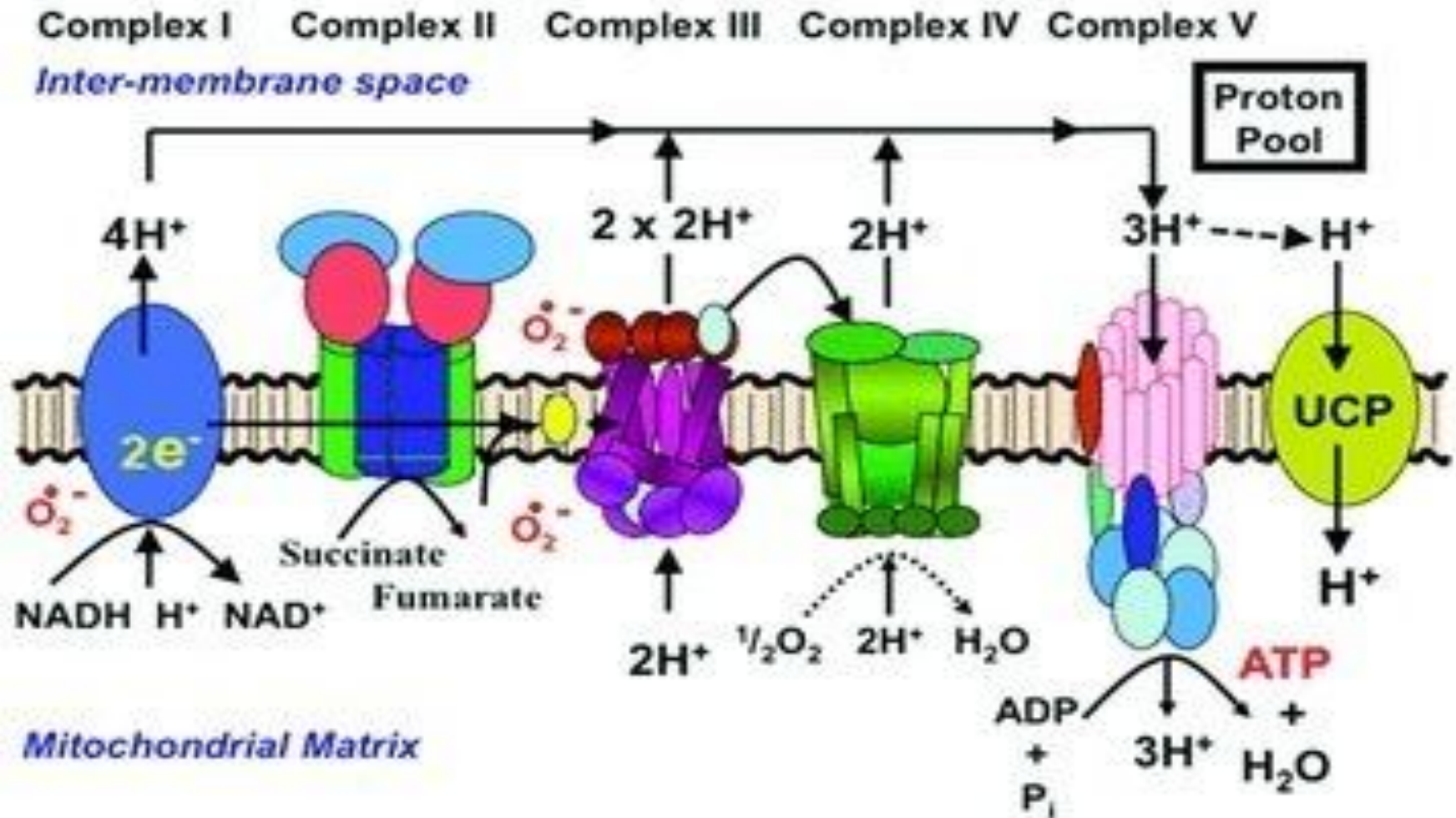


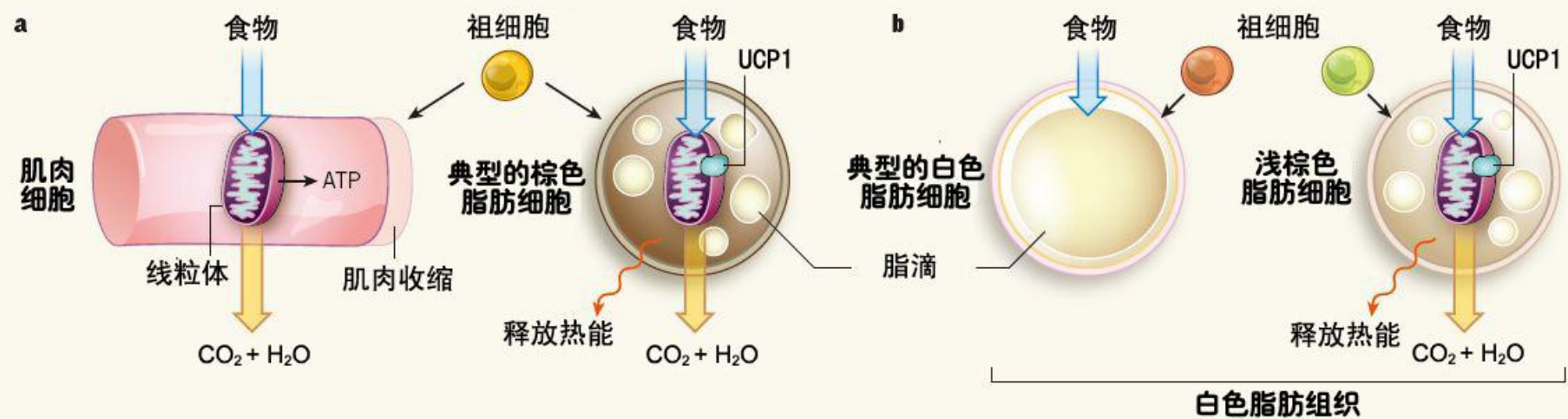
Brown fat in new-born infant

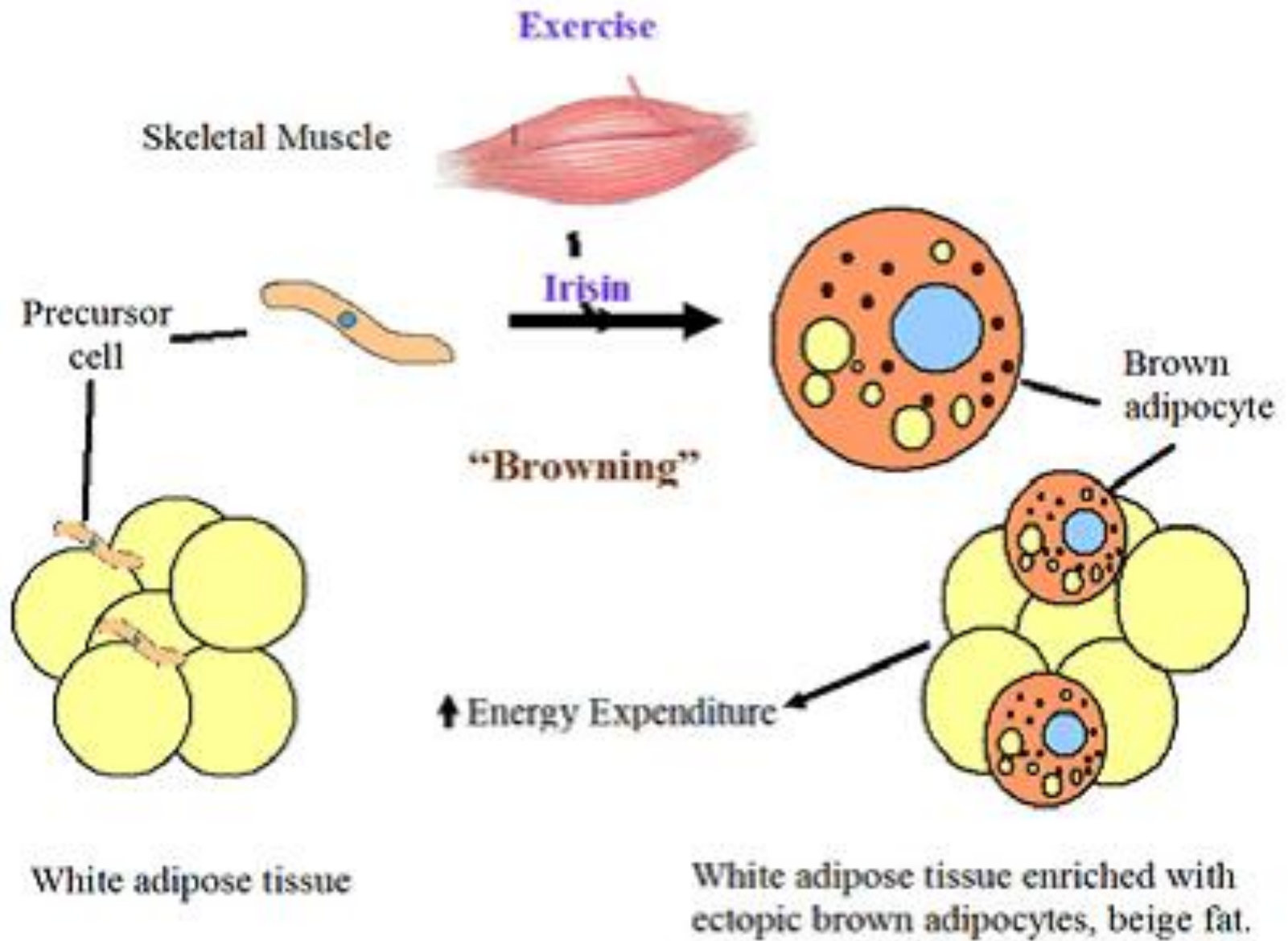
Action of Thermogenin (UCP1) in brown fat cells

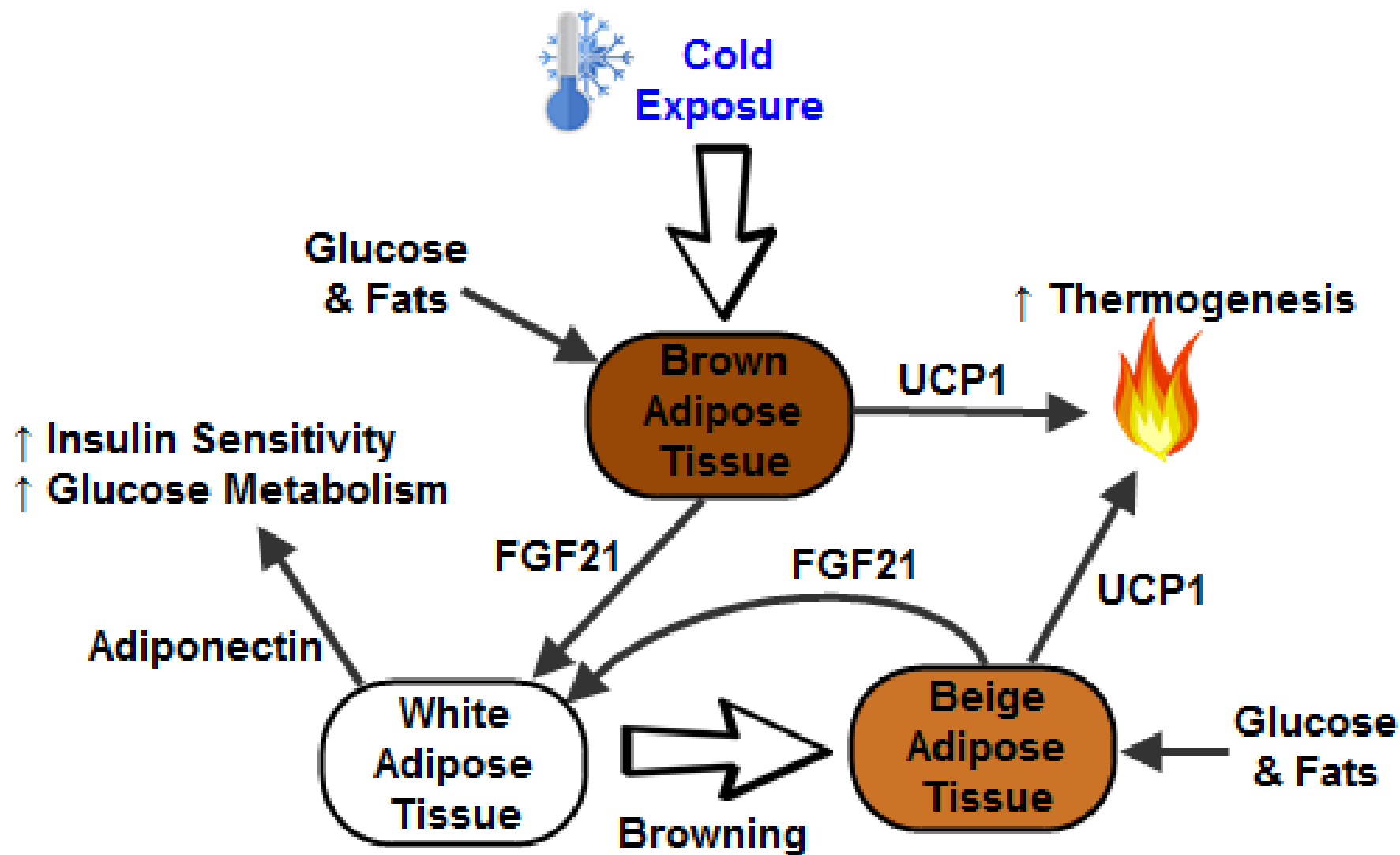


Oxidative phosphorylation and UCP

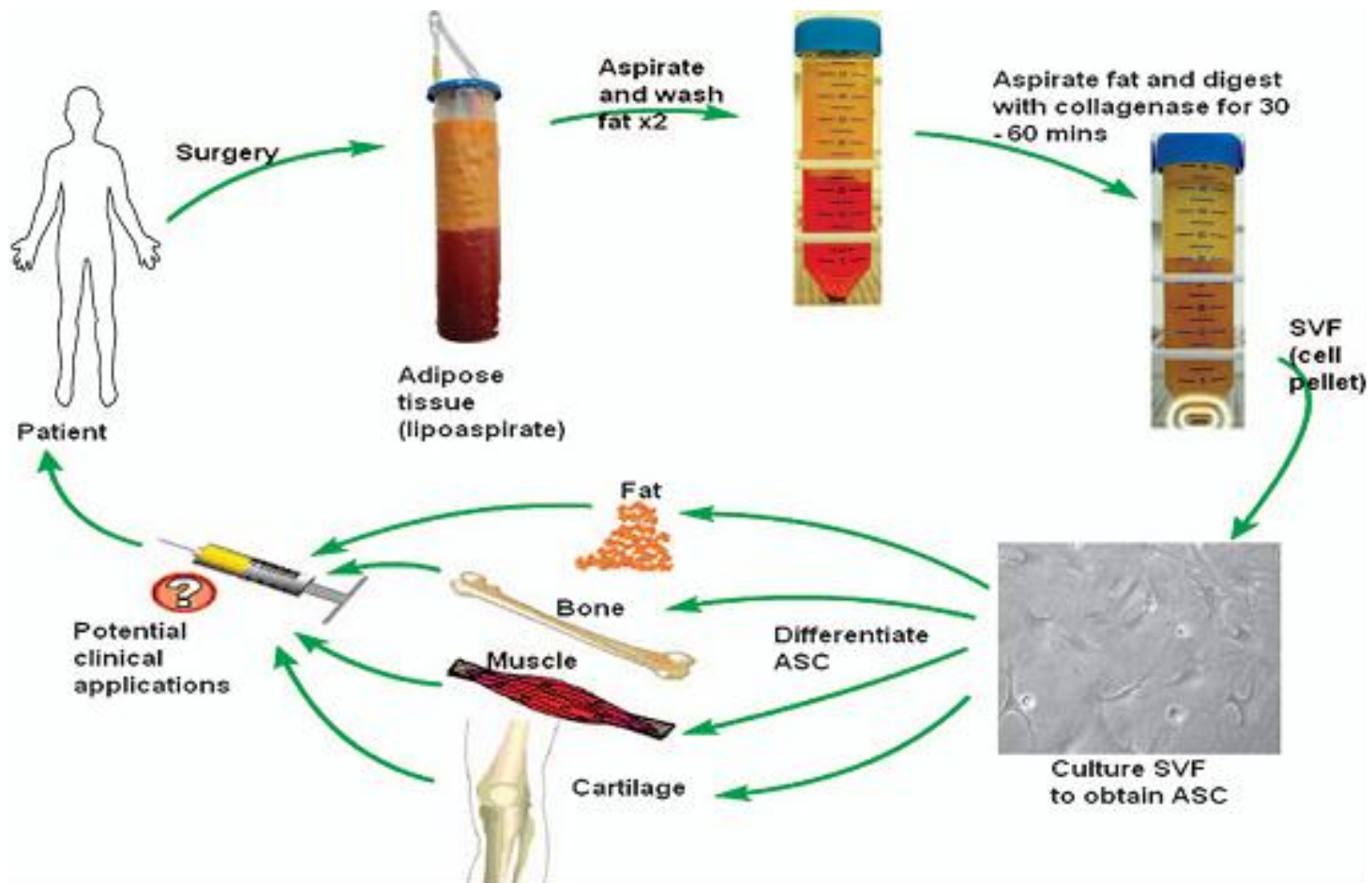








tissue repair and cells regeneration



ANZ J Surg. 2009 Apr;79(4):235-44

Stored metabolic fuel in a 70kg person

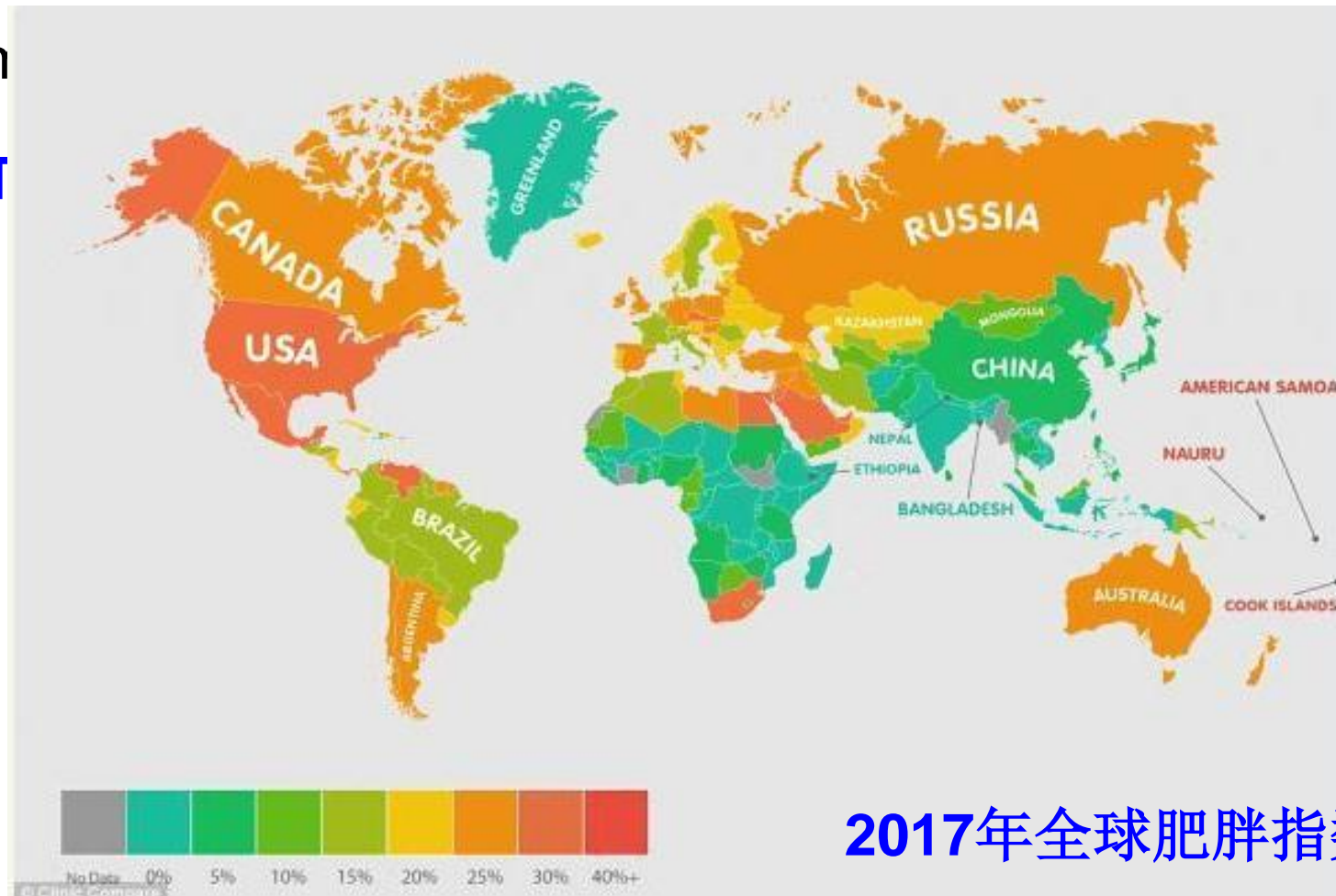
Constituent	Energy (KJ/g dry weight)	Dry weight (g)	Available energy (KJ)
Fat (adipose tissue)	37	15,000	555,000
Protein (Muscle)	17	6,000	102,000
Glycogen (muscle)	16	120	1,920
Glycogen (Liver)	16	70	1,120
Glucose (extracellular fluid)	16	20	320
Total			660,360

Fat from Diet & Adipose Cells

- **Diet fat** or **carbohydrates** or **aa**
- **TGs** represent the major energy input in the diet of the

n

- T

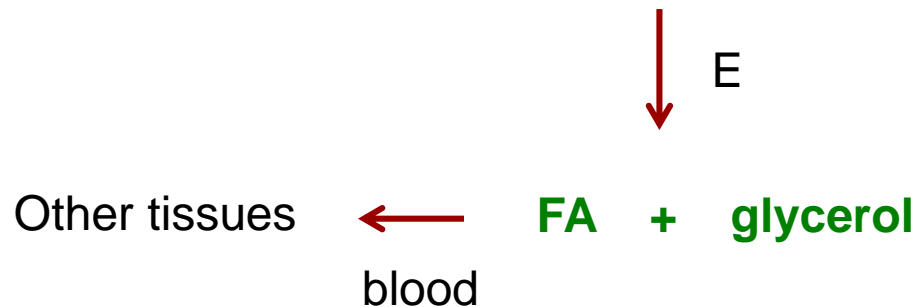


2017年全球肥胖指数

2. Mobilization of fats from dietary intake and adipose tissues

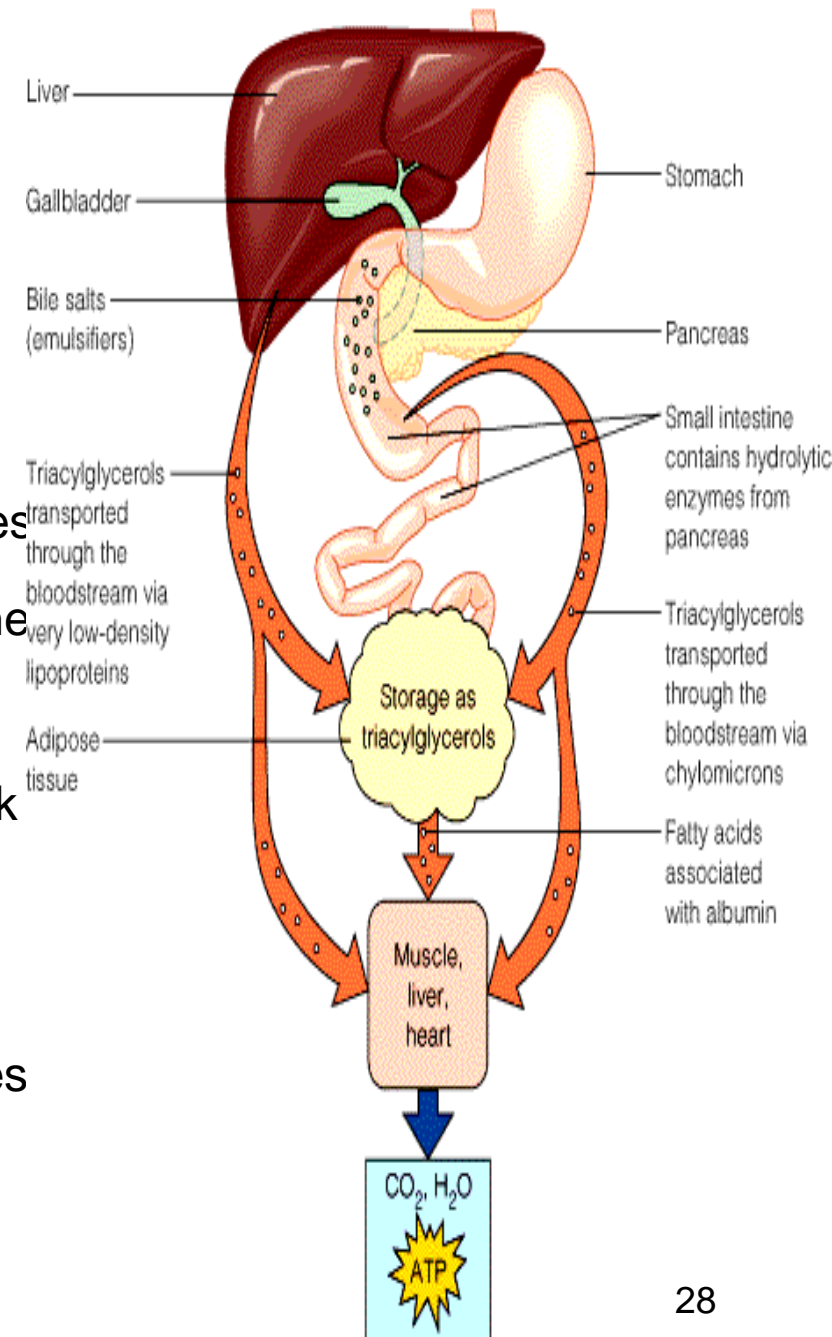
- Degradation of dietary triacylglycerols in the duodenum

- Mobilization of fats: fats (adipose)



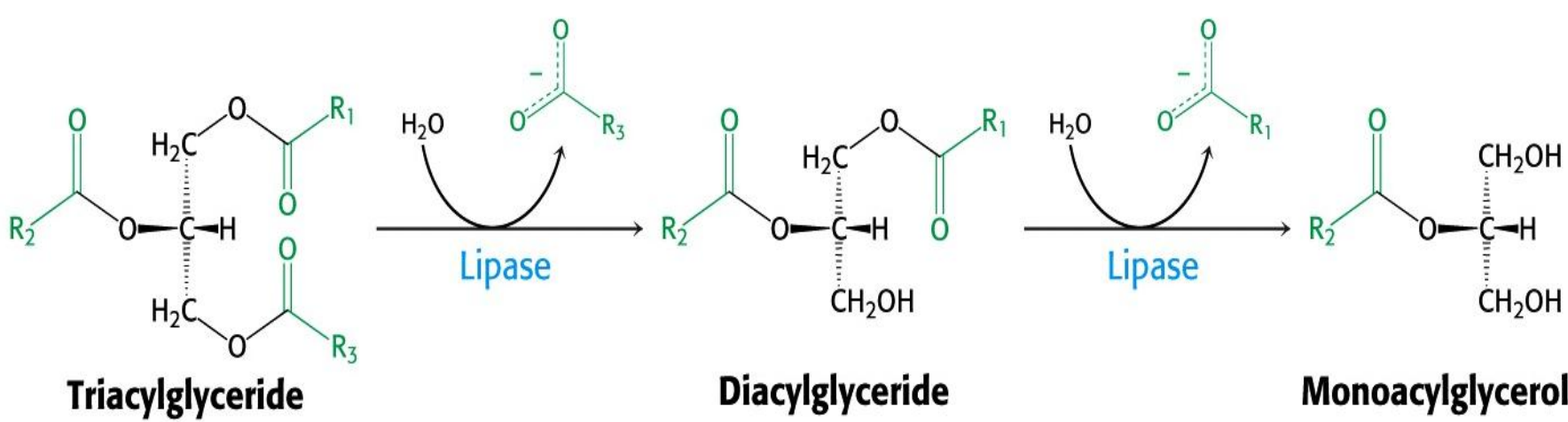
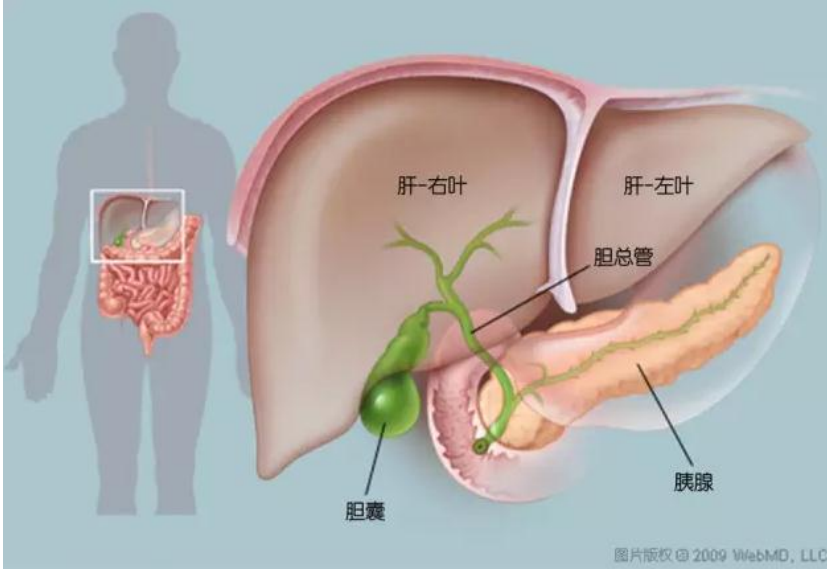
Degradation of dietary TGs

- In the **stomach**, a small extent by lipases
- In the **duodenum**, alkaline pancreatic juice raises pH, allowing hydrolysis of TG by pancreatic lipase and by non-specific esterases
- **Pancreatic lipase** releases fatty acids from the C-1 and C-3 position of TG
- Other lipases and nonspecific esterases attack the C-2 position
- **Bile salts** emulsifies (乳化) TGs and facilitate the activity of the lipase and esterases



dietary fat digestion (消化)

Pancreatic Lipases (胰脂肪酶)



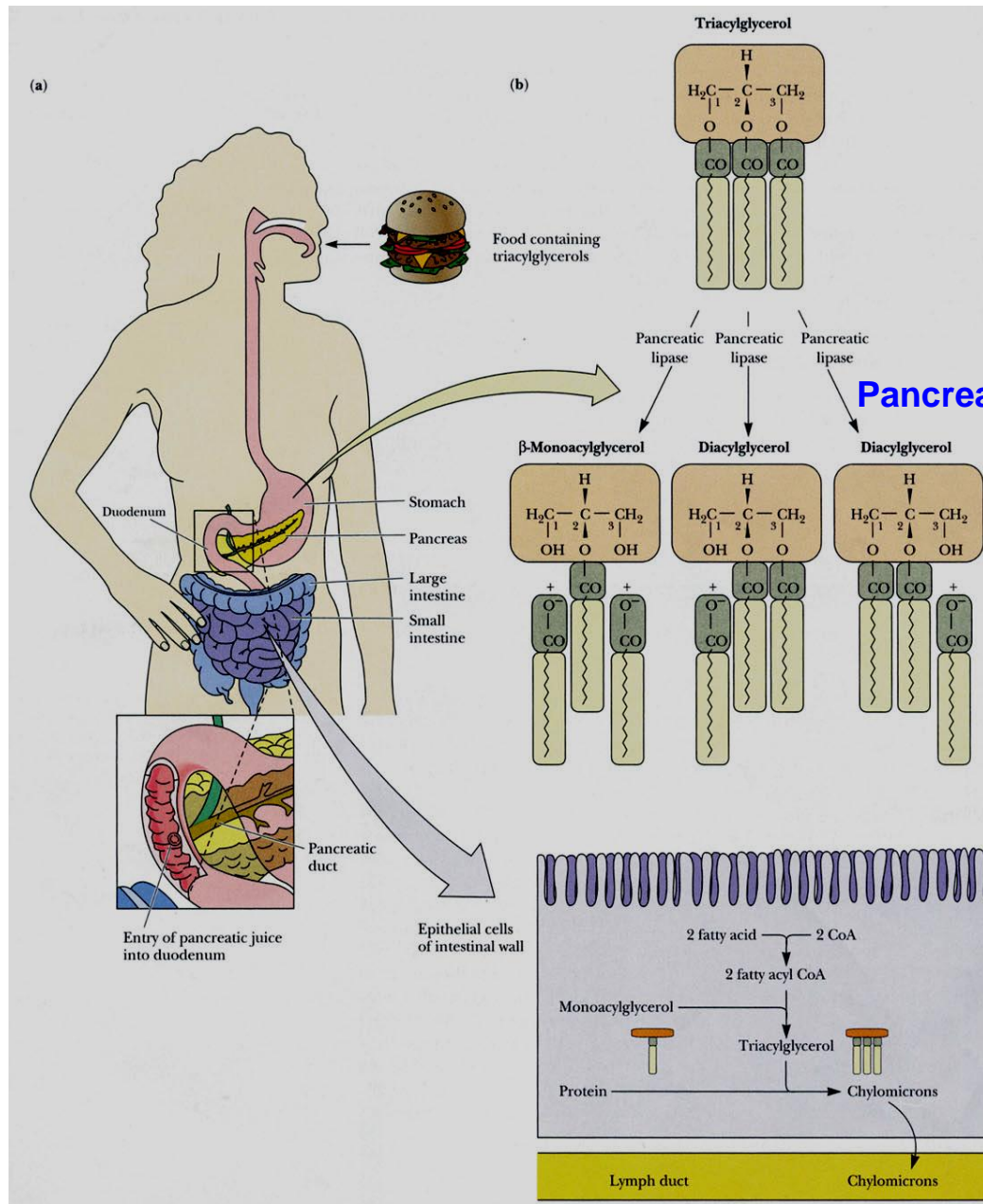
Pancreatic Lipases

Colipase (辅脂酶)

Pancreatic Lipases

Colipase (辅脂酶)

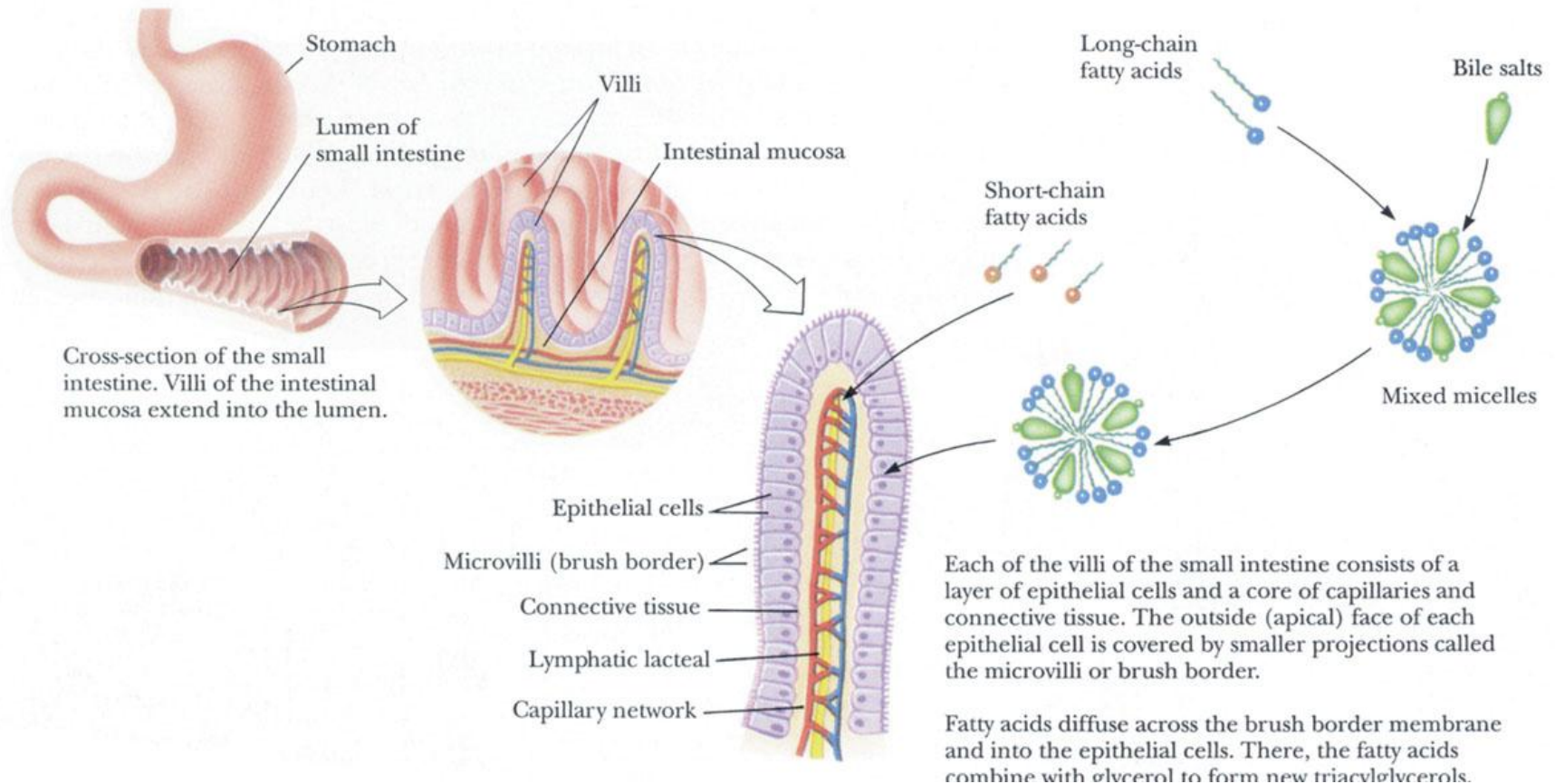
Degradation of dietary TGs

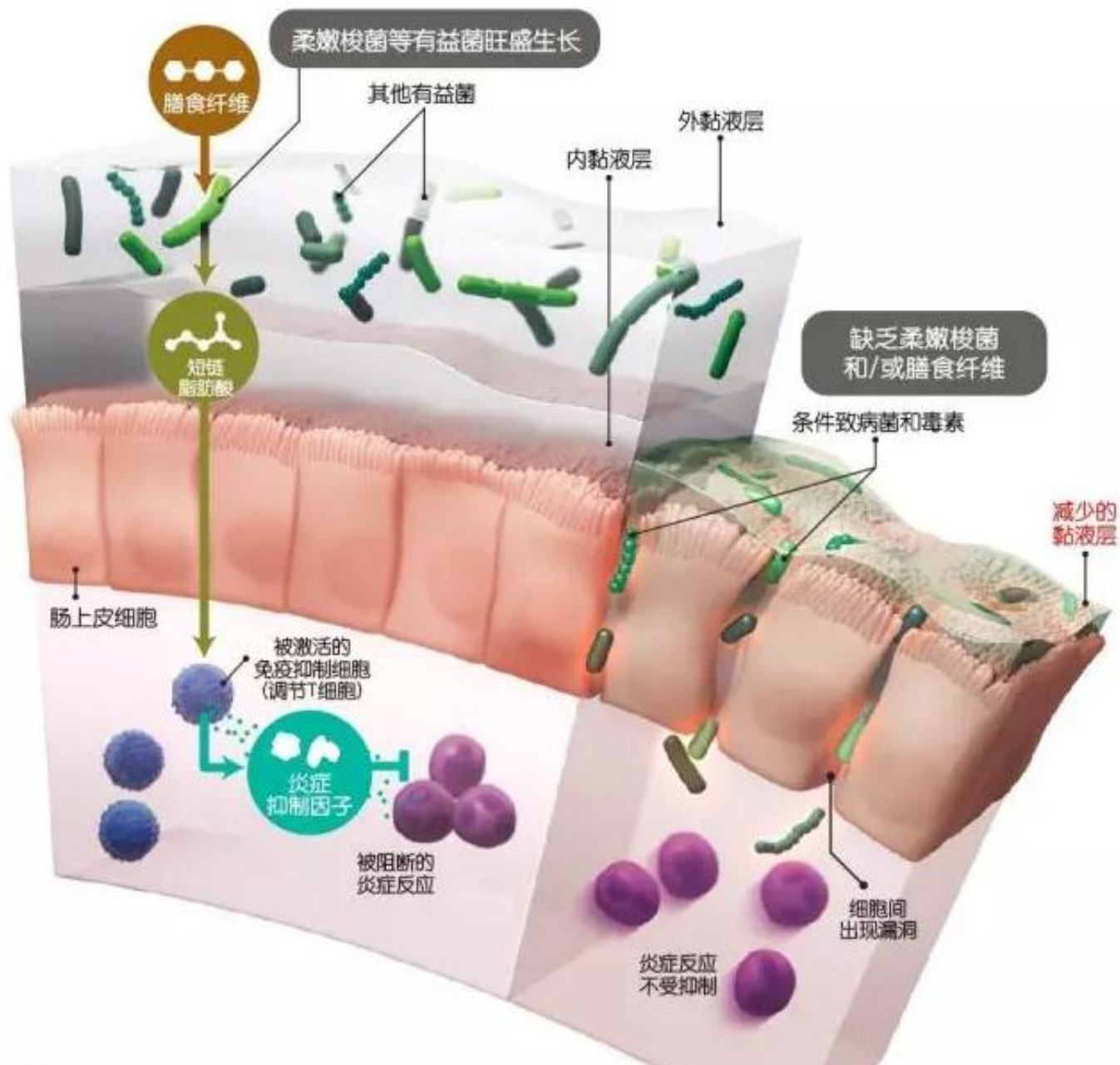


Pancreatic Lipases (胰脂肪酶)

Absorption (吸收) and storage

- Short chain FAs absorbed directly into the **intestinal mucosa**
- Long chain FAs ($\geq 12C$) with **bile salts** in mixed **micelles**, which deliver FAs to **epithelial cells** to form new TGs.

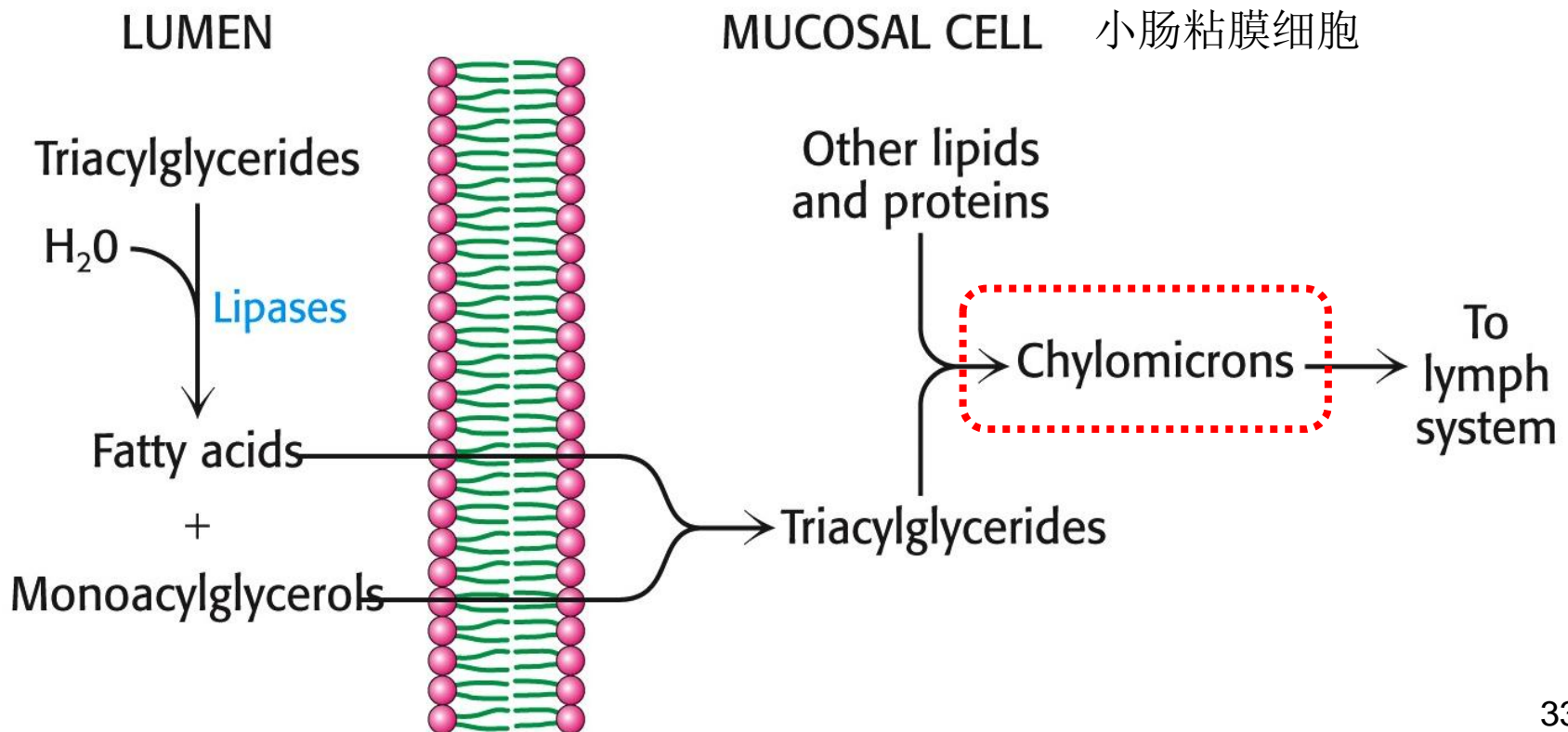




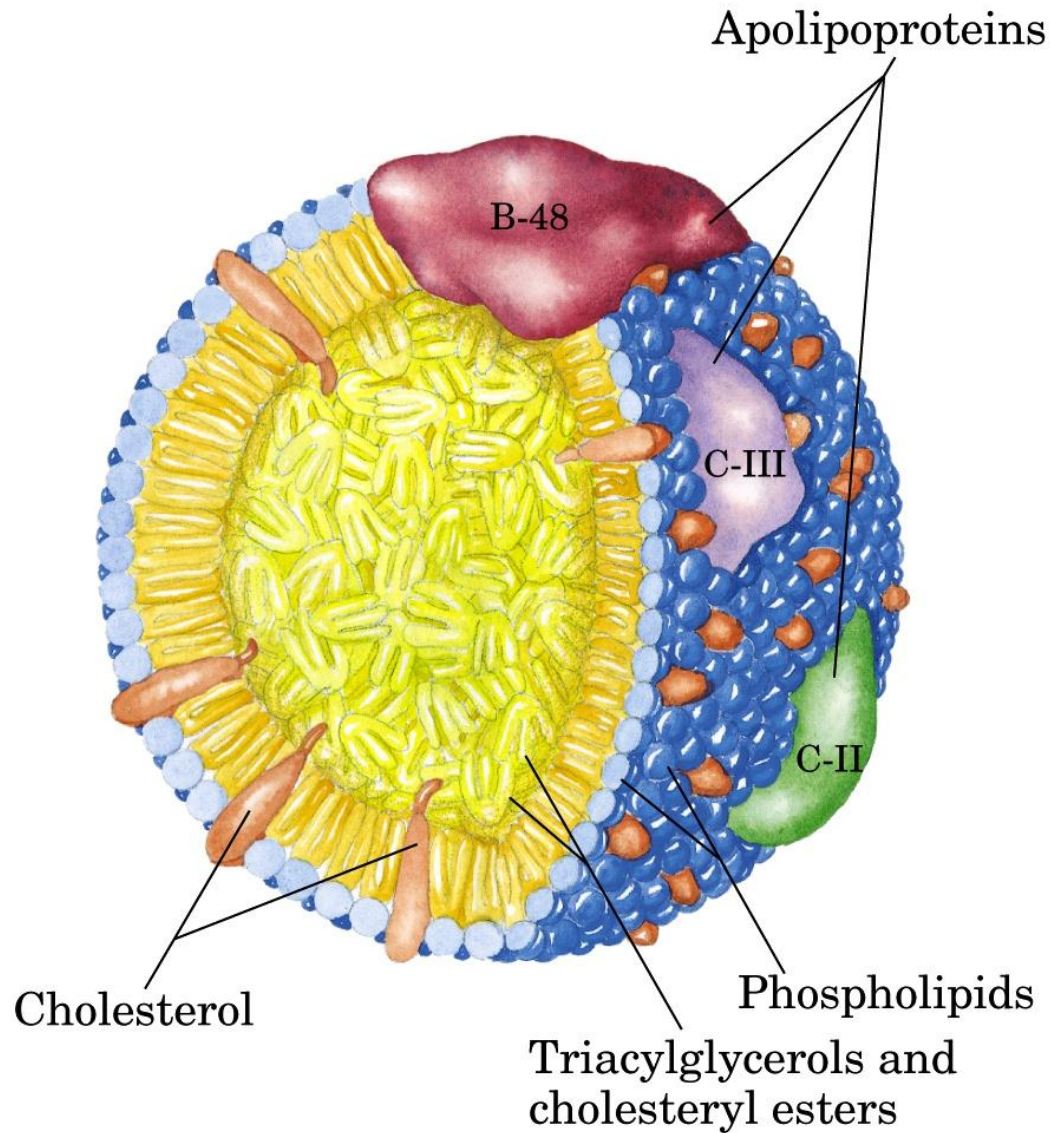
Nat Rev Gastroenterol Hepatol. 2015 Apr;12(4):205-17.

Absorption (吸收) and storage

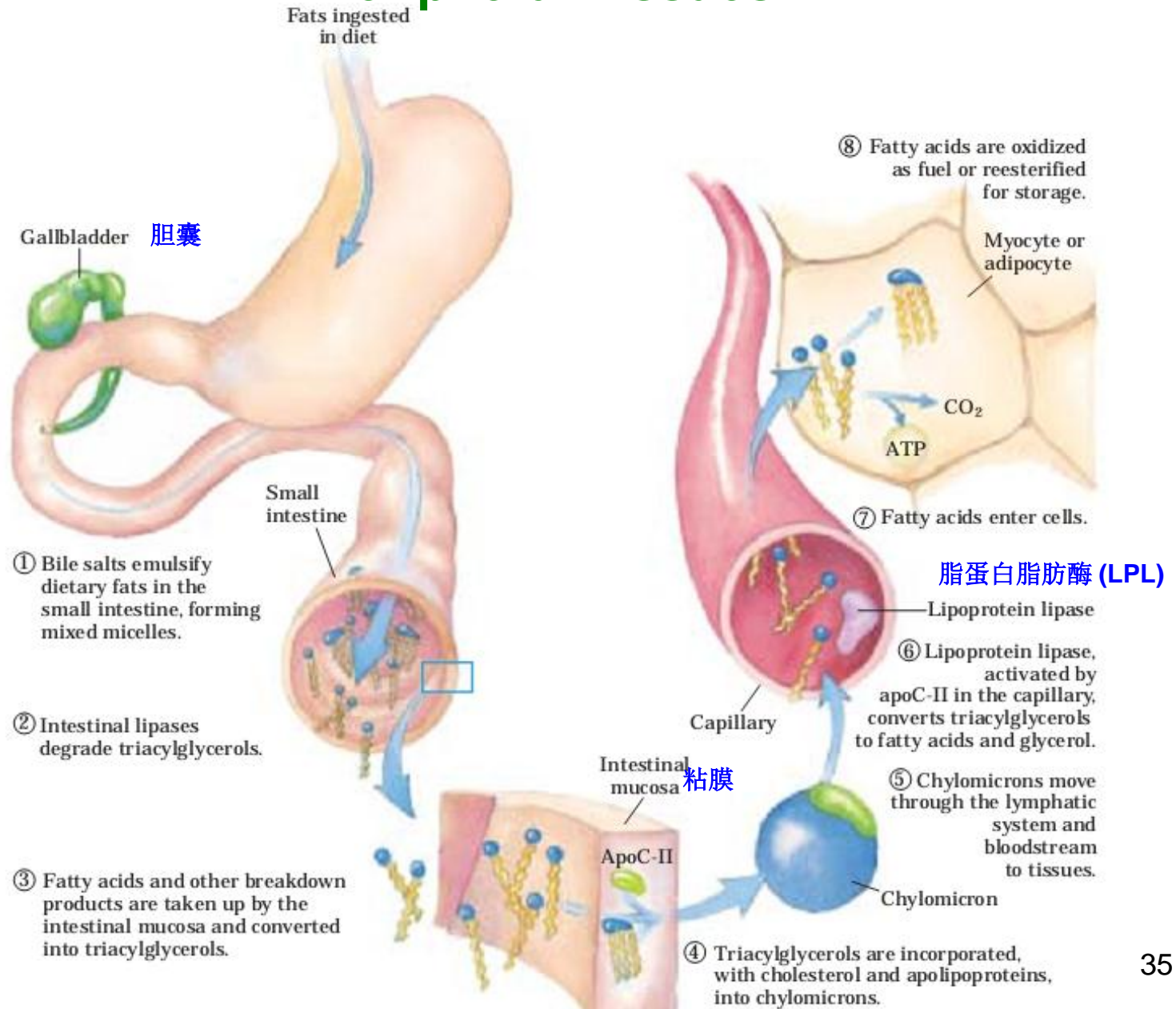
◆ In **intestinal mucosal cells** (肠粘膜细胞), FA and monoacylglycerides are resynthesized into TGs and packaged into **chylomicrons** (乳糜微粒).



*The chylomicron: **a lipoprotein***

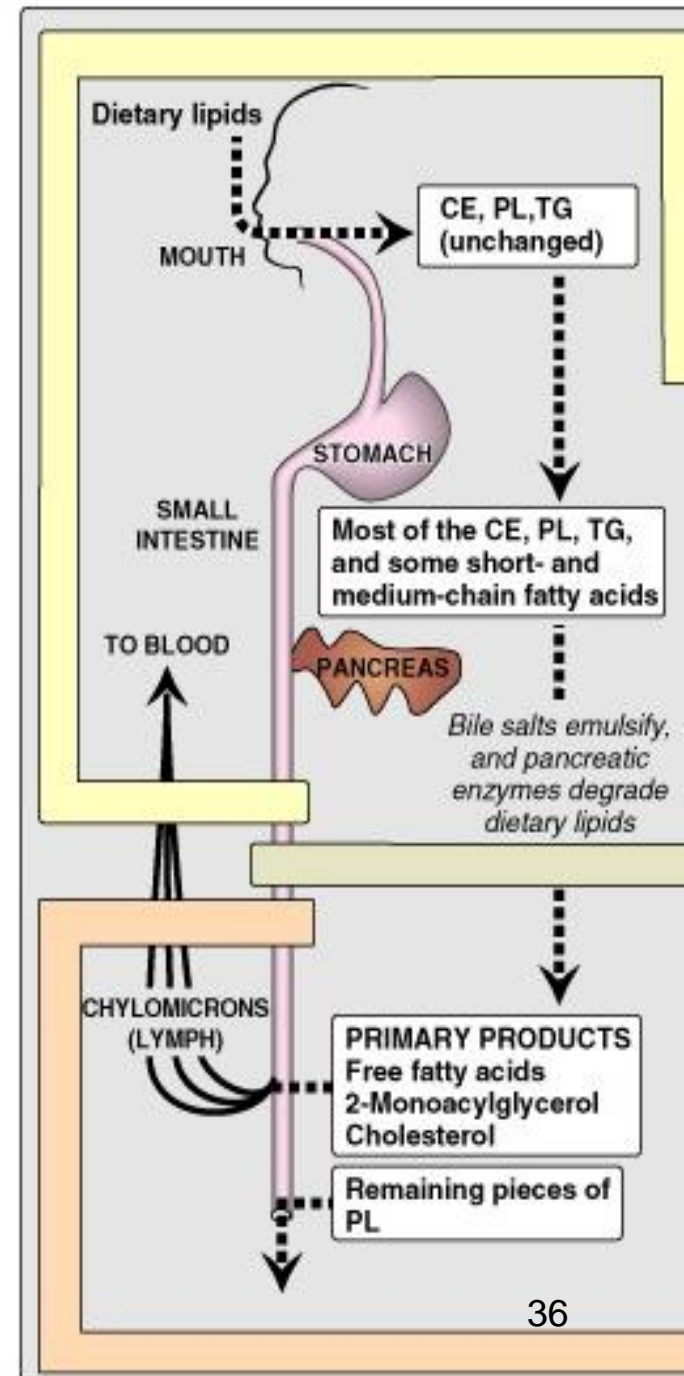


Movement of Dietary Lipid from Small Intestine to Peripheral Tissues



Lipid Digestion & absorb:

- **Highly Efficient: 60-160 g fat/day (90% as TGs); only 5% returns as “fecal fat”.**
- **To digest and absorb dietary fat must overcome 2 problems:**
 - poor solubility;
 - aggregate to form large complexes that make poor contact with the cell surface.

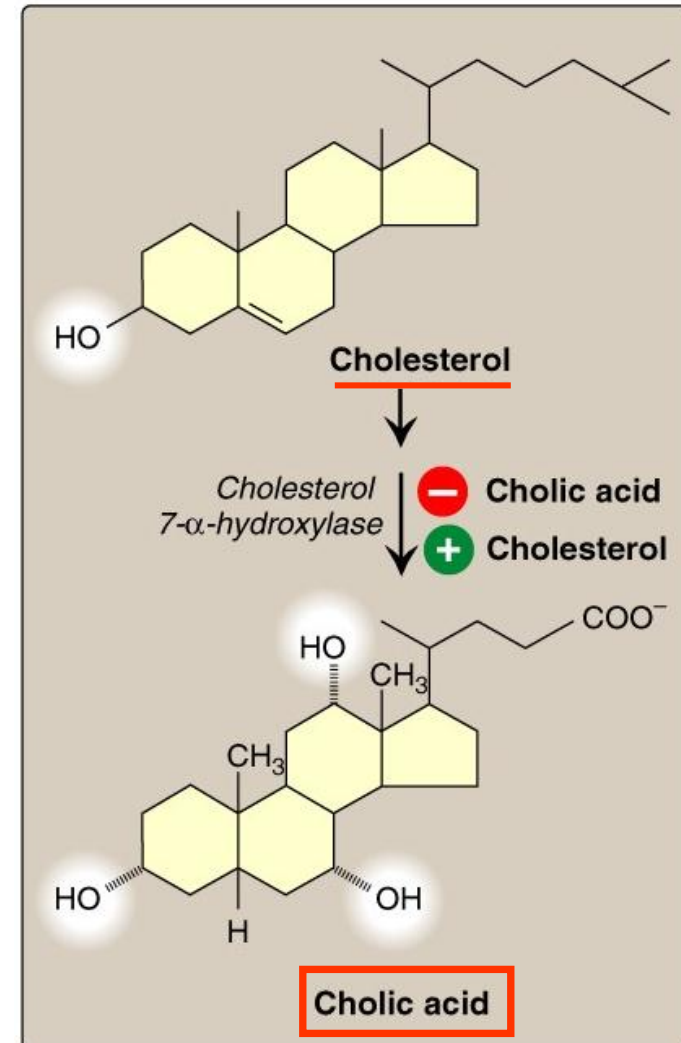


Solution:

- **Emulsification**（乳化） - **increase surface area** of lipid
 - Aided by **bile salts** detergent（去垢剂） + **mechanical mixing** due to peristalsis（蠕动）.
- **Solubilization** ↑ with **detergents**.

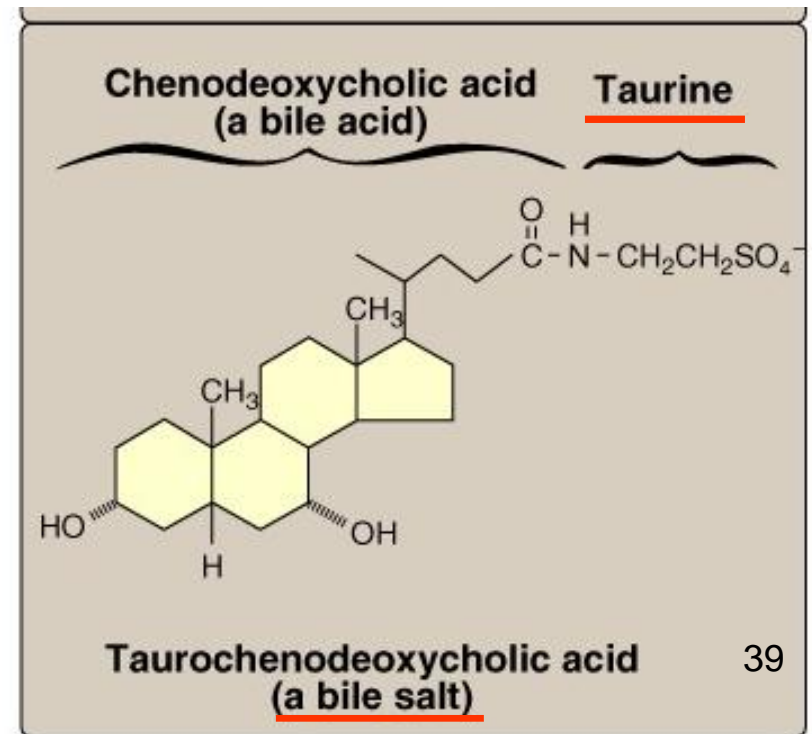
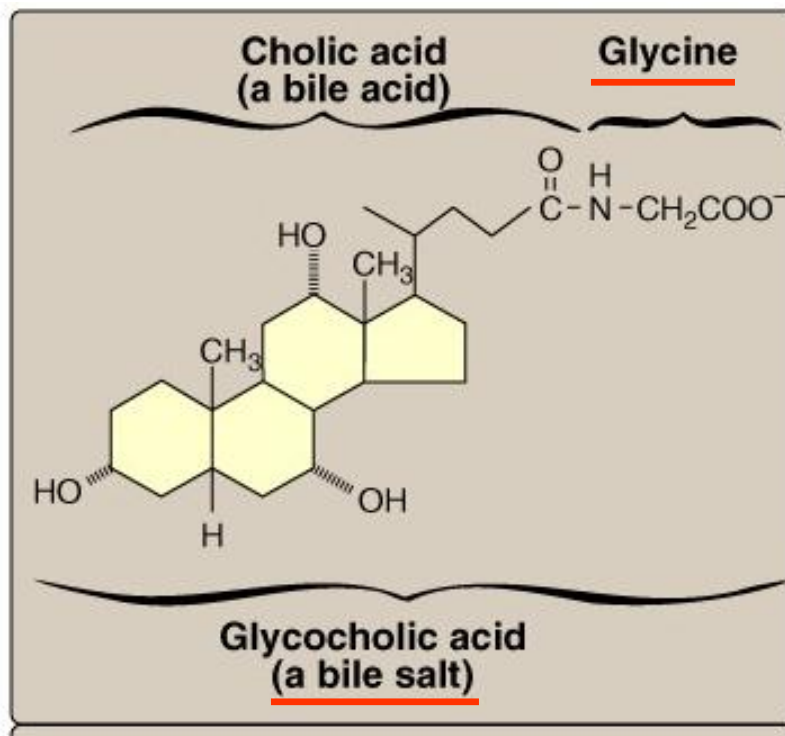
Synthesis of Bile Acids (Bile Salts) in liver

- **Cholic acid** synthesis is the rate-limiting step in bile salts production.
- **3-OHs** face upwards above the plane of the ring- a “**hydrophilic**” face
- The **-CH₃** groups face below the plane of the rings.



Bile Acids (Bile Salts)

- derivatives of cholesterol
- Formed in the liver
- A **sterol ring** + an **glycine** or **taurine** (牛磺酸)



● **stored in gallbladder** (胆囊)

● **secreted into the duodenum** (十二指肠)

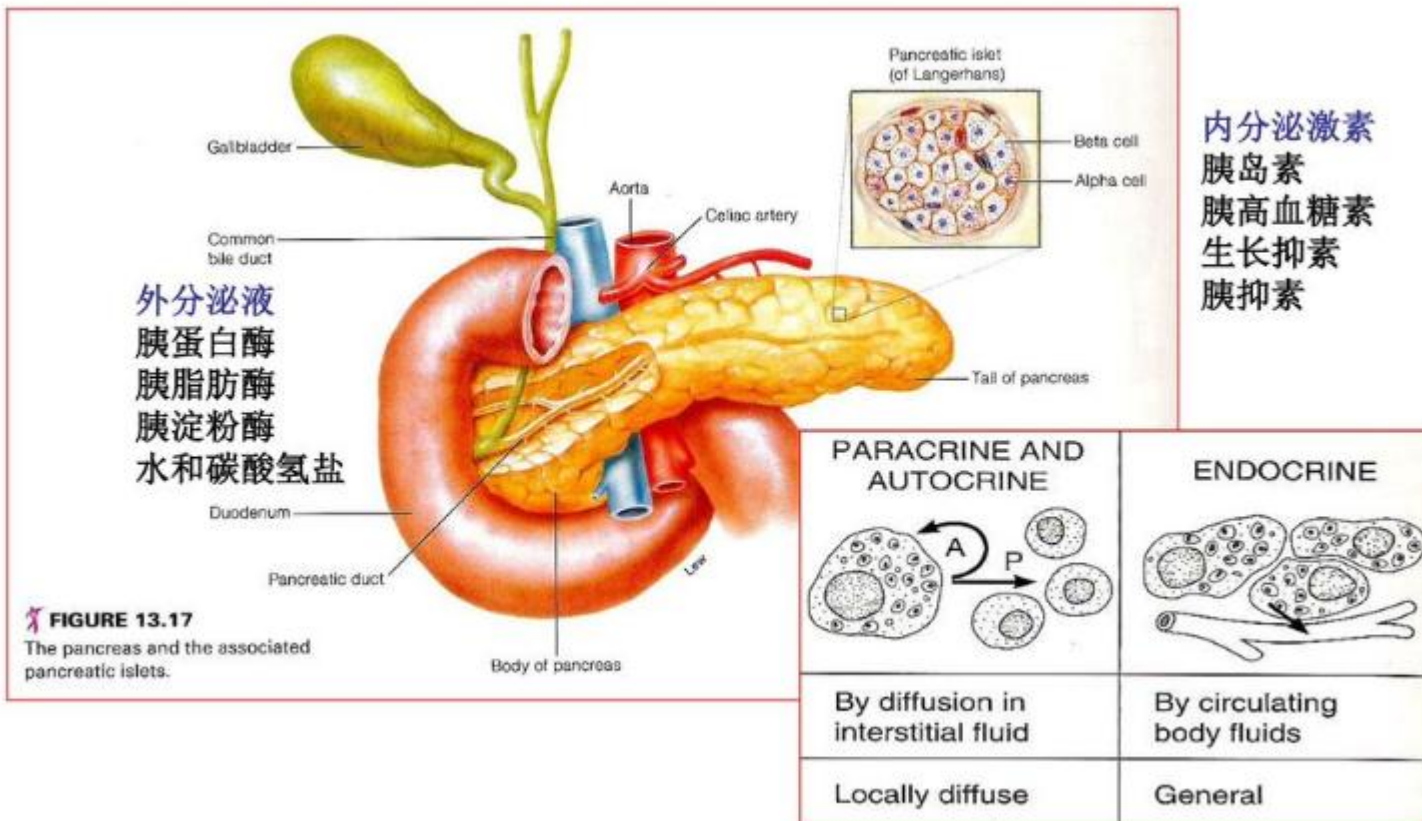
● **main function is to form micelles.**

● **stabilize lipid particles as they become smaller and prevent them from coalescing** (聚结) .

● **absorption of cholesterol and the fat-soluble vitamins (A,E, and K) across the intestinal epithelial membrane.**

Process of Lipid Digestion

- **Dietary** TGs, cholesteryl esters & phospholipids-degraded by **pancreatic enzymes** whose secretion into the small intestine is hormonally controlled.

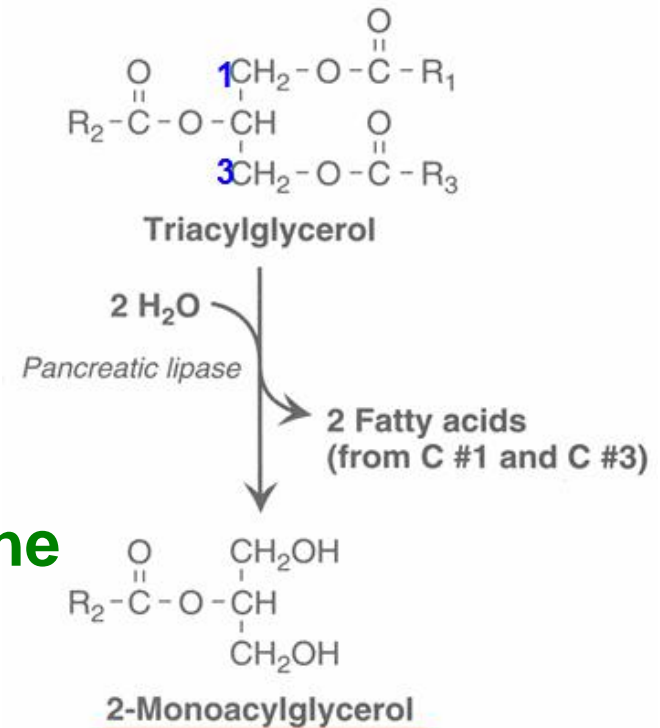


2.1 TGs Digestion

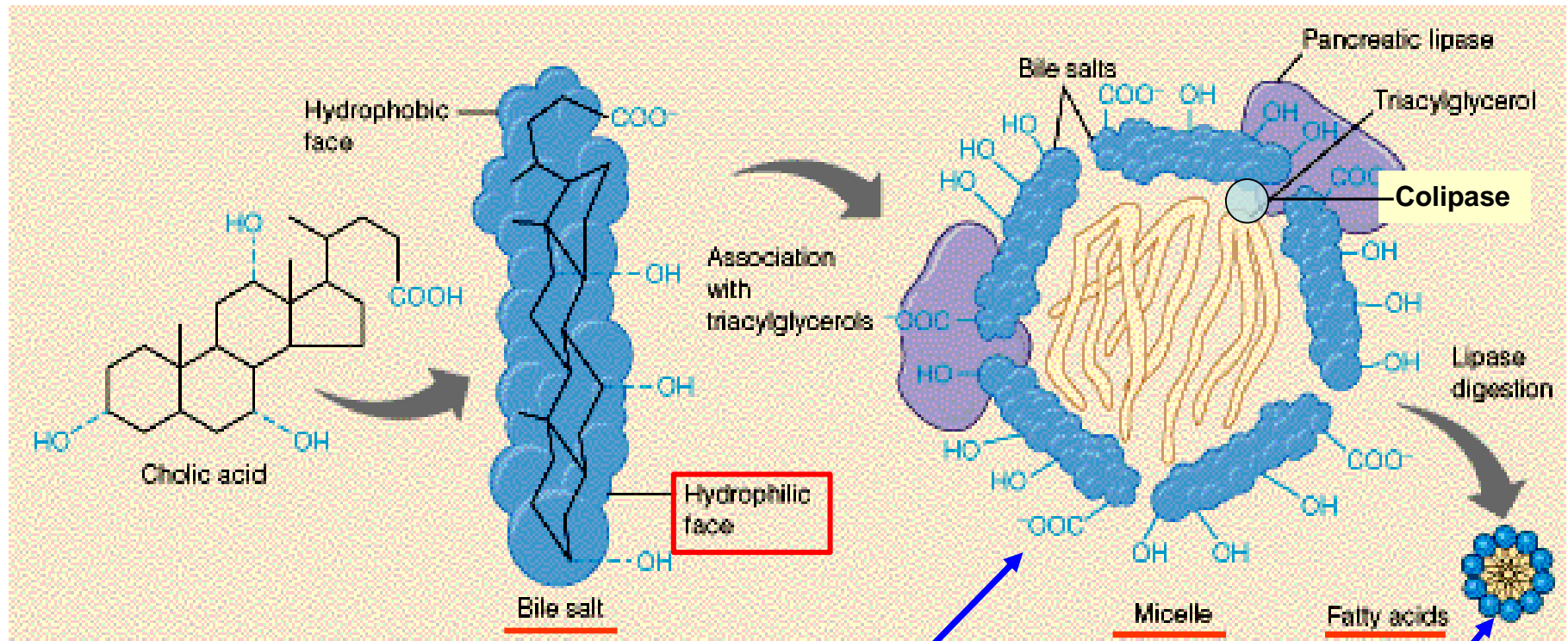
● Micelles composed of TGs are too large to be taken up efficiently by the mucosal cells.

● By *pancreatic lipase*

- specific for FAs at the C1 and C3
- **2-monoacylglycerols**
- reaction at water/lipid interface of the emulsion droplets
- colipase (辅脂肪酶) stabilizes the complex of **salts/TG/phospholipid**.



Pancreatic Lipase Associated with a Bile Salt /Triacylglycerol /Phospholipid Micelle



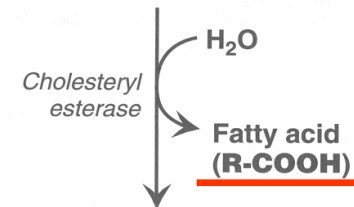
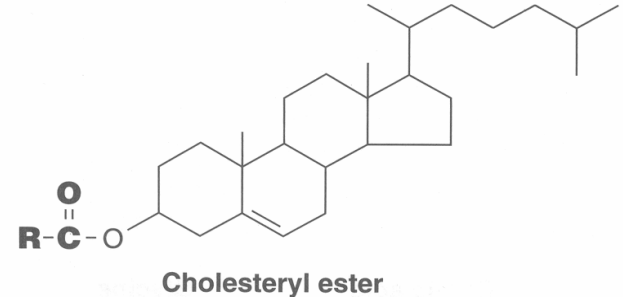
This micelle is too large to be absorbed.

via *pancreatic lipase* yields a smaller micelle

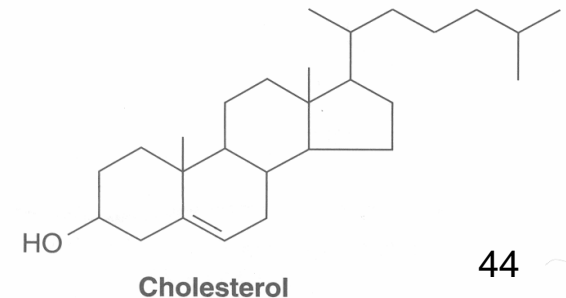
2.2 Cholesteryl Ester Degradation

- **Cholesteryl esters** (胆固醇酯) are hydrolyzed by *cholesteryl ester hydrolase / esterase* which produces **cholesterol** + free **FA**.

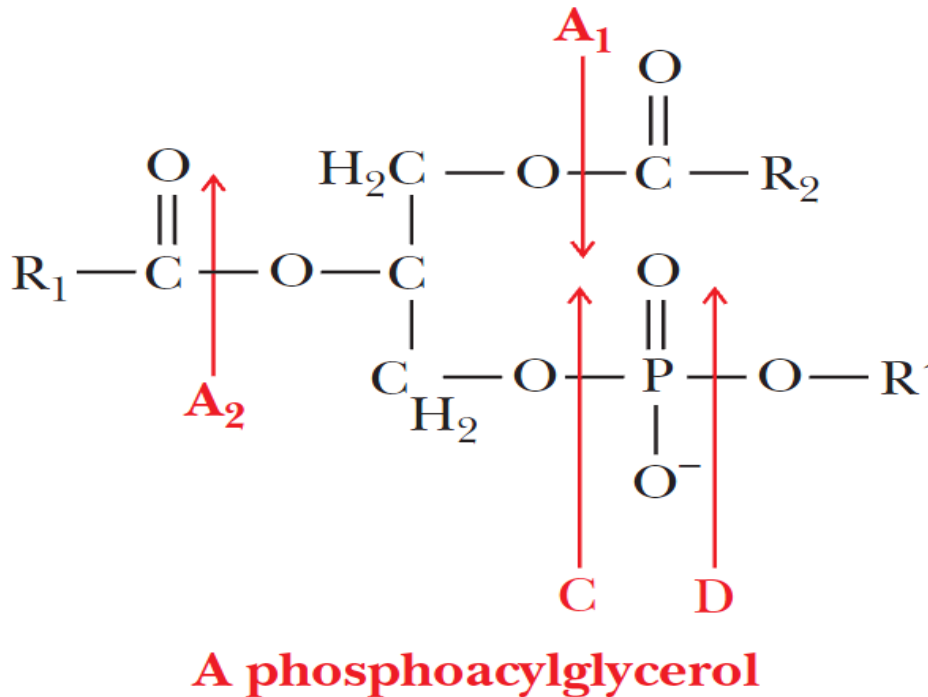
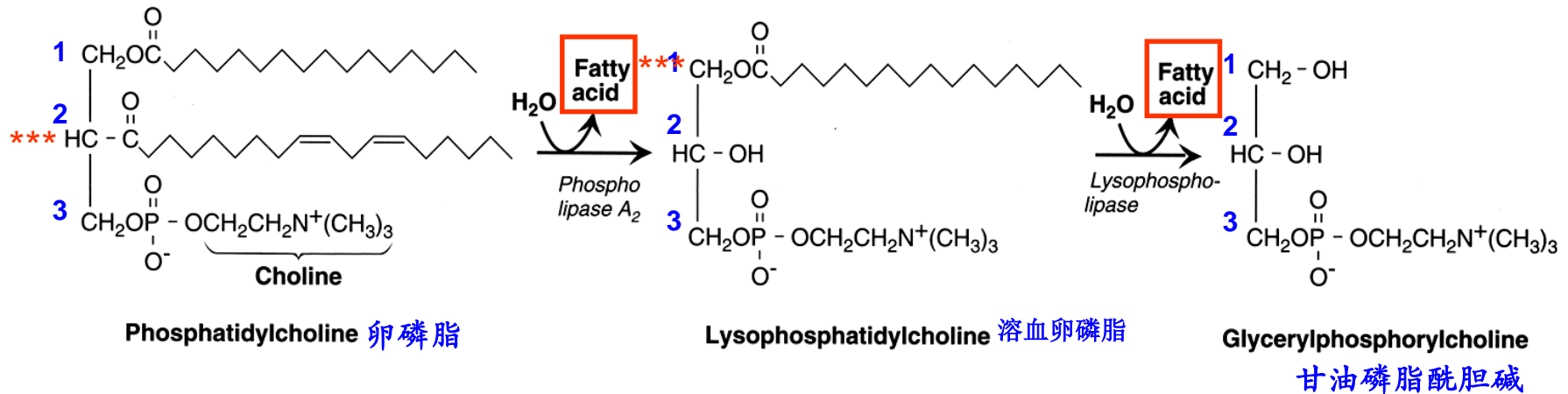
More
hydrophobic

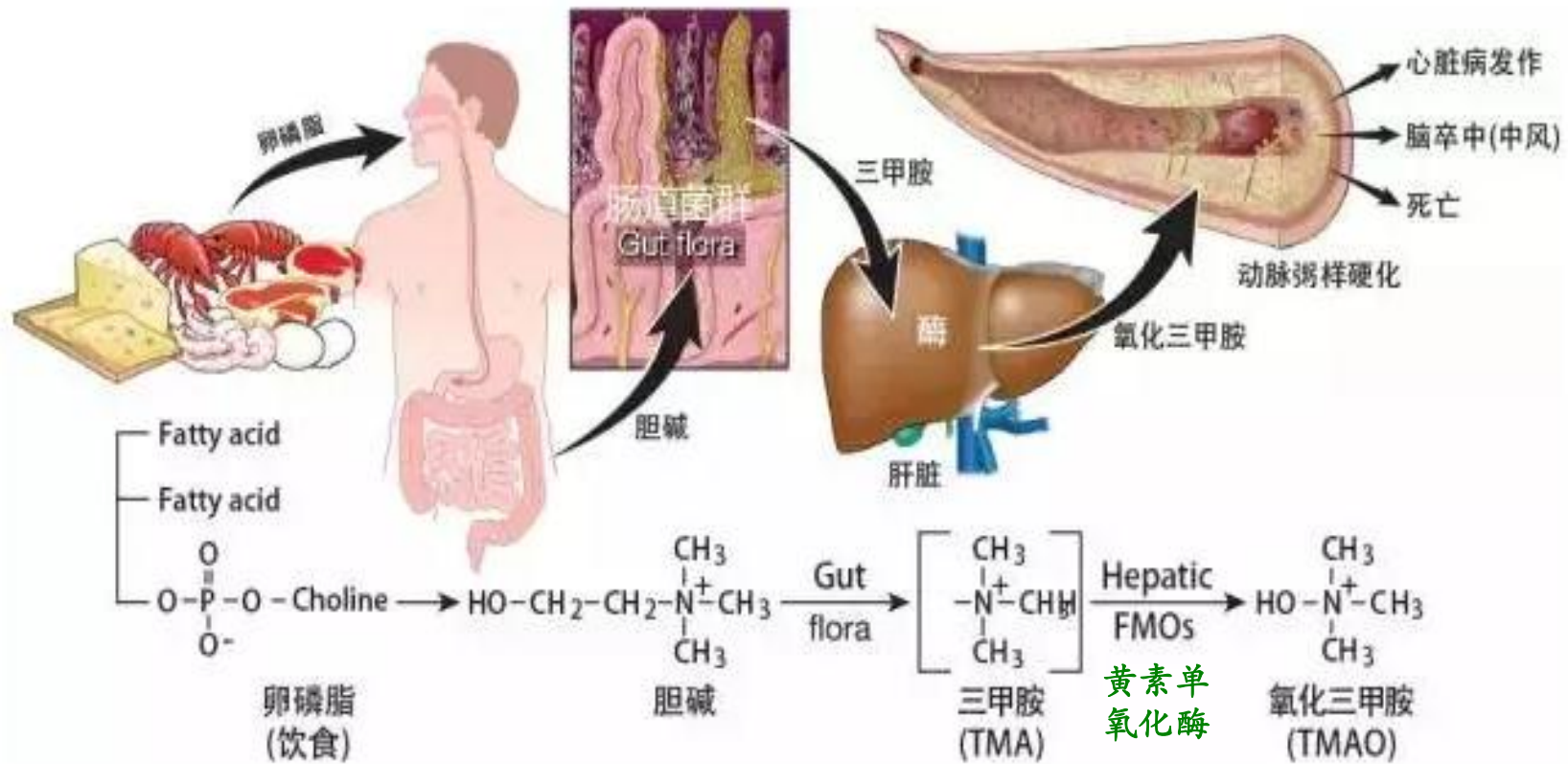


Less
hydrophobic



2.3 Phospholipid Degradation





Nature. 2011 Apr 7;472(7341):57-63.

Absorption of Lipids in a **Small Mixed Micelle** by Intestinal Mucosal Cells

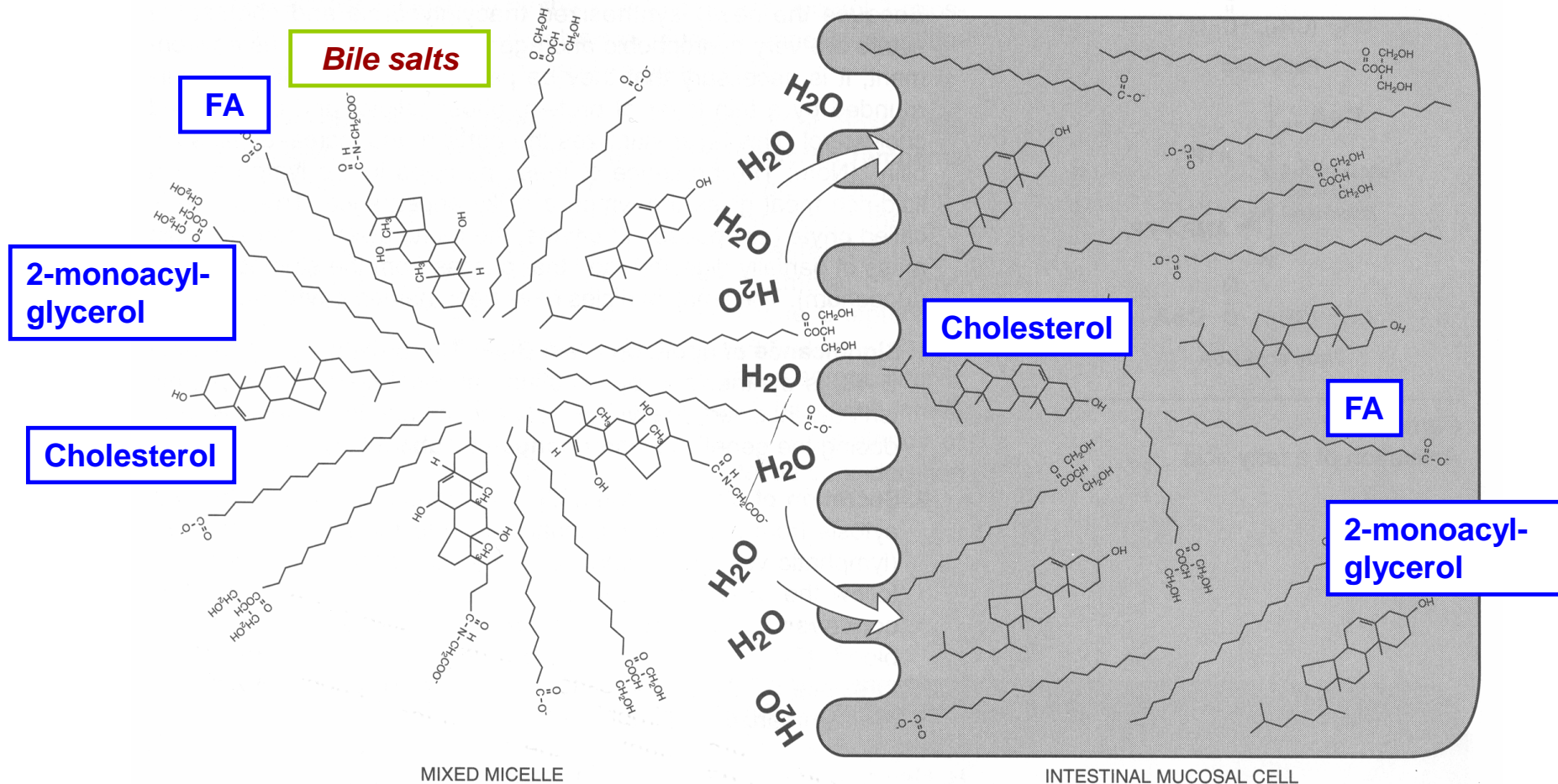
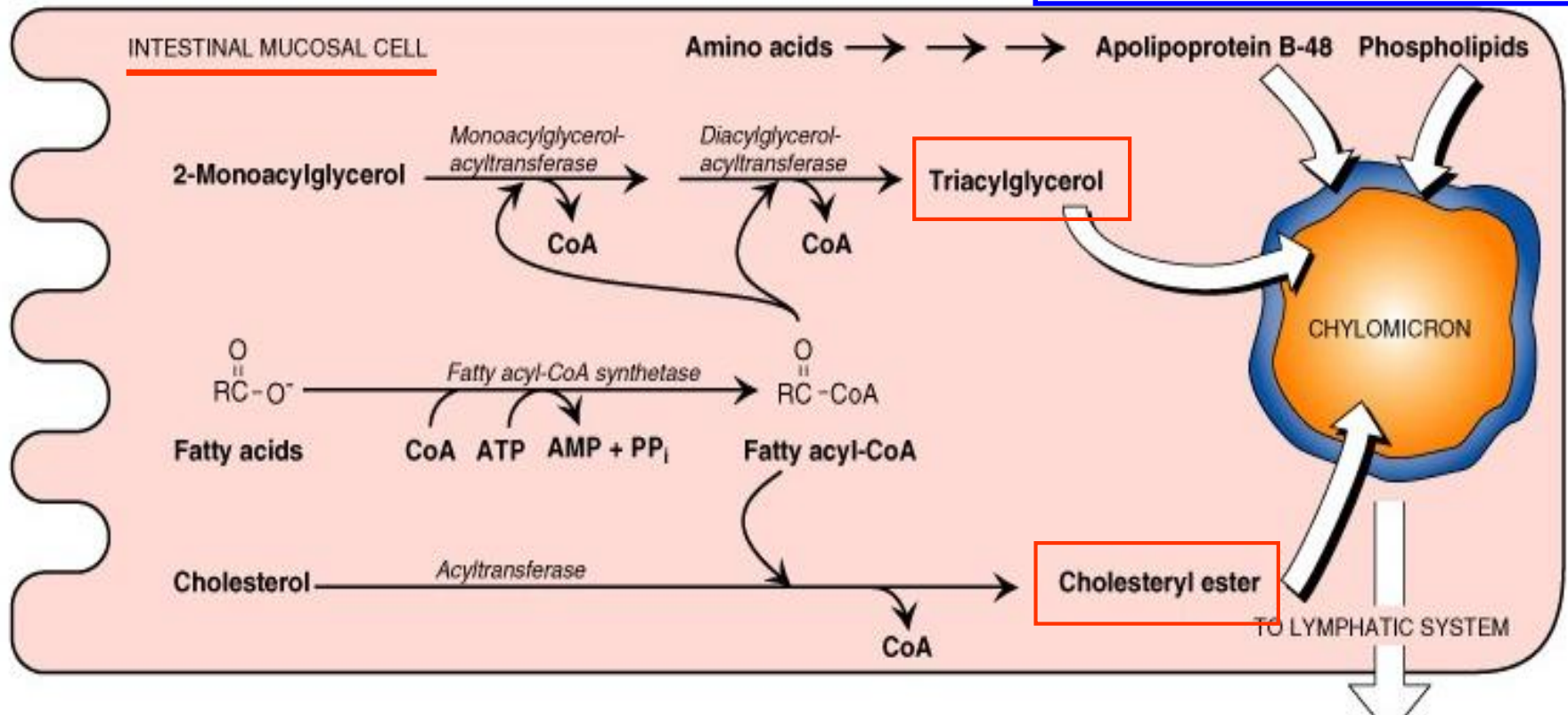


Figure 16.6

Absorption of lipids contained in mixed micelle by intestinal mucosal cells.

Assembly and Secretion of Chylomicrons from Intestinal Mucosal Cells

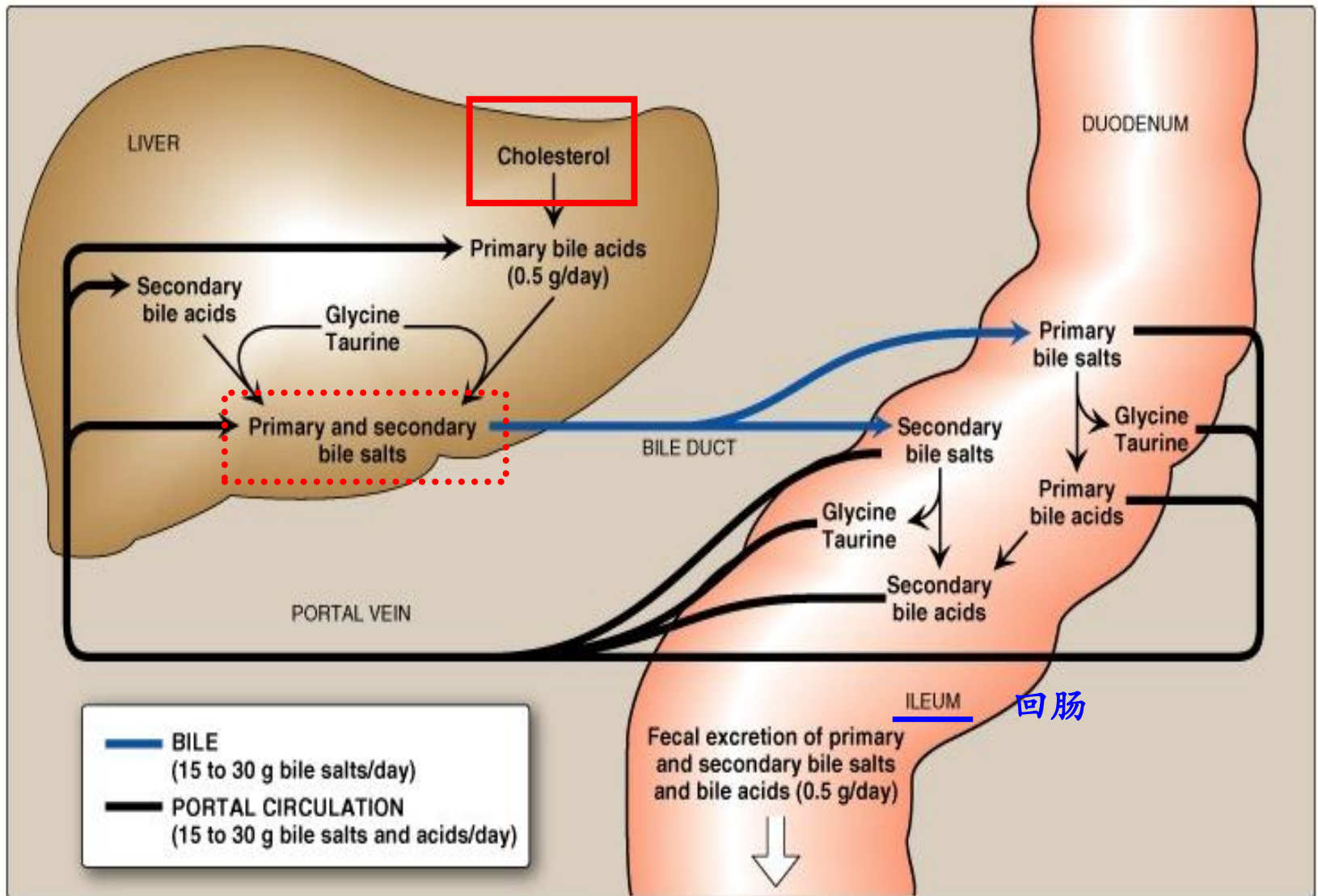
Increase the solubility of chylomicrons.



Glycerol and short FAs pass thru intestinal cell via passive diffusion.

To bloodstream & then to tissues.

Enterohepatic Circulation (肠肝循环) of Bile Salts/Acids



Summary of Diet TG Digestion

- *Pancreatic lipase* (with colipase) generates FAs and 2-monacylglycerol. (TG)
- FAs and monoacylglycerols with bile salts are solubilized & transported to enterocytes (肠上皮) via **passive diffusion**.
- Glycerol & FAs $\leq 12\text{C}$ pass thru the cell into the blood.
- 2-monacylglycerols and FAs > 12 carbons are resynthesized into TGs in the **ER**.

- TGs form large lipid globules in the ER called **nascent chylomicrons**. Several **apolipoproteins** are required.
- **Nascent chylomicrons** are released by **exocytosis** into the lymph system.
- **Bile salts** are recycled to the liver via **active transport**.

----- **Enterohepatic Cycling** (肠肝循环)

Questions

- 饮食中的**TG**、磷脂和胆固醇如何代谢？
- 脂肪酸如何被机体吸收和储存？
- 肠肝循环