Lecture 8

BT 203

Biochemistry

3-0-0-6

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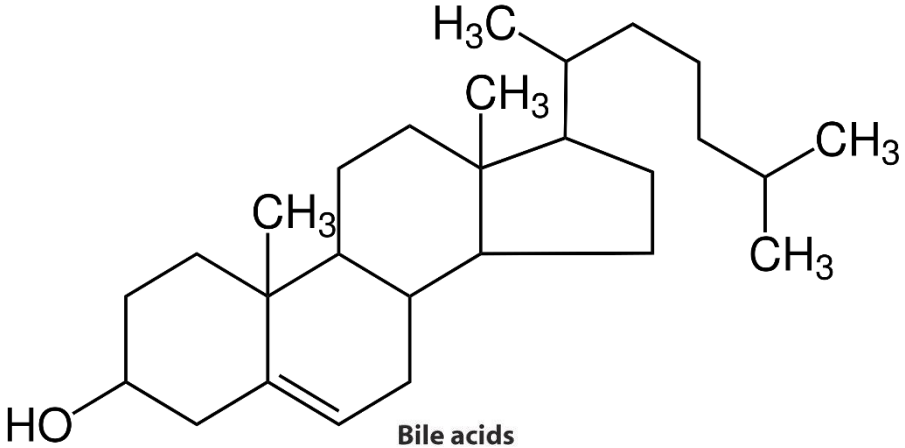
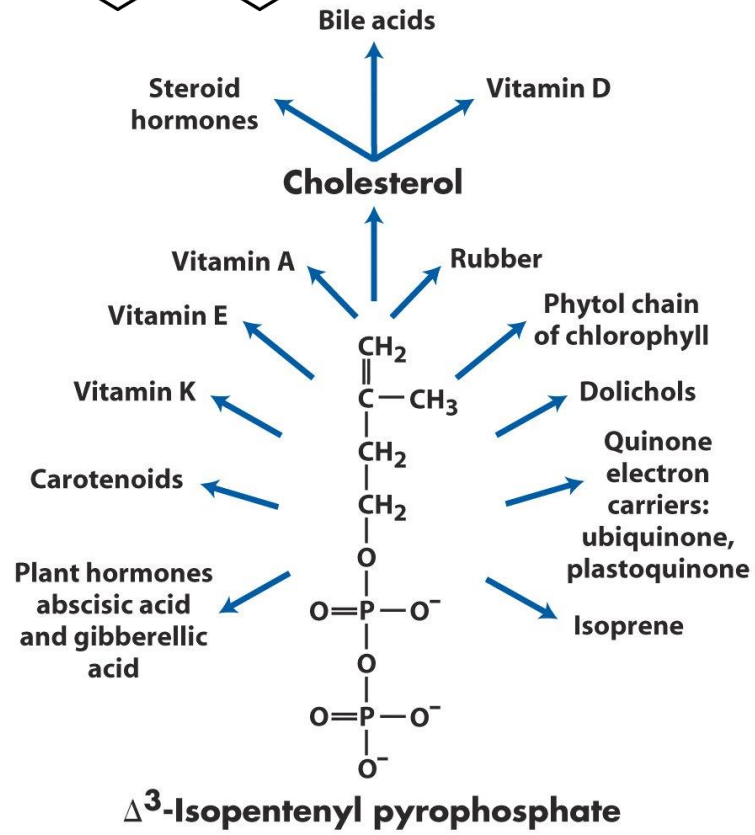
Key Concepts

- What is an isoprenoid unit?
- How is cholesterol formed in the body?
- What are the different steps of cholesterol biosynthesis?
- What is the fate of cholesterol in the body?
- What is lipoproteins?

Cholesterol

- An **isoprenoid**
- Cell membrane constituent
- **Precursor to steroid hormones**, bile acids
- Associated with many chronic diseases like cardiovascular disorders
- Obtained in the body
  - ✓ Diet
  - ✓ Synthesis

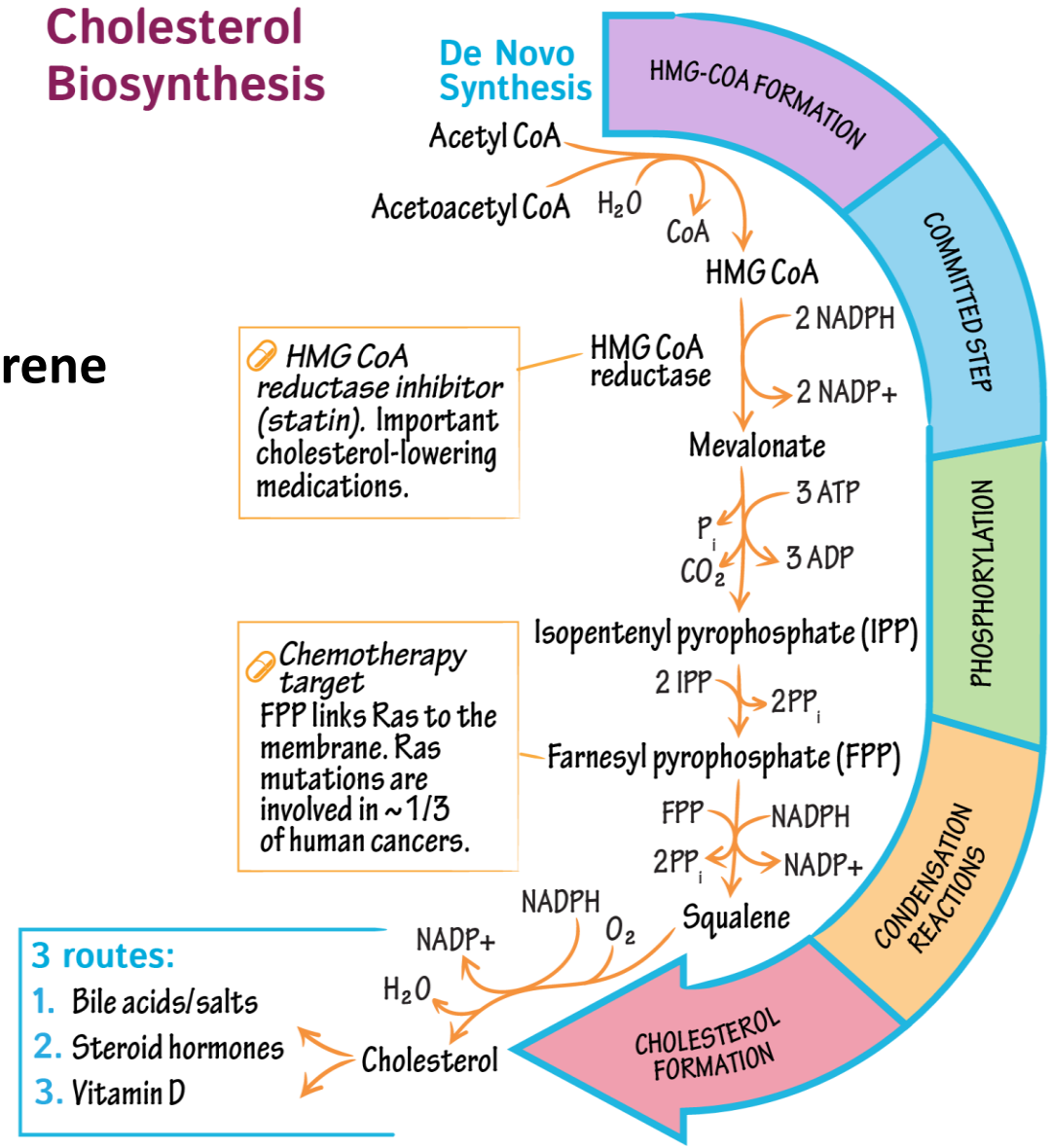




Biosynthesis of Cholesterol

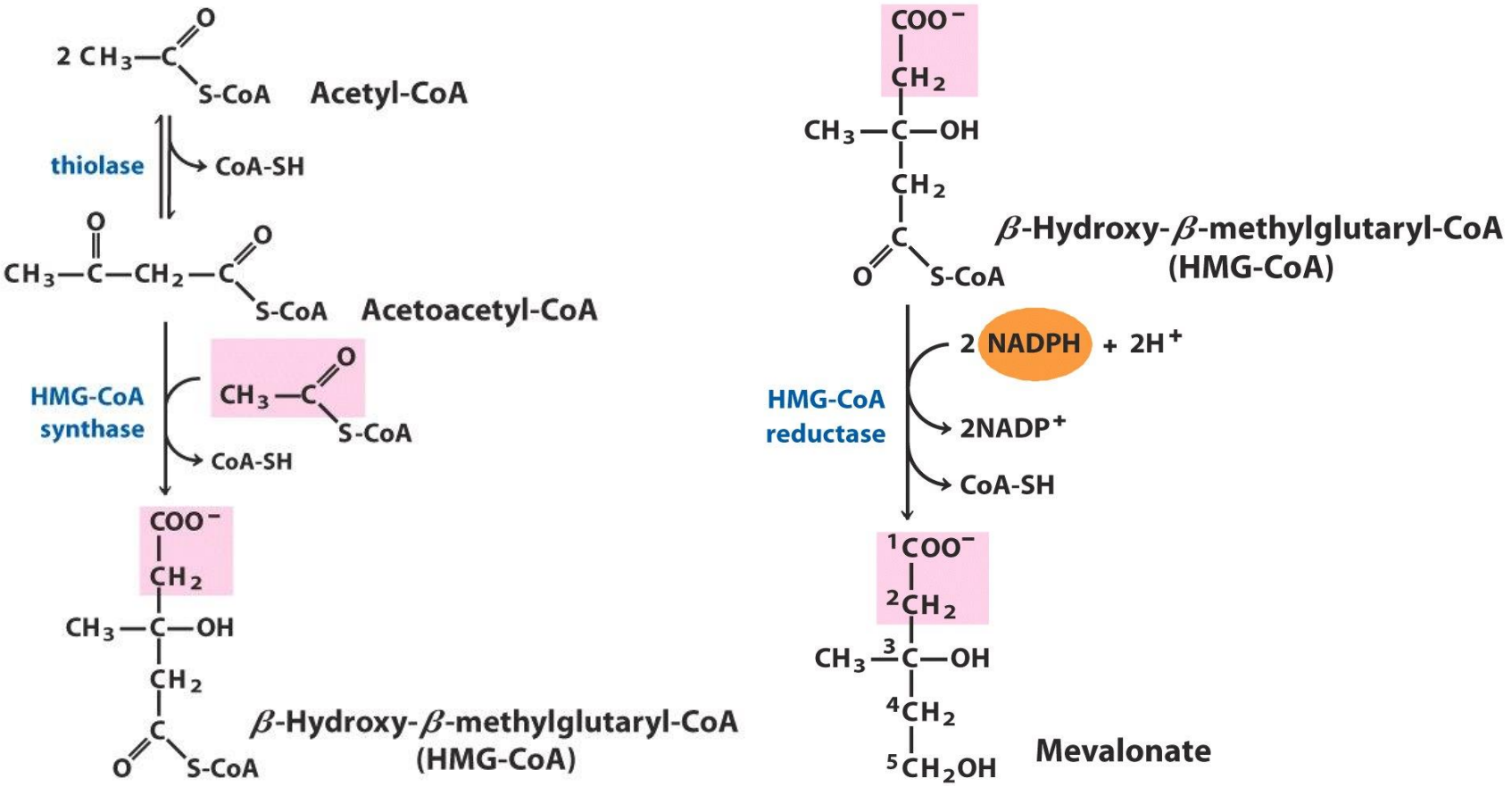
Five stages

1. Formation of mevalonate
2. Conversion to activated isoprene
3. Polymerization of isoprene
4. Cyclization of squalene
5. Modification of structure



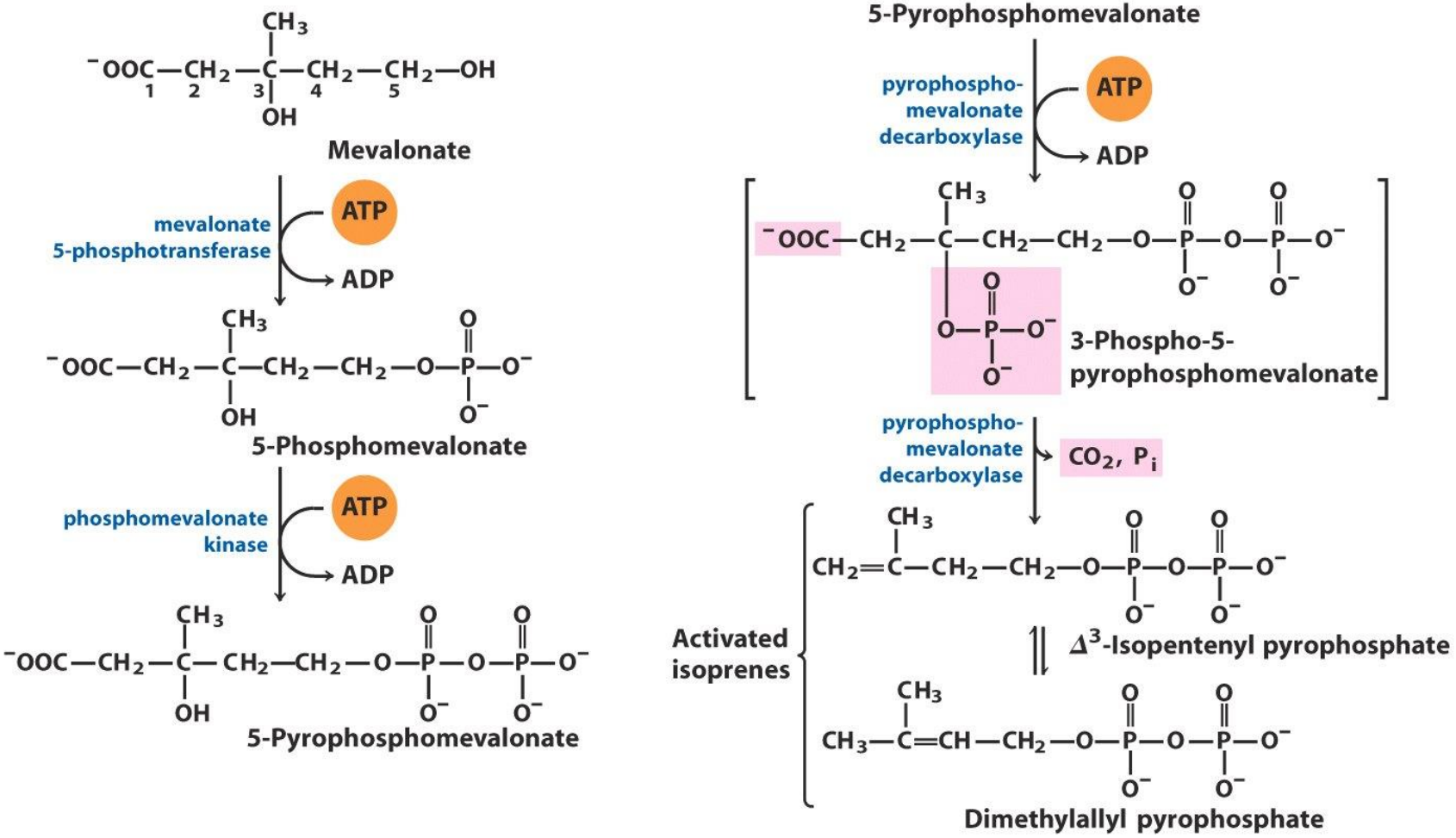
Biosynthesis of Cholesterol

Stage 1: Synthesis of Mevalonate



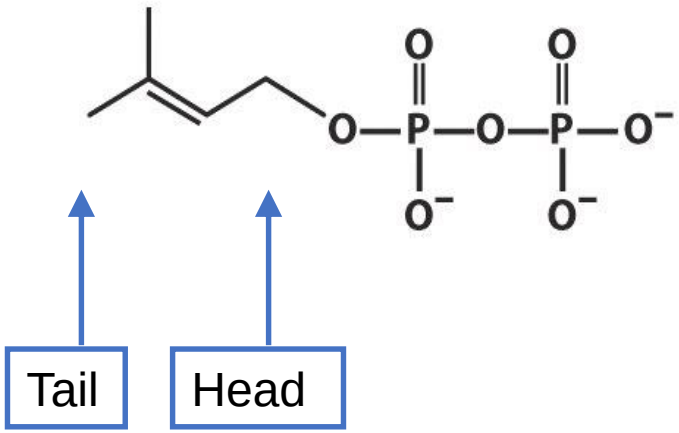
Biosynthesis of Cholesterol

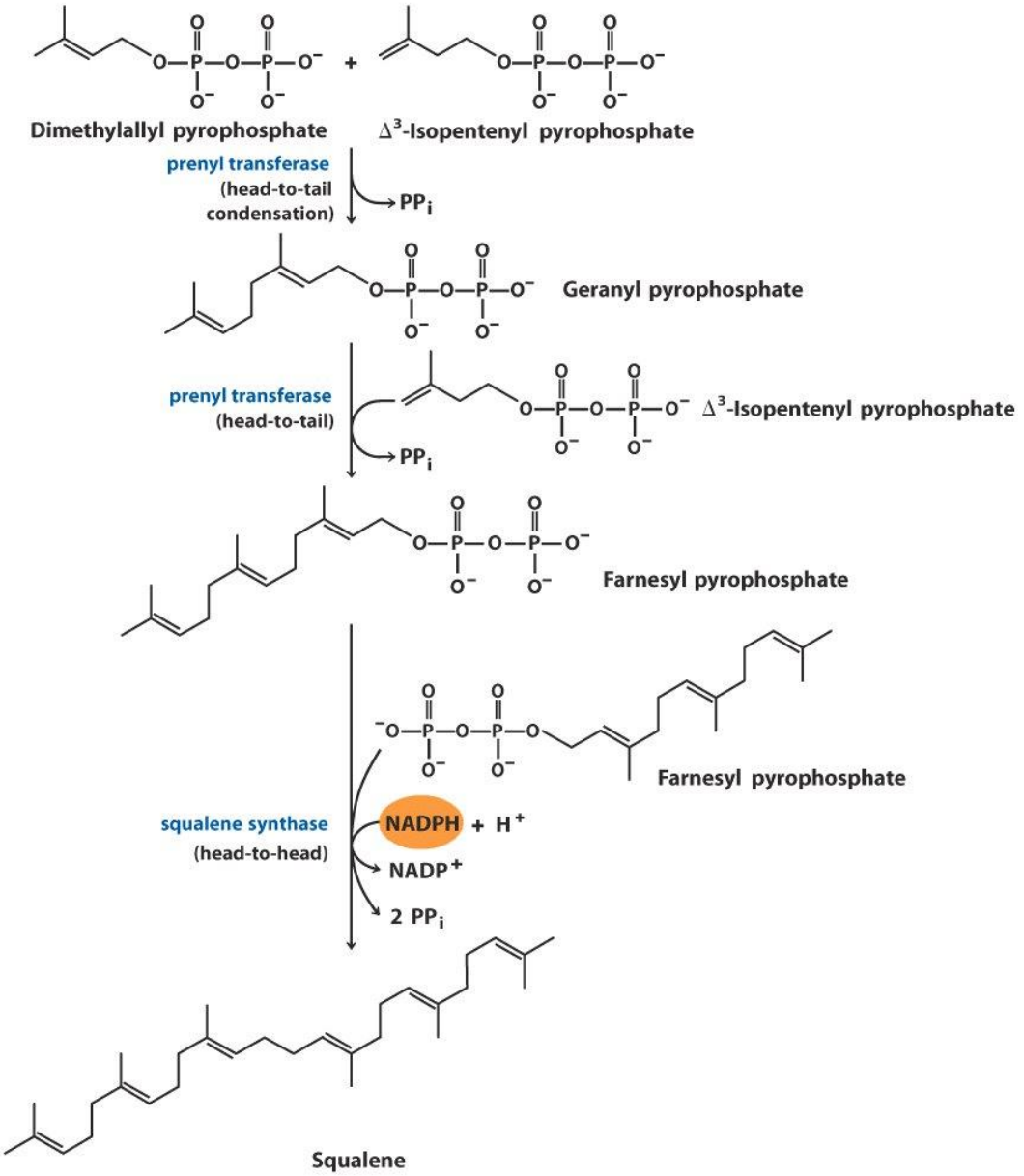
Stage 2: Conversion of Mevalonate to Activated Isoprene Units



Biosynthesis of Cholesterol

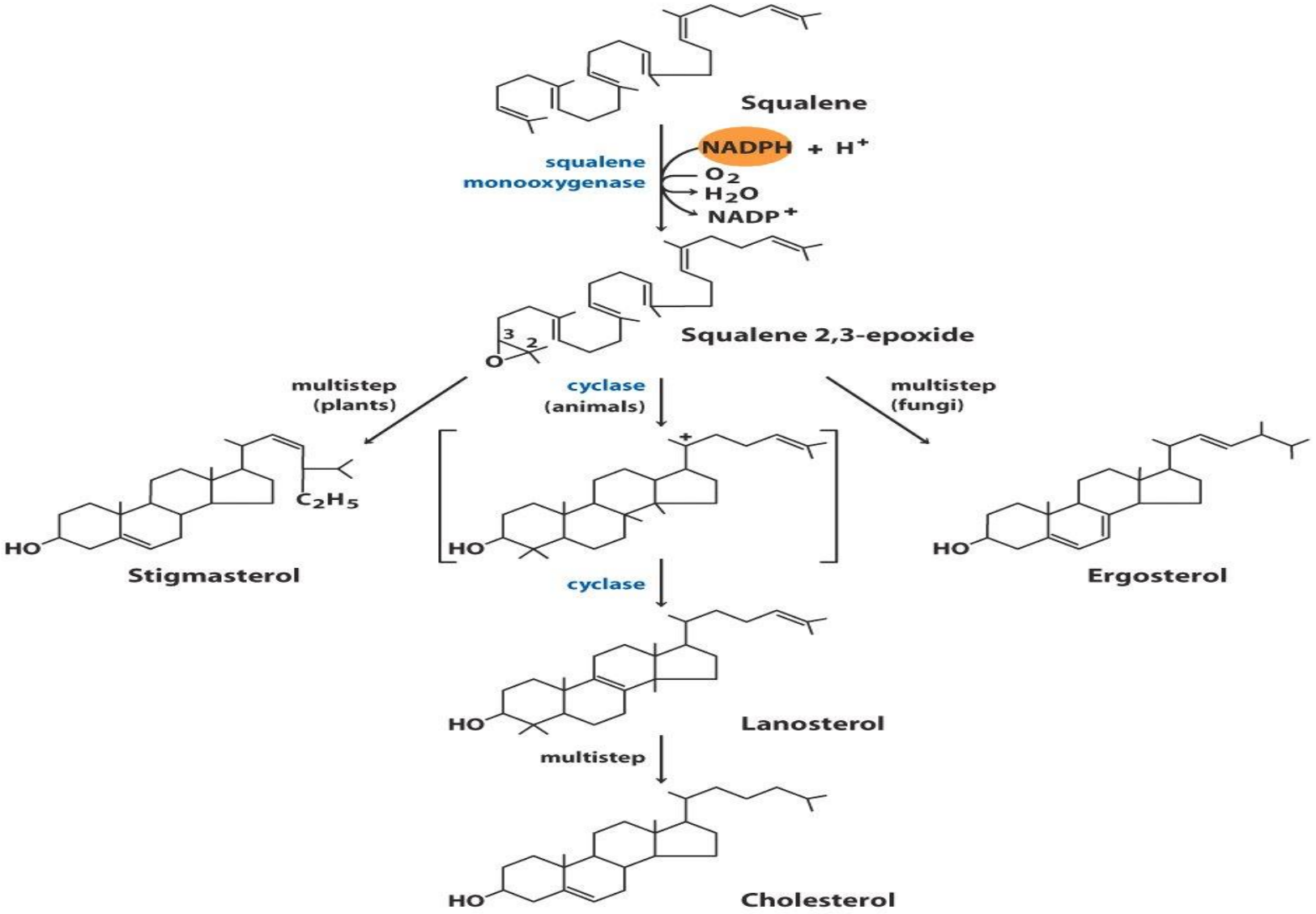
Stage 3: Formation of Squalene





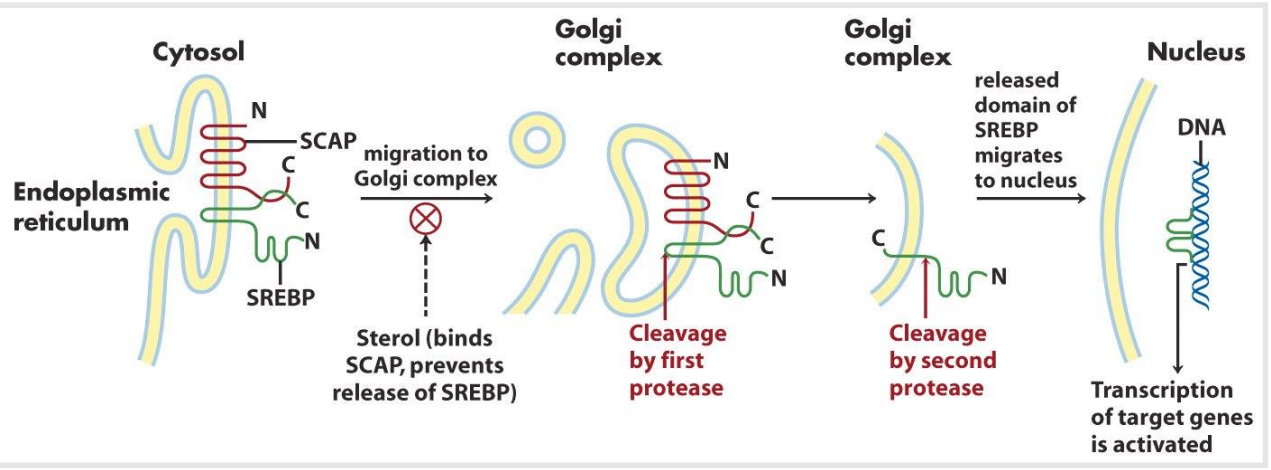
Biosynthesis of Cholesterol

Stage 4: Cyclization



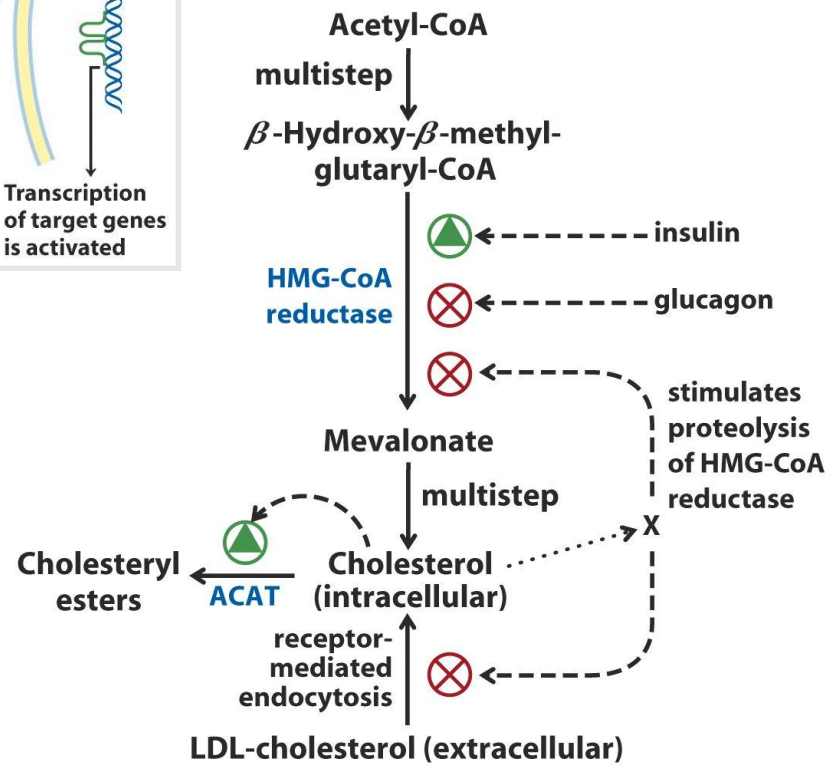
Biosynthesis of Cholesterol

Regulation of Cholesterol Synthesis



SREBP = Sterol regulatory element-binding proteins

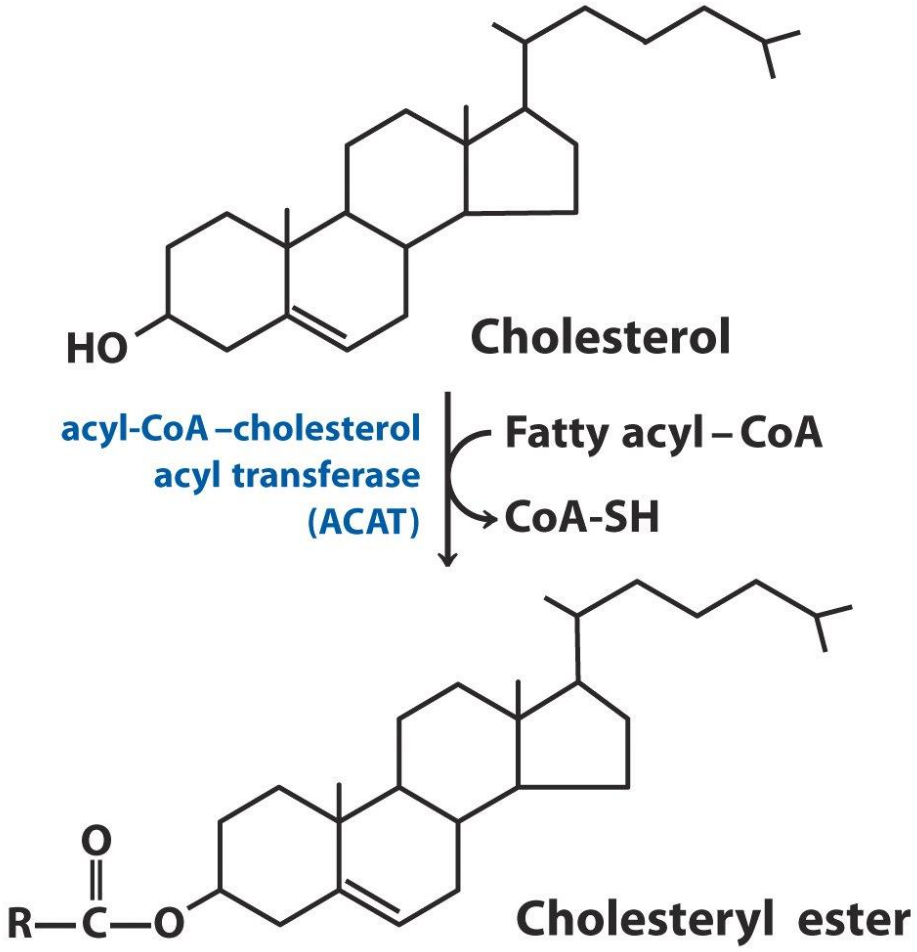
SCAP = SREBP cleavage-activating protein



Biosynthesis of Cholesterol

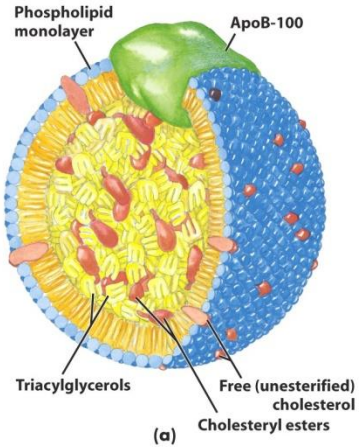
Regulation of Cholesterol Synthesis

- **Incorporated into hepatocyte membranes**
- **Exported**
  - Bile acids
  - Cholesterol esters
  - Free cholesterol



Lipoproteins

Substances made of protein and fat that carry cholesterol



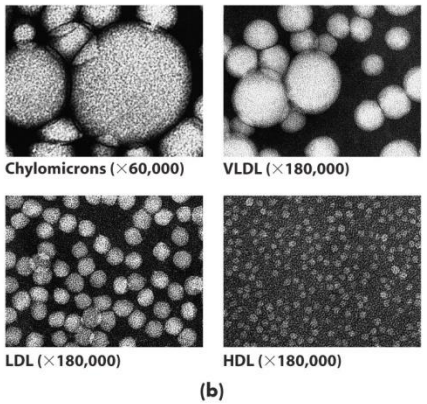


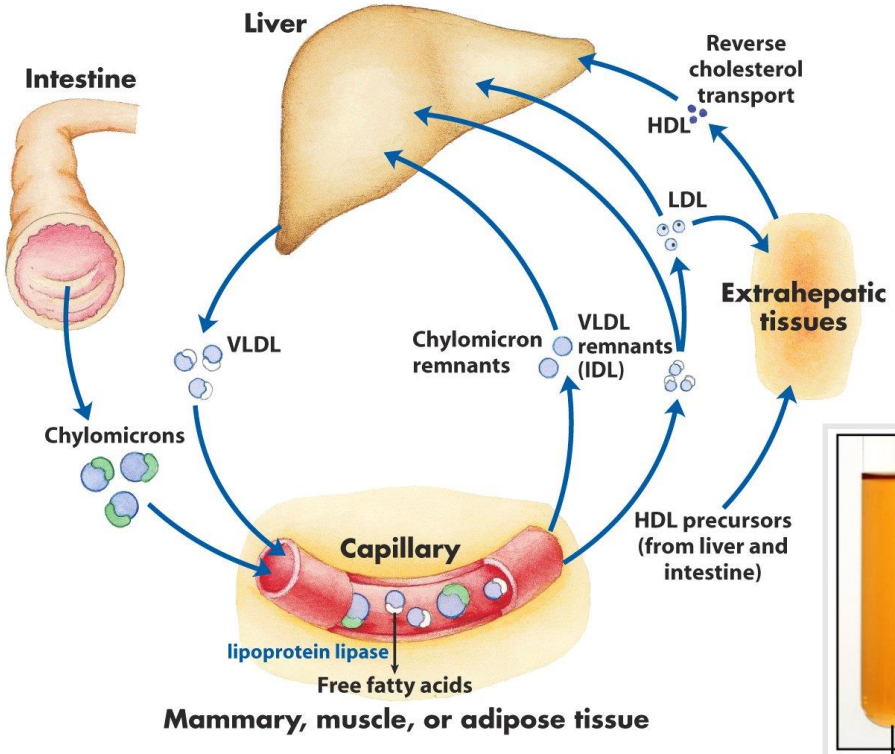
TABLE 21–2 Major Classes of Human Plasma Lipoproteins: Some Properties

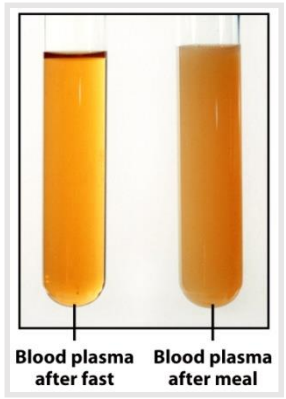
		Composition (wt %)				
Lipoprotein	*Density (g/mL)*	*Protein*	*Phospholipids*	*Free cholesterol*	*Cholesteryl esters*	*Triacylglycerols*
Chylomicrons	<1.006	2	9	1	3	85
VLDL	0.95–1.006	10	18	7	12	50
LDL	1.006–1.063	23	20	8	37	10
HDL	1.063–1.210	55	24	2	15	4

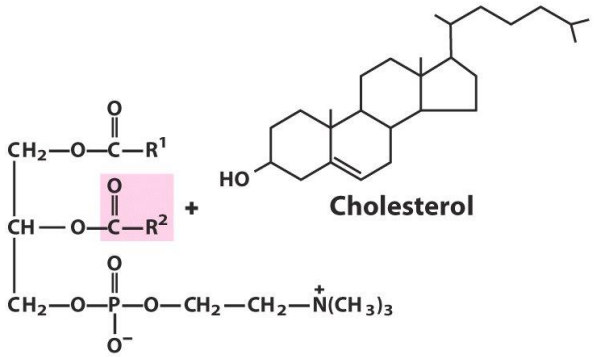
TABLE 21–3 Apolipoproteins of the Human Plasma Lipoproteins

Apolipoprotein	*Molecular weight*	*Lipoprotein association*	*Function (if known)*
ApoA-I	28,331	HDL	Activates LCAT; interacts with ABC transporter
ApoA-II	17,380	HDL	
ApoA-IV	44,000	Chylomicrons, HDL	
ApoB-48	240,000	Chylomicrons	
ApoB-100	513,000	VLDL, LDL	Binds to LDL receptor
ApoC-I	7,000	VLDL, HDL	
ApoC-II	8,837	Chylomicrons, VLDL, HDL	Activates lipoprotein lipase
ApoC-III	8,751	Chylomicrons, VLDL, HDL	Inhibits lipoprotein lipase
ApoD	32,500	HDL	
ApoE	34,145	Chylomicrons, VLDL, HDL	Triggers clearance of VLDL and chylomicron remnants

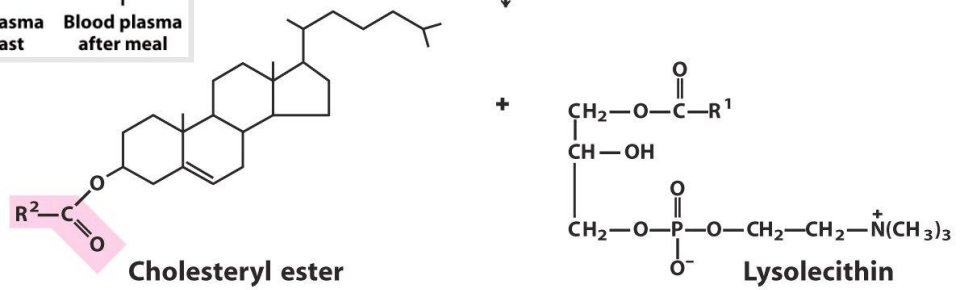
Lipoproteins and Lipid Transport



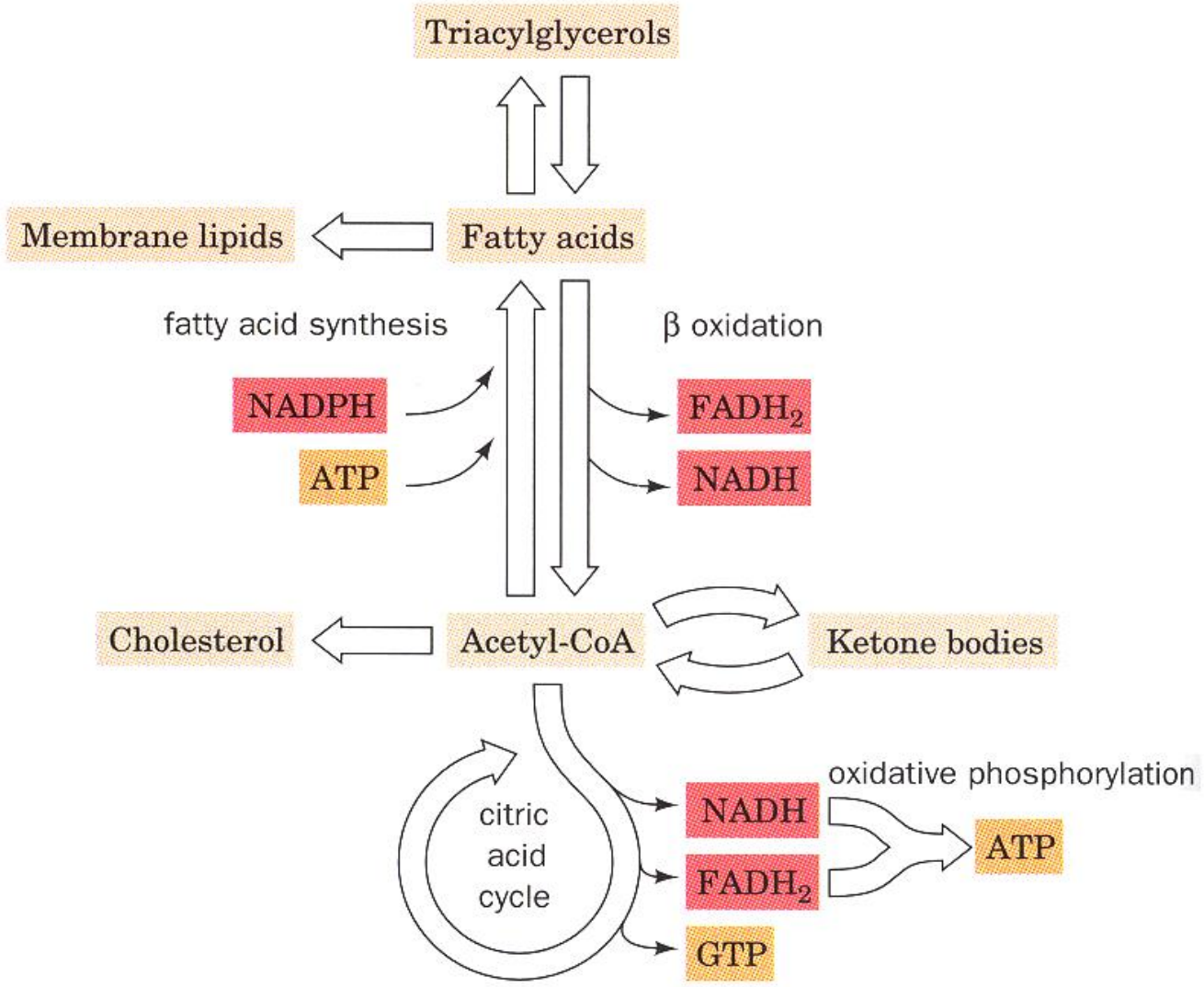




lecithin-cholesterol acyl transferase (LCAT)



Summary


Triacylglycerols
Membrane lipids
Fatty acids
fatty acid synthesis
β oxidation
NADPH
ATP
FADH2
NADH
Cholesterol
Acetyl-CoA
Ketone bodies
citric acid cycle
oxidative phosphorylation
NADH
FADH2
GTP
ATP