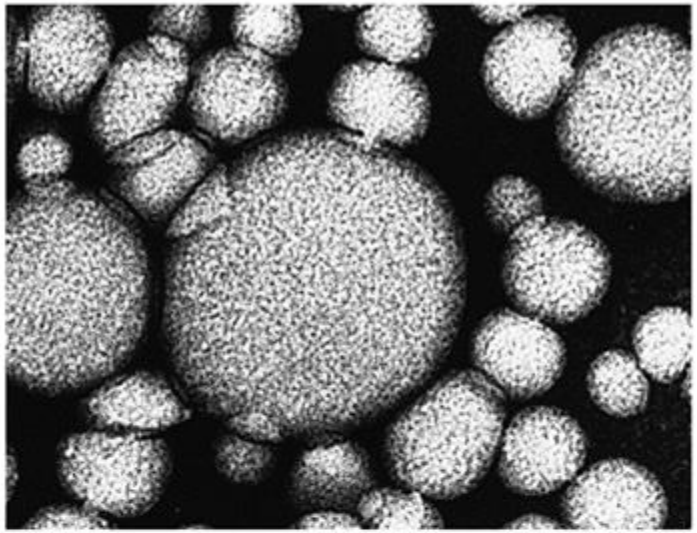
METABOLISM OF PLASMA LIPOPROTEINS

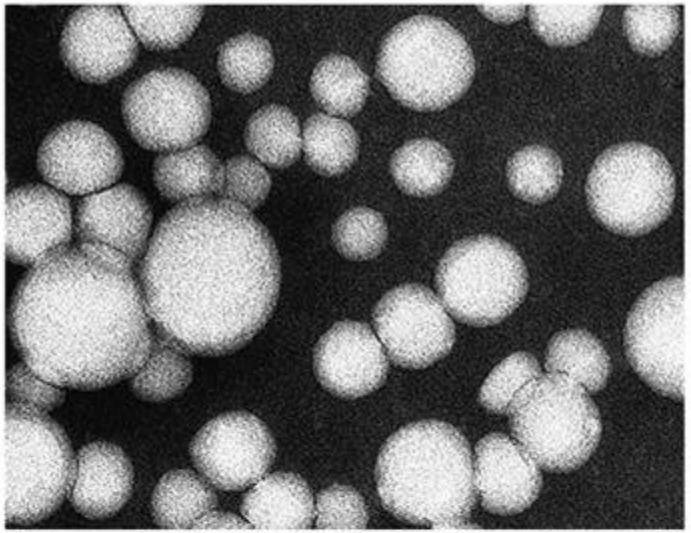
Plasma Lipoproteins

- Differerent types of and ratios of lipids and proteins
- Visible by electron microscopy
- Different size and density
- Detected by
    - electrophoresis
    - density gradient centrifugation

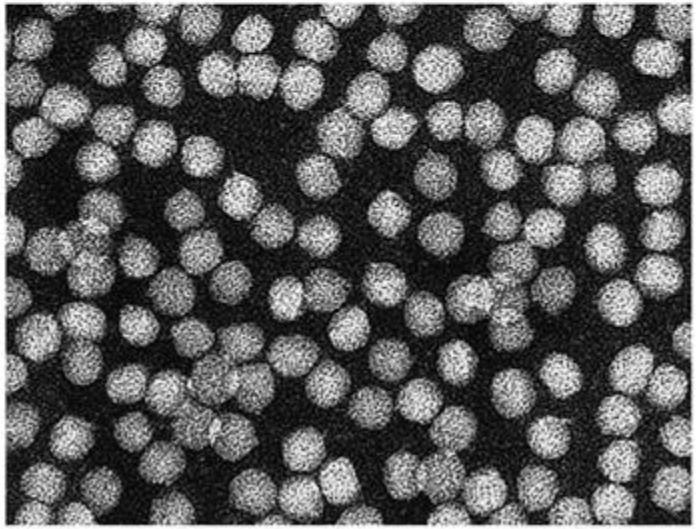
Plasma Lipoproteins



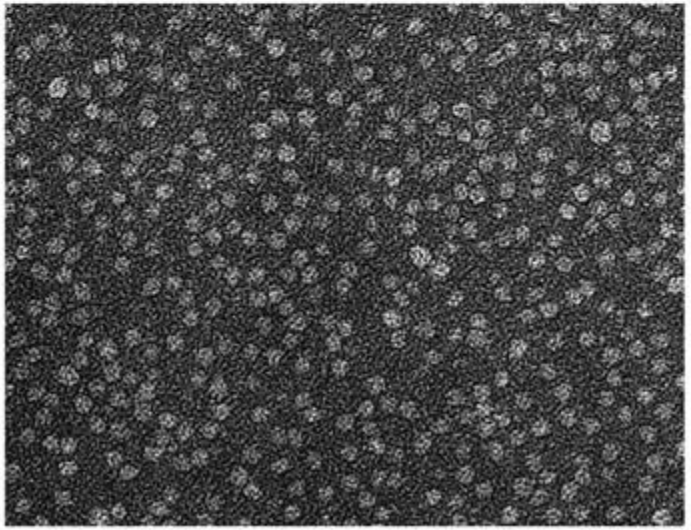
Chylomicrons (x60,000)



VLDL (x180,000)

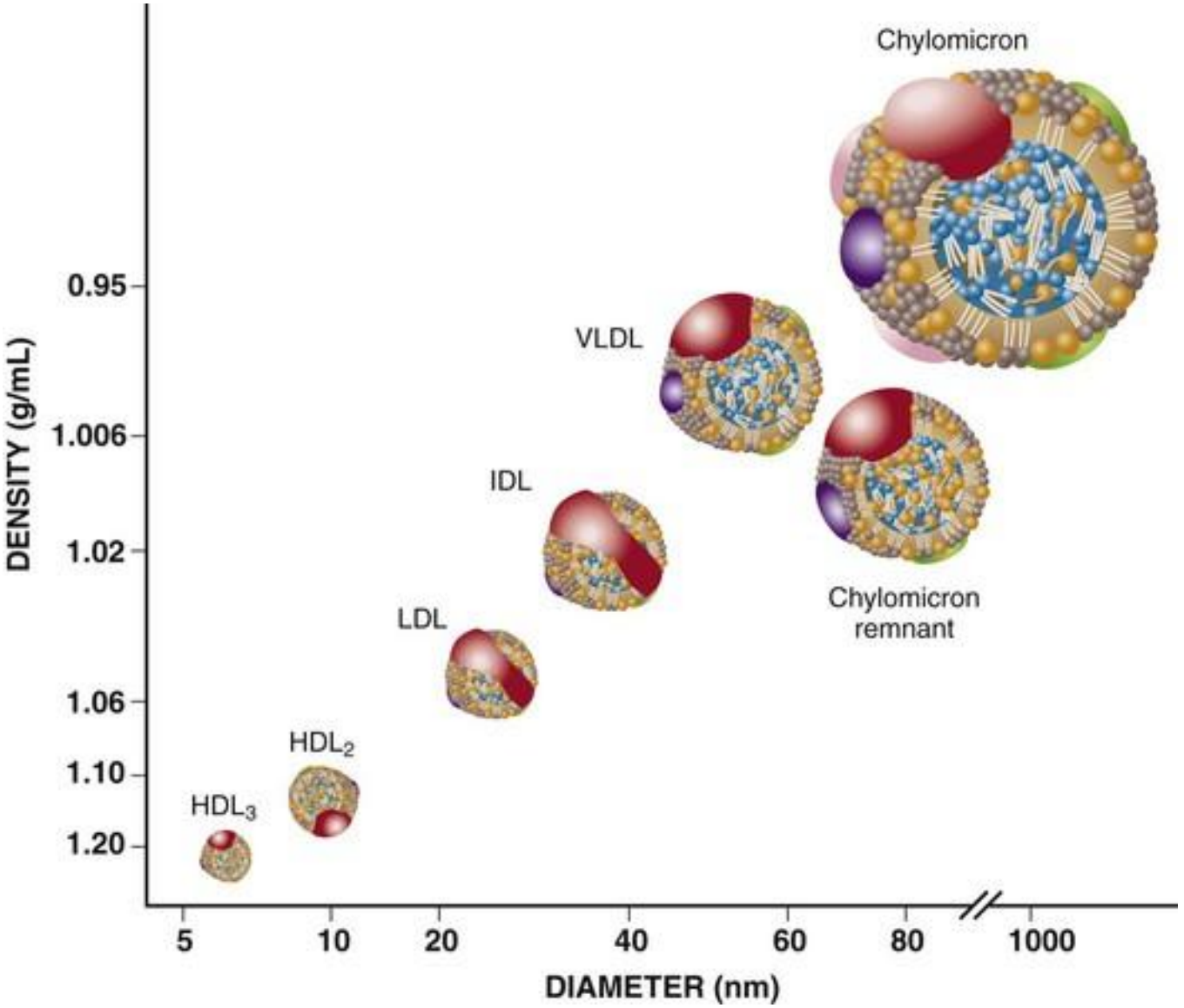


LDL (x180,000)

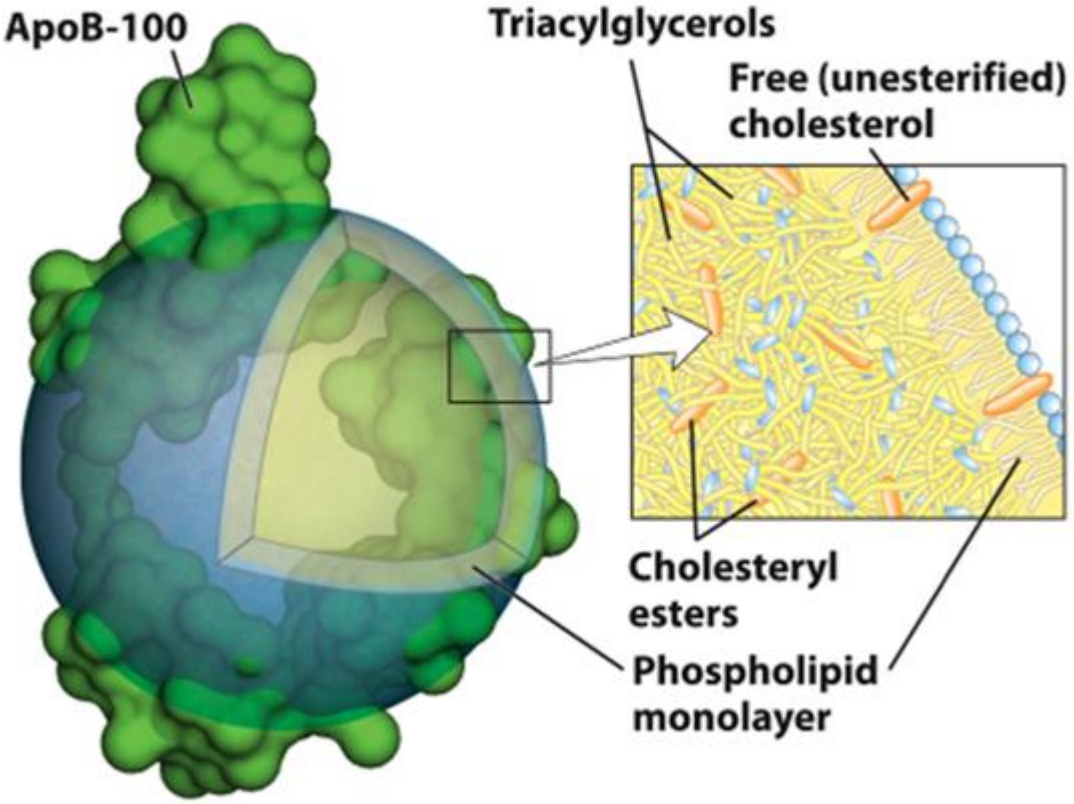


HDL (x180,000)

Plasma Lipoproteins



Plasma Lipoproteins



Major Classes of Human Plasma Lipoproteins: Some Properties

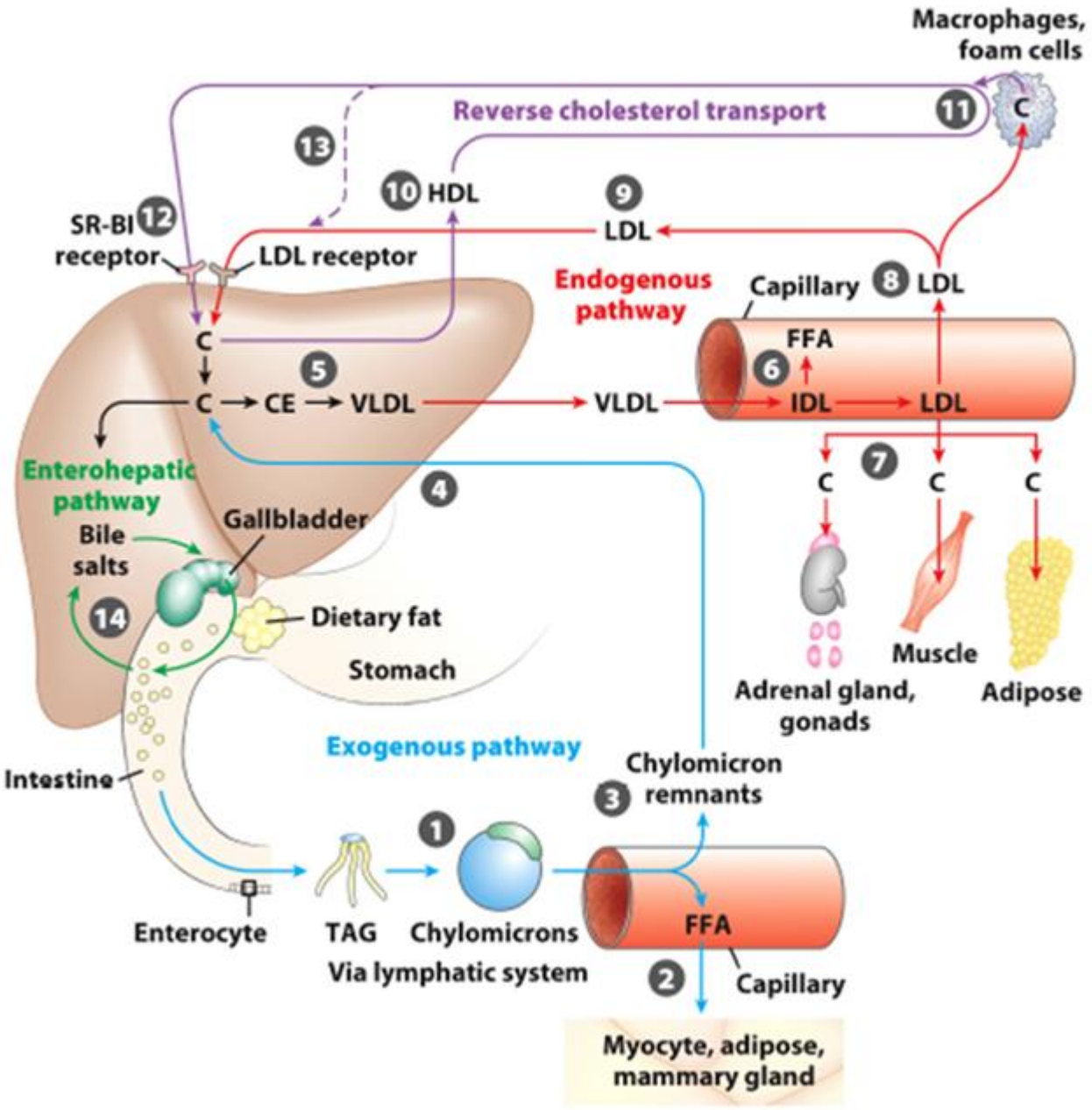
Lipoprotein	Density (g/mL)	Composition (wt %)				
		Protein	Phospholipids	Free cholesterol	Cholesteryl esters	Triacylglycerols
Chylomicrons	<1.006	2	9	1	3	85
VLDL	0.95–1.006	10	18	7	12	50
LDL	1.006–1.063	23	20	8	37	10
HDL	1.063–1.210	55	24	2	15	4

Source: Modified from Kritchevsky, D. (1986) Atherosclerosis and nutrition. *Nutr. Int.* **2,** 290 – 297.

Apolipoproteins of the Human Plasma Lipoproteins

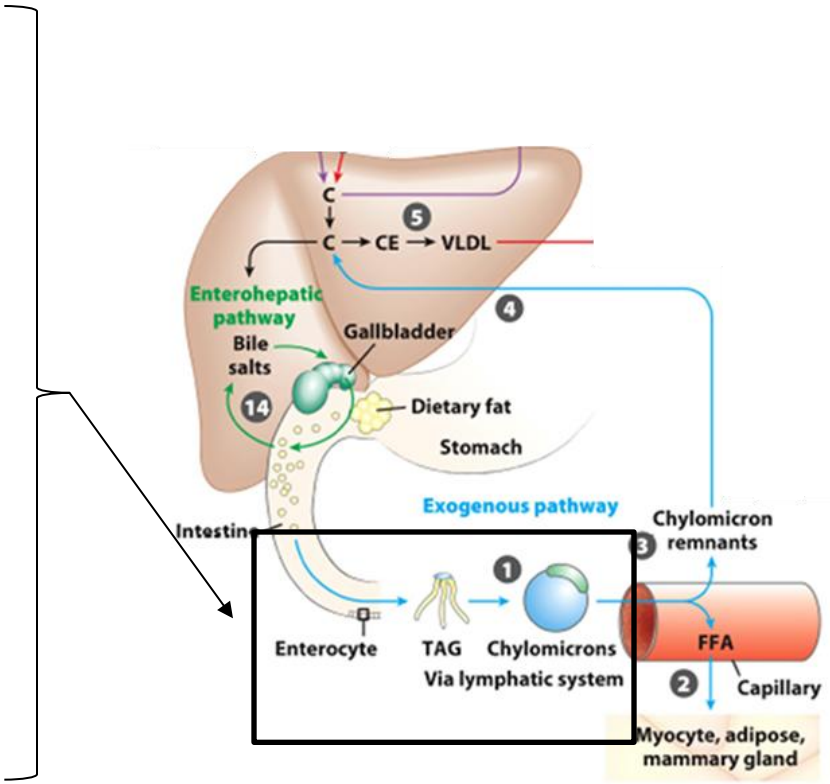
Apolipoprotein	Polypeptide molecular weight	Lipoprotein association	Function (if known)
ApoA-I	28,100	HDL	Activates LCAT; interacts with ABC transporter
ApoA-II	17,400	HDL	Inhibits LCAT
ApoA-IV	44,500	Chylomicrons, HDL	Activates LCAT; cholesterol transport/clearance
ApoB-48	242,000	Chylomicrons	Cholesterol transport/clearance
ApoB-100	512,000	VLDL, LDL	Binds to LDL receptor
ApoC-I	7,000	VLDL, HDL	
ApoC-II	9,000	Chylomicrons, VLDL, HDL	Activates lipoprotein lipase
ApoC-III	9,000	Chylomicrons, VLDL, HDL	Inhibits lipoprotein lipase
ApoD	32,500	HDL	
ApoE	34,200	Chylomicrons, VLDL, HDL	Triggers clearance of VLDL and chylomicron remnants

Source: Modified from Vance, D.E. & Vance, J.E. (eds) (2008) *Biochemistry of Lipids and Membranes*, 5th edn, Elsevier Science Publishing.



Exogenous pathway

Chylomicrons are the largest of the lipoproteins and the least dense, containing a high proportion of triacylglycerols.
Chylomicrons are synthesized in the ER of epithelial cells that line the small intestine, then move through the lymphatic system and enter the bloodstream via the left subclavian vein. The apolipoproteins of chylomicrons include apoB-48 (unique to this class of lipoproteins), apoE, and apoC-II.

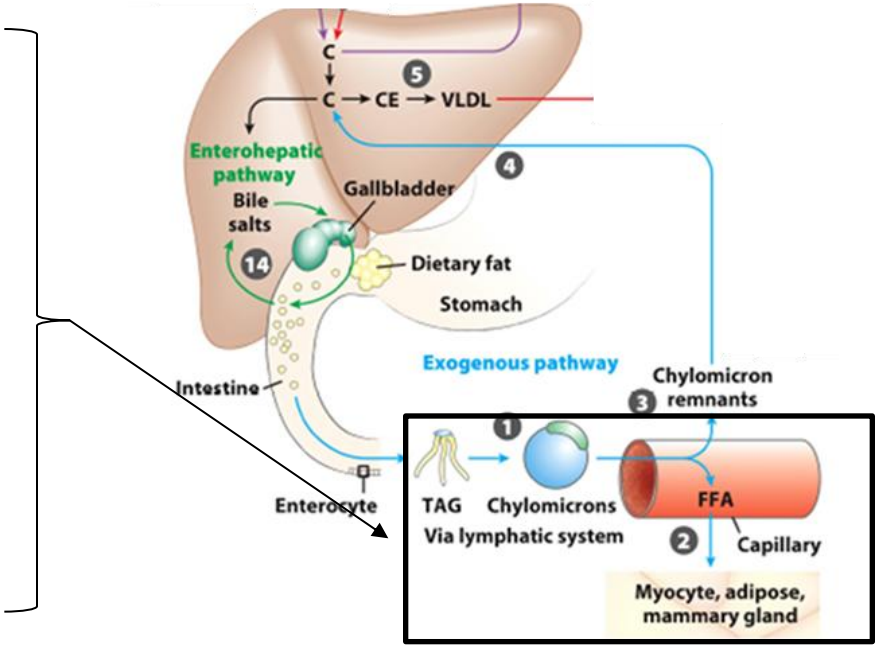


	Density (g/mL)	Composition (wt %)				
		Protein	Phospholipids	Free cholesterol	Cholesteryl esters	Triacylglycerols
Chylomicrons	<1.006	2	9	1	3	85

Exogenous pathway

ApoC-II activates lipoprotein lipase in the capillaries of adipose, heart, skeletal muscle, and lactating mammary tissues, allowing the release of free fatty acids to these tissues.

Chylomicrons thus carry dietary fatty acids to tissues where they will be consumed or stored as fuel.



	Density (g/mL)	Composition (wt %)				
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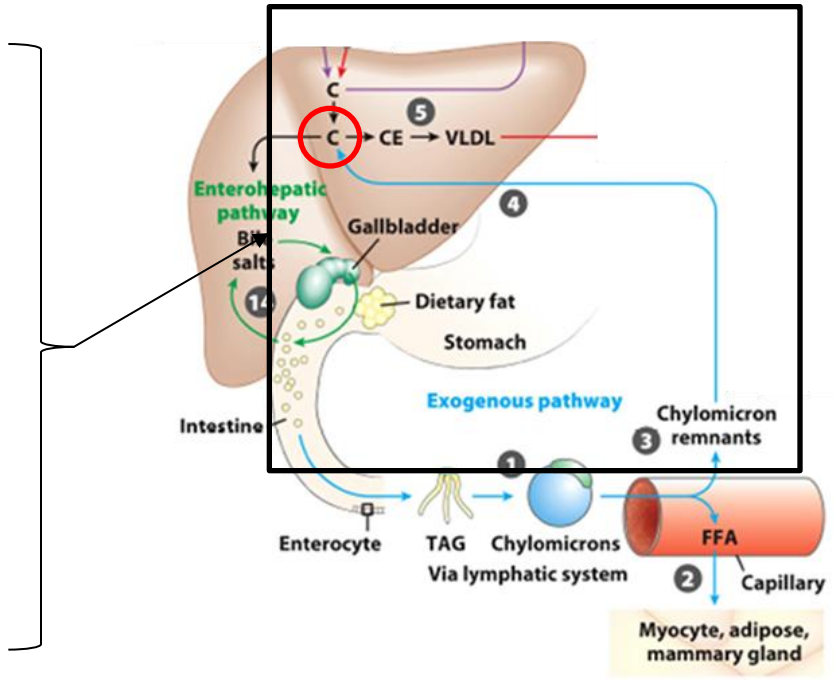
Exogenous pathway

The remnants of chylomicrons (depleted of most of their triacylglycerols but still containing cholesterol, apoE, and apoB-48) move through the bloodstream to the liver.

Receptors in the liver bind to the apoE in the chylomicron remnants and mediate their uptake by endocytosis. In the liver, the remnants release their cholesterol and are degraded in lysosomes.



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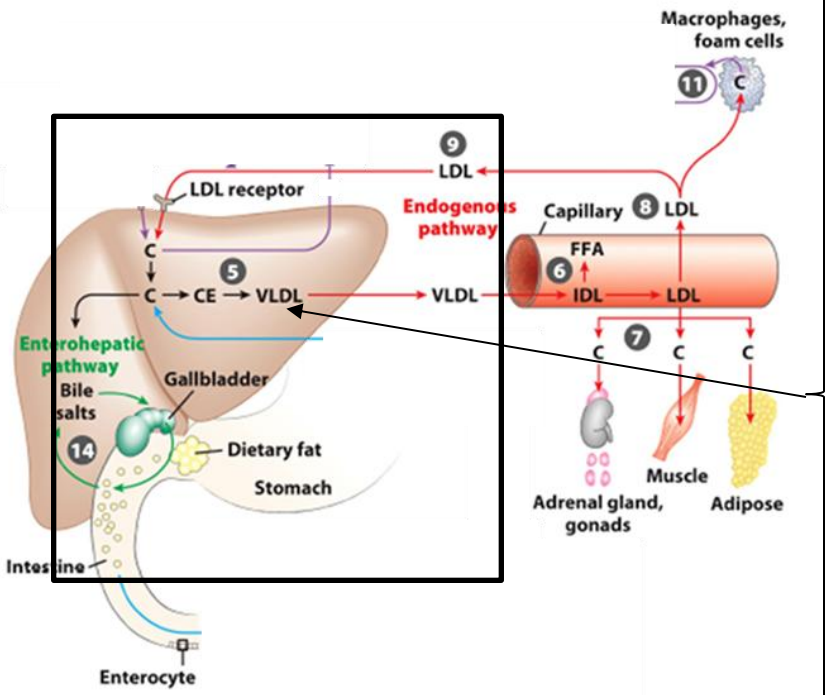
Endogenous pathway



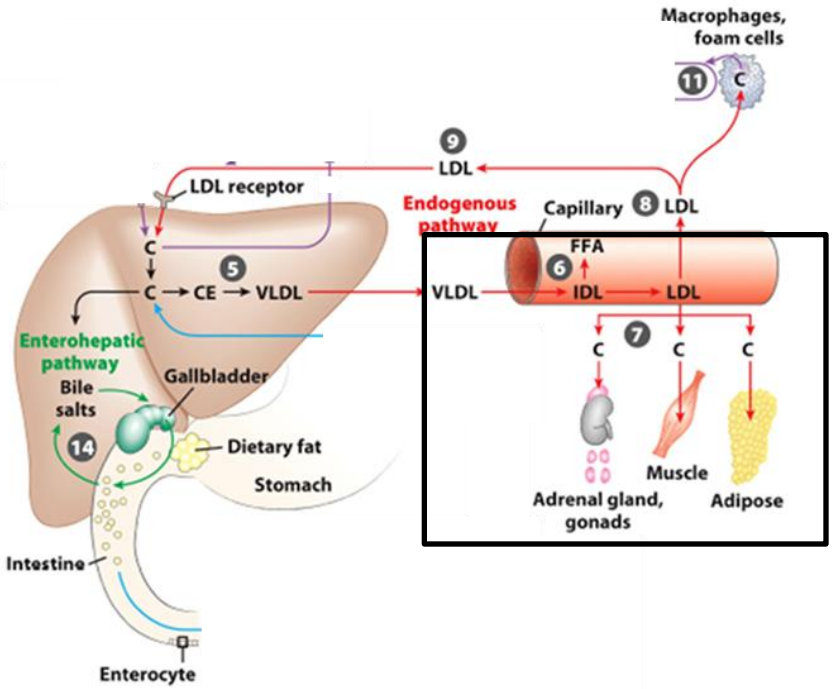
When the diet contains more fatty acids than are needed immediately as fuel, they are converted to triacylglycerols in the liver and packaged with specific apolipoproteins into **very-low-density lipoprotein (VLDL)**.

Excess carbohydrate in the diet can also be converted to triacylglycerols in the liver and exported as VLDLs.

In addition to triacylglycerols, VLDLs contain some cholesterol and cholesteryl esters, as well as apoB-100, apoC-I, apoC-II, apoC-III, and apo-E.

		Composition (wt %)				
	Density (g/mL)	Protein	Phospholipids	Free cholesterol	Cholesteryl esters	Triacylglycerols
VLDL	0.95–1.006	10	18	7	12	50

Endogenous pathway



These lipoproteins are transported in the blood from the liver to muscle and adipose tissue, where activation of lipoprotein lipase by apoC-II causes the release of free fatty acids from the VLDL triacylglycerols.

Adipocytes take up these fatty acids, reconvert them to triacylglycerols, and store the products in intracellular lipid droplets; myocytes, in contrast, primarily oxidize the fatty acids to supply energy.

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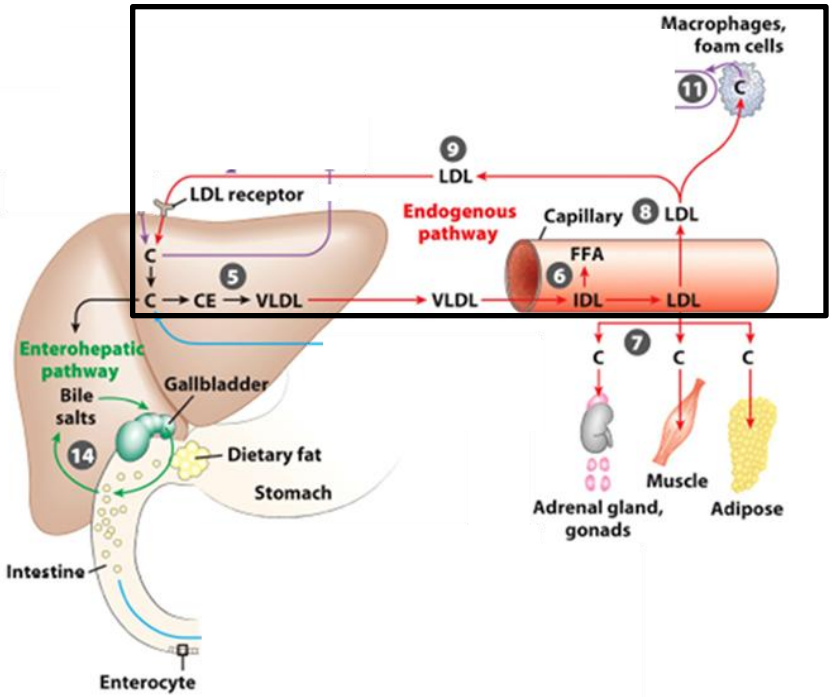
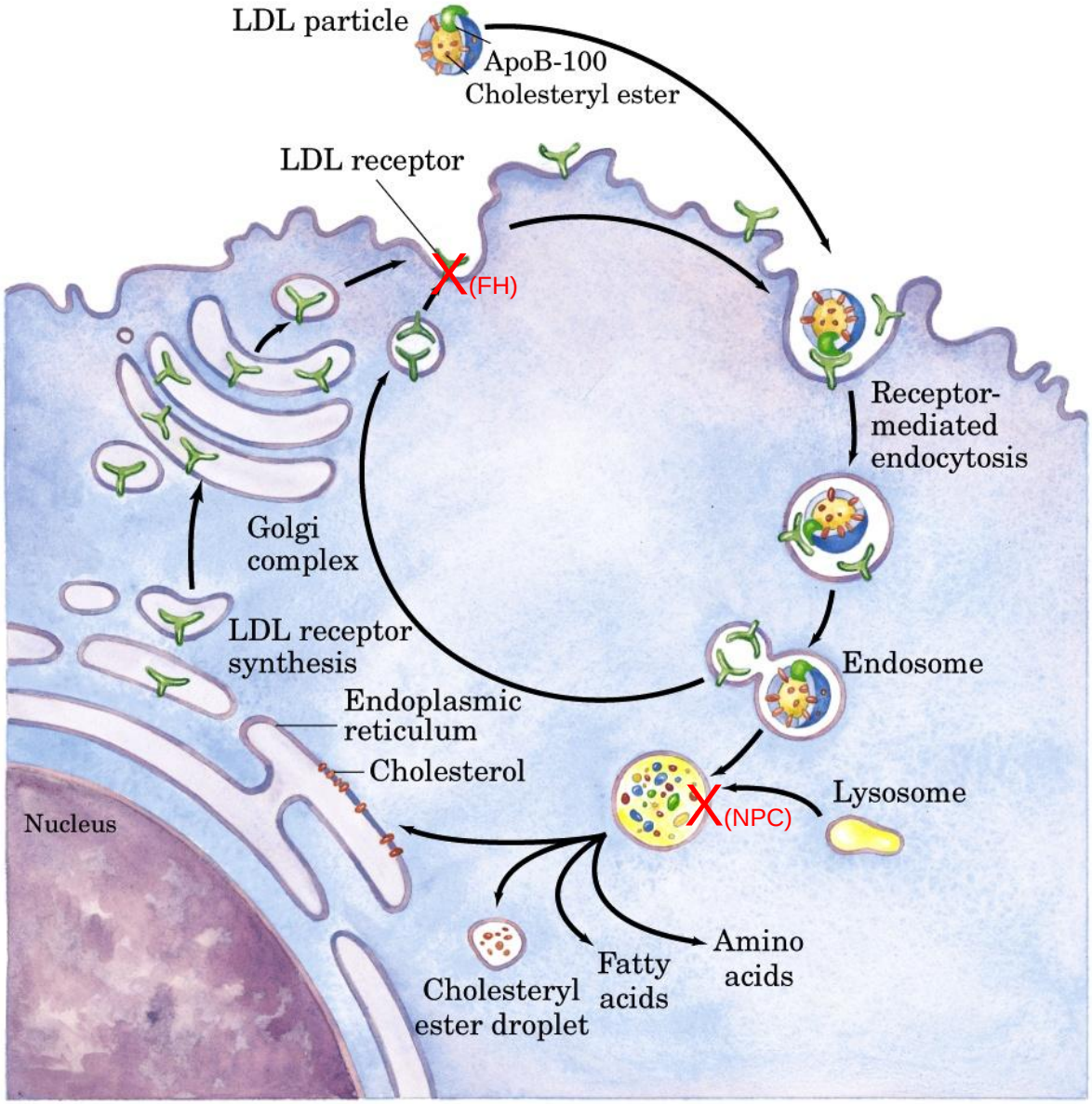
Endogenous pathway



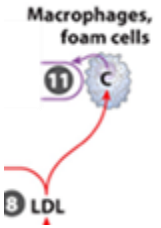
Most VLDL remnants are removed from the circulation by hepatocytes. The uptake, like that for chylomicrons, is receptor-mediated and depends on the presence of apoE in the VLDL remnants.

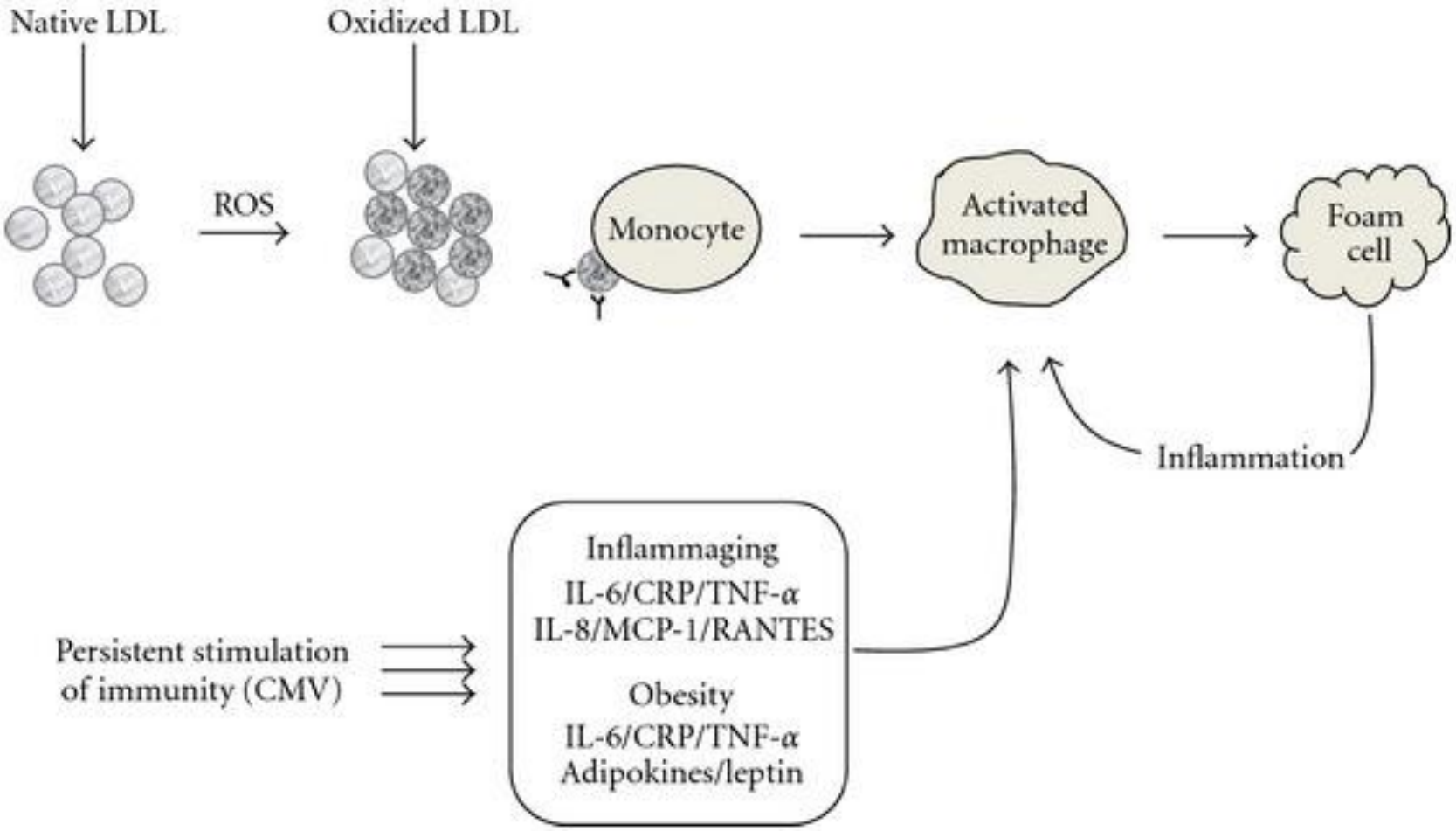
The loss of triacylglycerol converts VLDL to VLDL remnants and **low-density lipoprotein (LDL)**. Very rich in cholesterol and cholesteryl esters and containing apoB-100 as their major apolipoprotein, LDLs carry cholesterol to membrane receptors that recognize apoB-100.

		Composition (wt %)				
	Density (g/mL)	Protein	Phospholipids	Free cholesterol	Cholesteryl esters	Triacylglycerols
LDL	1.006–1.063	23	20	8	37	10

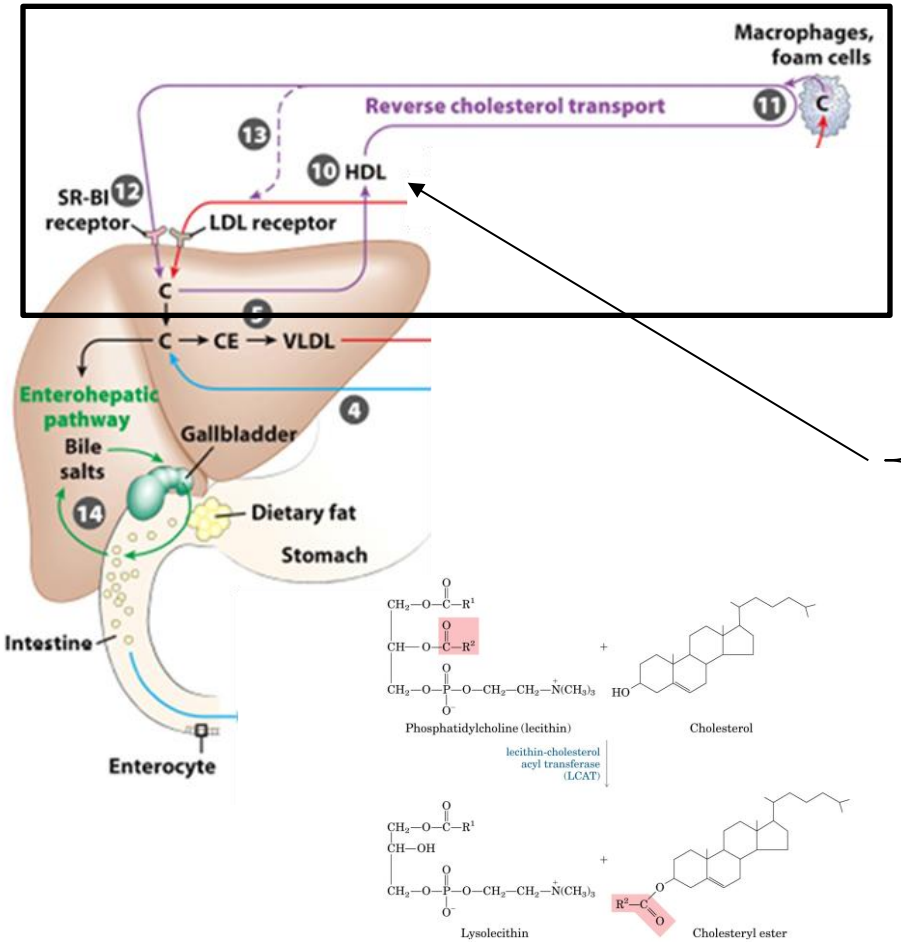


Role of oxidized LDL





Reverse cholesterol transport



The fourth major lipoprotein type, **high-density lipoprotein (HDL)**, originates in the liver as small, protein-rich particles that contain relatively little cholesterol and cholesteryl esters.

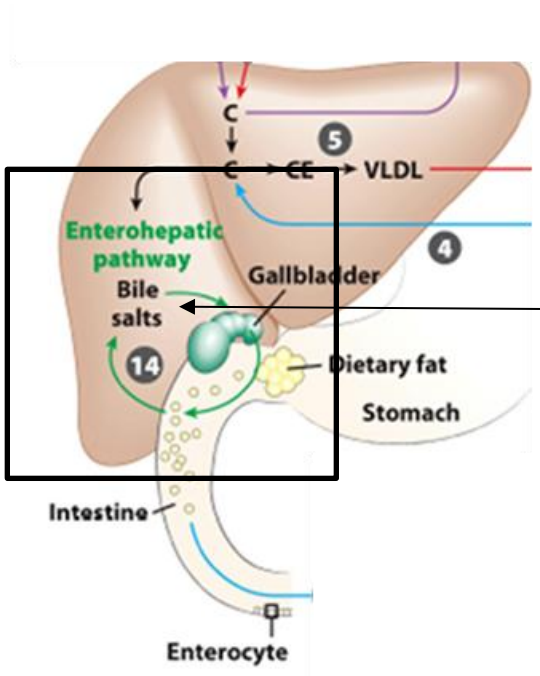
HDLs contain apoA-I, apoC-I, apoC-II, and other apolipoproteins, as well as the enzyme lecithin-cholesterol acyl transferase (LCAT), which catalyzes the formation of cholesteryl esters from lecithin (phosphatidylcholine) and cholesterol.

		Composition (wt %)				
	Density (g/mL)	Protein	Phospholipids	Free cholesterol	Cholesteryl esters	Triacylglycerols
HDL	1.063–1.210	55	24	2	15	4

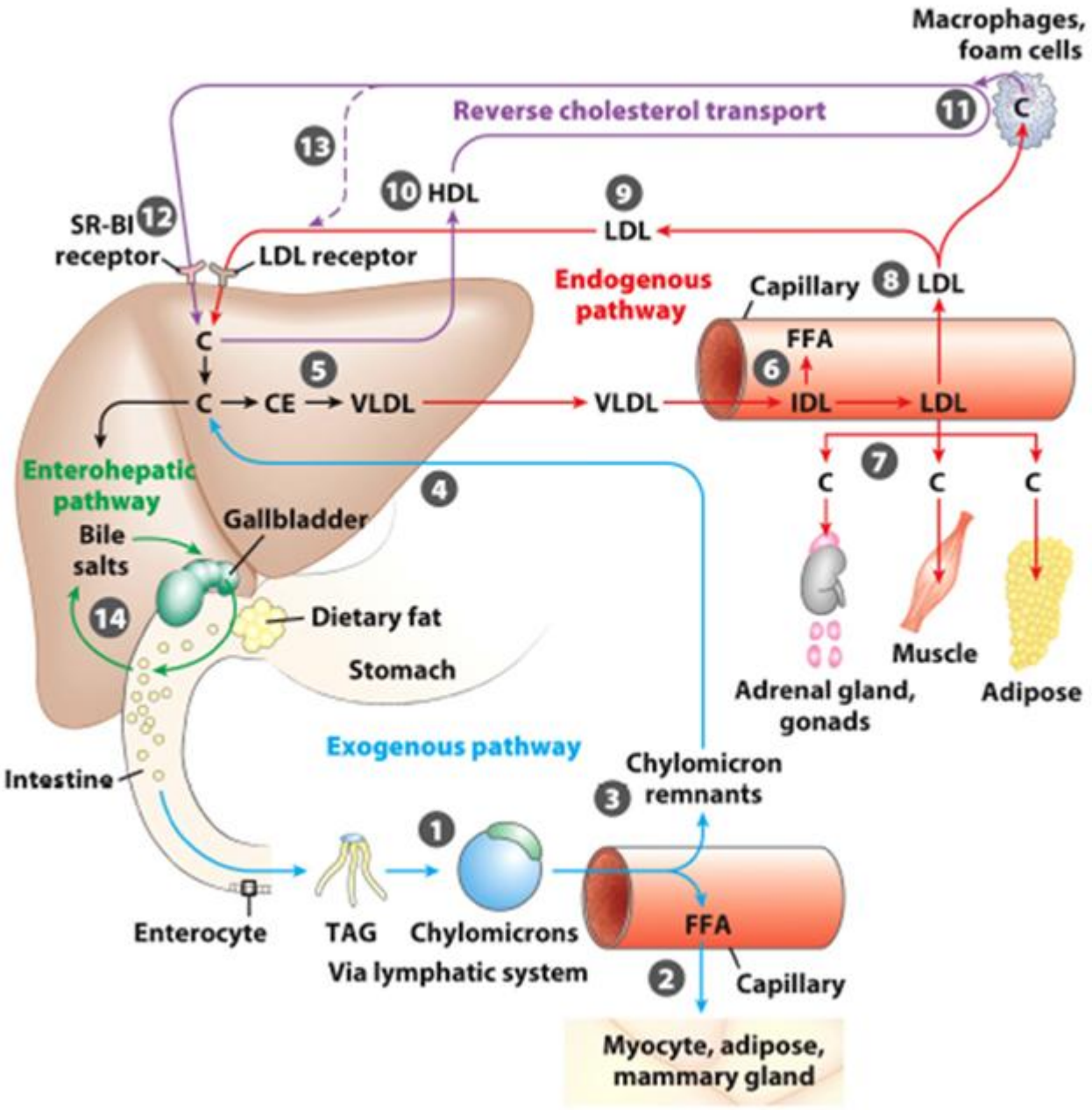
HDL

- After synthesis they are poor of lipids.
- Pick up cholesterol from extrahepatic tissues and blood vessels
- Acquire cholesterol esters by the action of LCAT on other lipoproteins
- Release cholesterol esters to liver and to steroidogenic tissues

Reverse cholesterol transport



Much of the cholesterol deliverd to the liver by HDL is converted into bile salts and stored in the gallbladder



Cholesterol and atherosclerosis

High cholesterol blood levels are found associated to atherosclerosis and cardiovascular disease.

- LDL deliver cholesterol to tissues, including blood vessels
- HDL picks up cholesterol from tissues