

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

Lipoprotein Metabolism

By

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Introduction

Lipid compounds:

Relatively water insoluble

Therefore, they are transported in plasma (aqueous) as Lipoproteins

Lipoproteins and Related Clinical Problems

- **Atherosclerosis and hypertension**
- **Coronary heart diseases**
- **Lipoproteinemias (hypo- and hyper-)**
- **Fatty liver**

Lipoprotein Structure

Protein part: Apoproteins or apolipoproteins

Abbreviations: Apo-A, B, C, D, E

Functions:

Structural and transport function

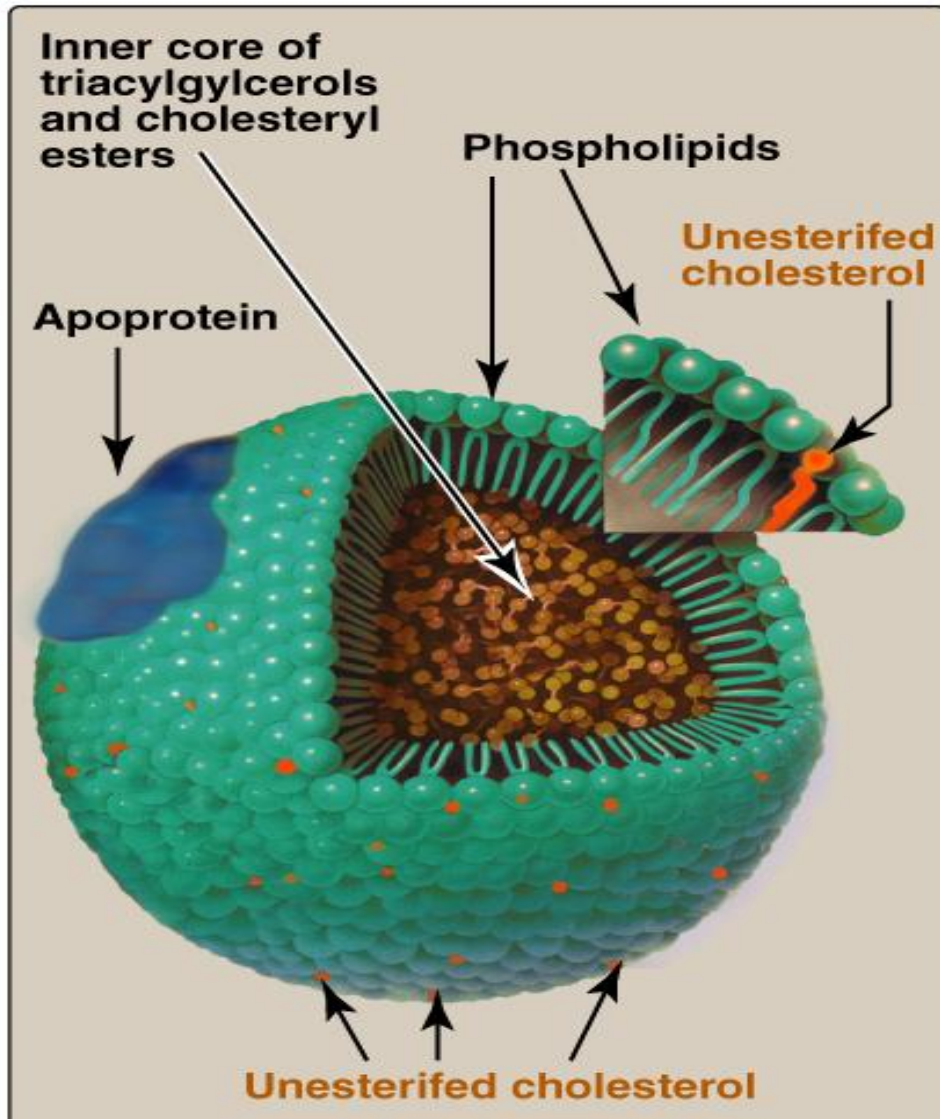
Enzymatic function

Ligands for receptors

Lipid part:

- **According to the type of lipoproteins**
- **Different lipid components in various combinations**

Spherical molecules of lipids and proteins (apoproteins)



Outer coat:

- **Apoproteins**
- **Phospholipids**
- **Cholesterol (Unesterified)**

Inner core:

- **TG**
- **Cholesterol ester (CE)**

Lipoprotein Structure

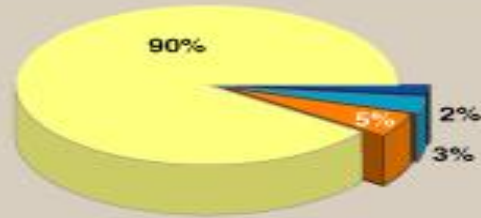
Types of Lipoproteins

- **What's different in various types of lipoproteins?**

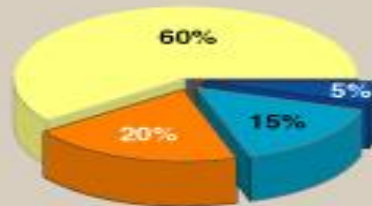
They differ in lipid and protein composition and therefore, they differ in

- **Size and density**
- **Electrophoretic mobility**

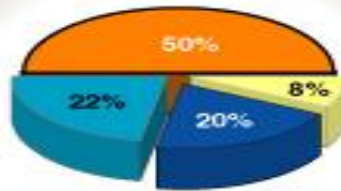
Types and Composition of Lipoproteins



Chylomicron



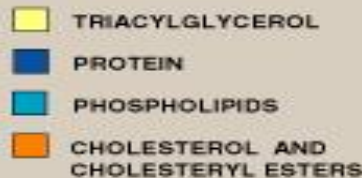
Very-Low-Density Lipoprotein (VLDL)



Low-Density Lipoprotein (LDL)



High-Density Lipoprotein (HDL)

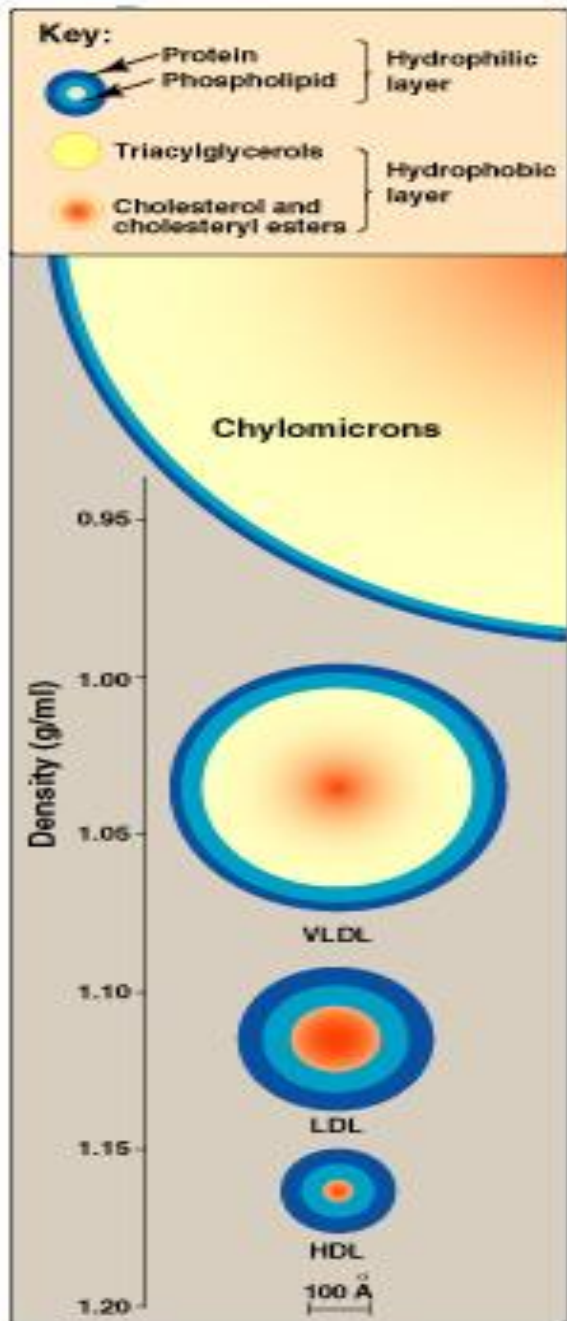


Chylomicrons

Very low density Lipoprotein (VLDL)

Low density Lipoprotein (LDL)

High density Lipoprotein (HDL)



Ultracentrifugation of Lipoproteins

Lipoprotein Electrophoresis

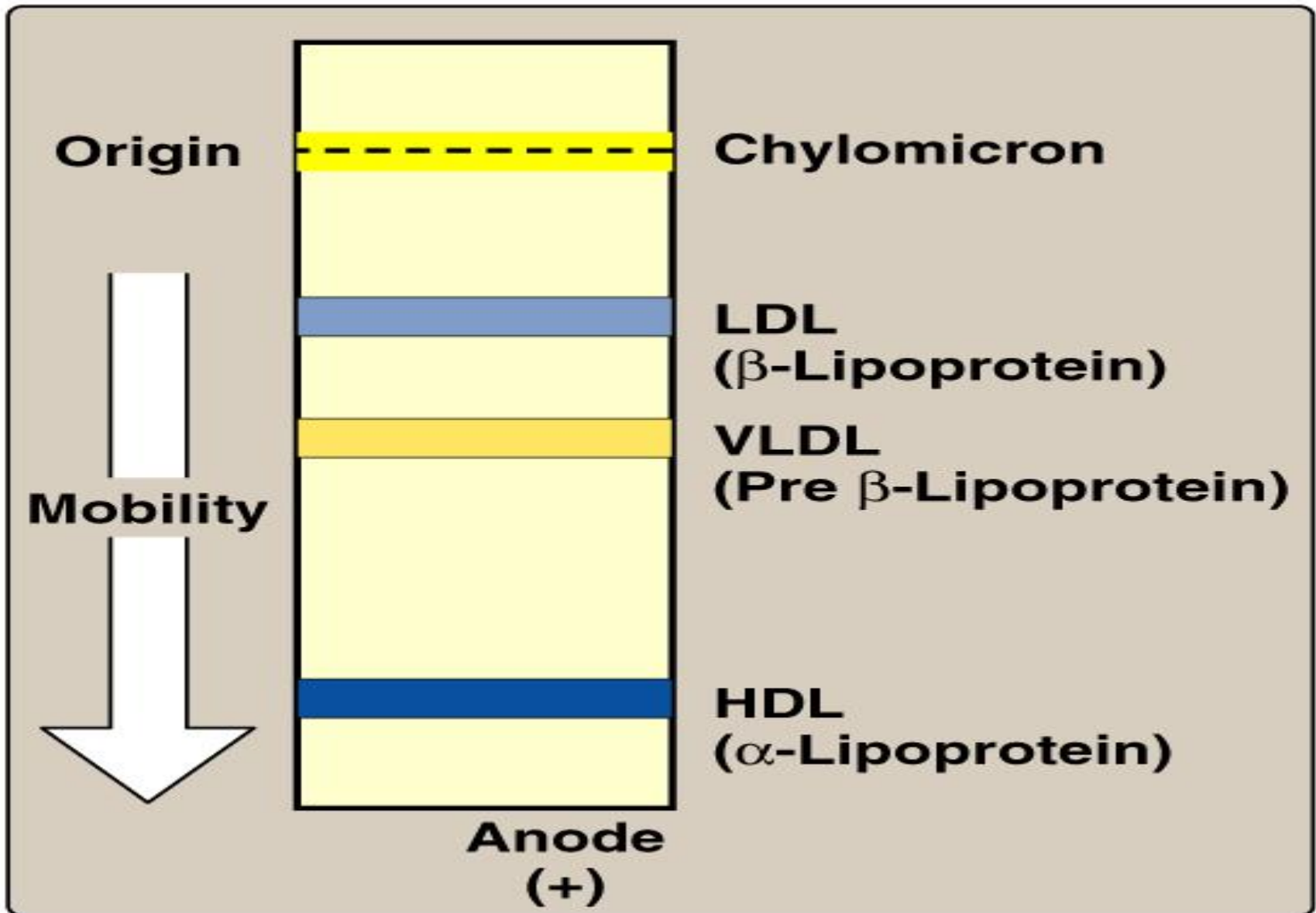


Figure 18.15

Plasma Lipoproteins

For triacylglycerol transport (TG-rich):

- **Chylomicrons:** TG of dietary origin
- **VLDL:** TG of endogenous (hepatic) synthesis

For cholesterol transport (cholesterol-rich):

LDL: Mainly free cholesterol

HDL: Mainly esterified cholesterol

Chylomicrons

- Assembled in intestinal mucosal cells
- Lowest density
- Largest size
- Highest % of lipids and lowest % proteins
- Highest triacylglycerol (**dietary origin**)
- Carry **dietary** lipids to peripheral tissues
- Responsible for physiological milky appearance of plasma (**up to 2 hours after meal**)

Very Low Density Lipoproteins VLDLs

- Assembled in liver
- High triacylglycerol (**hepatic origin**)
- Carry lipids from **liver** to peripheral tissues
- Nascent VLDL: contains Apo B-100
- Mature VLDL: Apo B-100 **plus**
Apo C-II and Apo E
(**from HDL**)

Metabolism of VLDLs

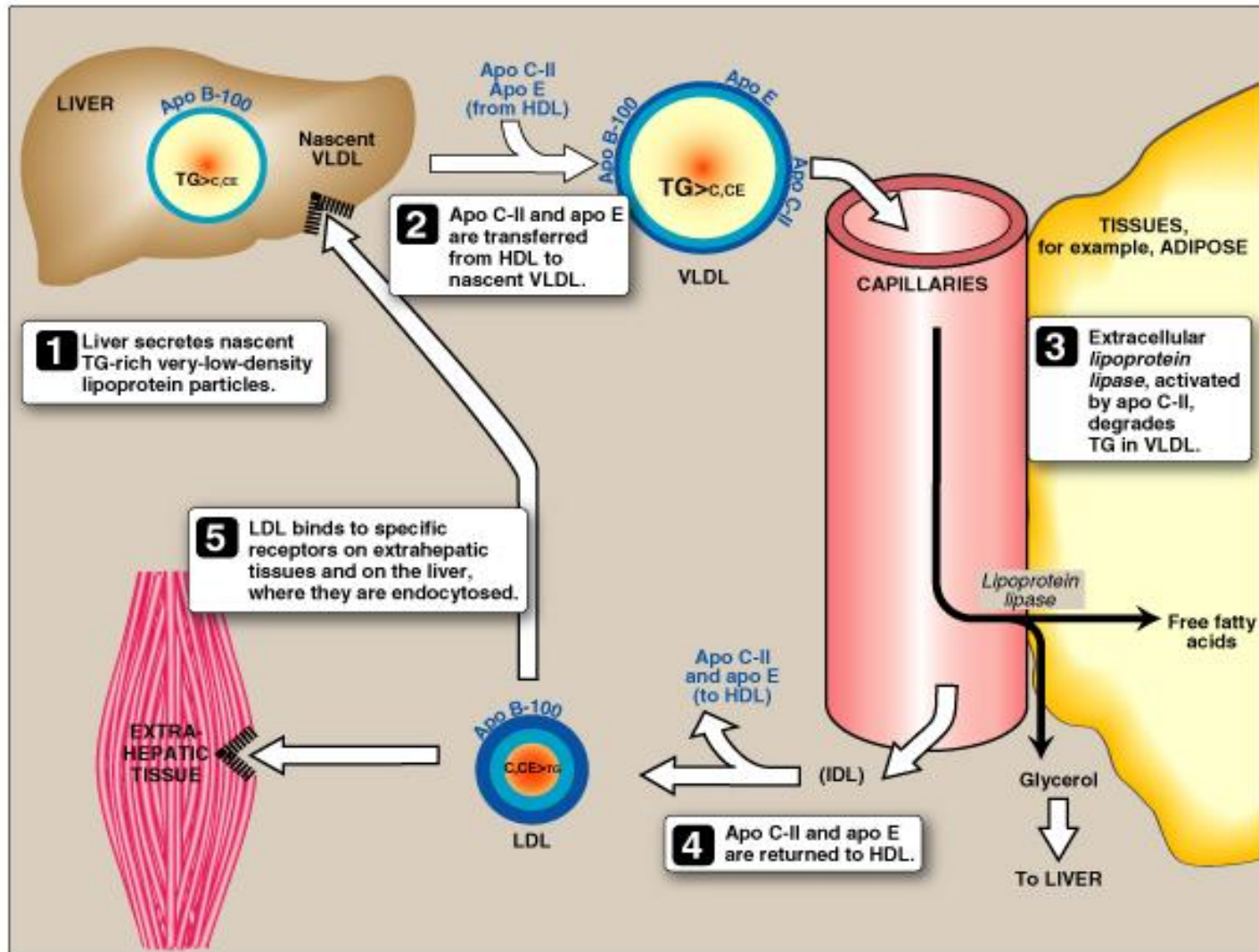
- Assembled and secreted by **liver**
- Mature VLDLs in blood
- Modifications of circulating VLDLs
- End products: IDL and LDL
- Related diseases:

Hypolipoproteinemia: Abetalipoproteinemia

Hyperlipoproteinemias:

Type I hyperlipoproteinemia

Familial type III hyperlipoproteinemia



VLDL Metabolism

Metabolism of VLDLs: Mature VLDLs

- Assembled and secreted by liver directly into blood as nascent form
- Mature VLDLs: contain Apo B-100 **plus** Apo C-II and Apo E. ApoC-II is required for activation of lipoprotein lipase
- Lipoprotein lipase is required to degrade TG into glycerol and fatty acids

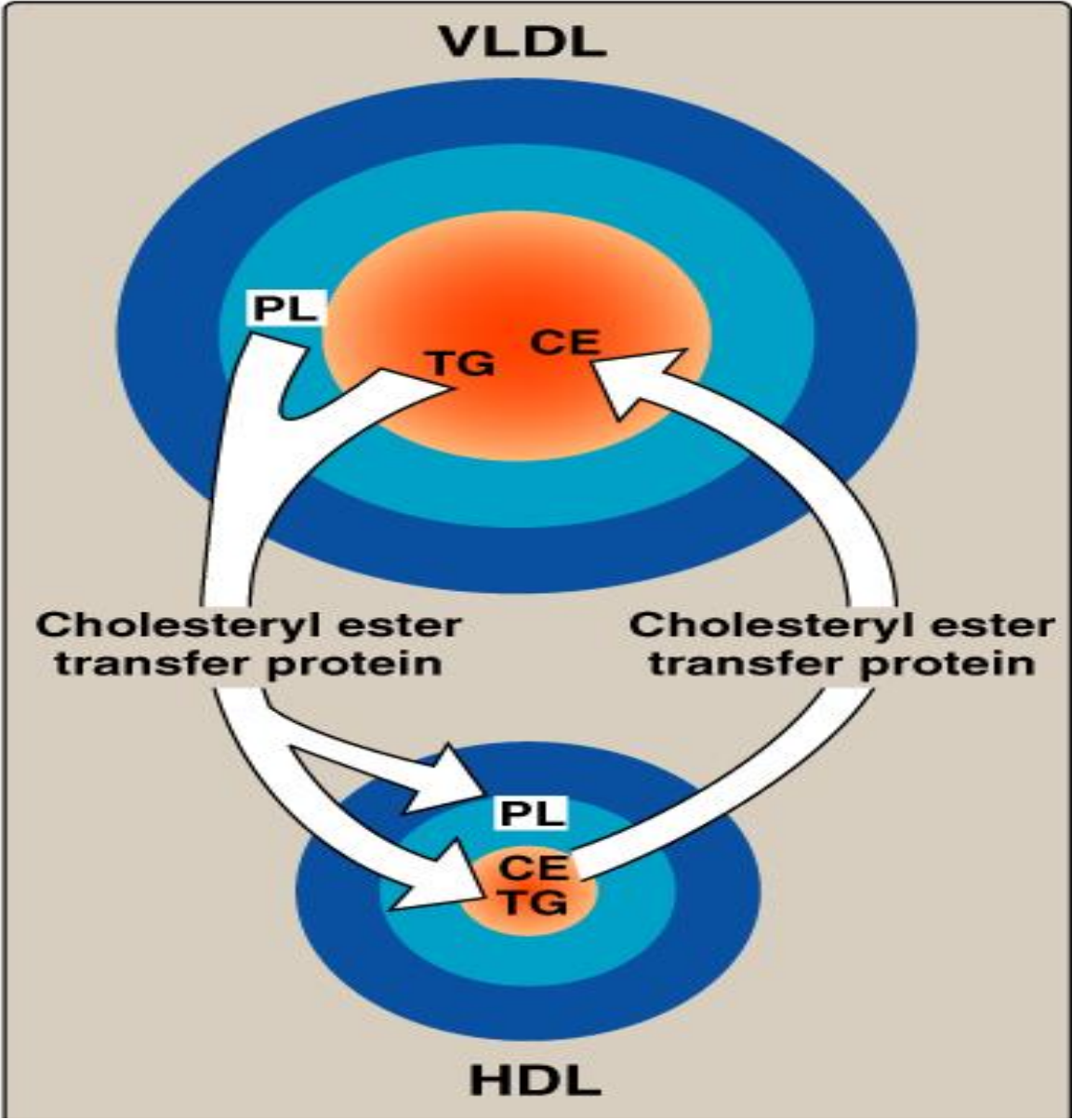
Lipoprotein lipase

- Extracellular enzyme, anchored by heparan sulfate to the capillary walls of most tissues
- Predominantly present in **adipose tissue, cardiac & skeletal muscle**
- Requires ApoC-II for activation
- Degrades TG into glycerol and free fatty acids
- Insulin stimulates its synthesis and transfer to the luminal surface of the capillary
- If deficient (or if apo C-II is deficient) → type 1 hyperlipoproteinemia = familial lipoprotein lipase deficiency)

Modifications of Circulating VLDLs

- 1- Degradation of TG by lipoprotein lipase →, VLDLs become**
 - Smaller in size**
 - More dense**
- 2- Apo C & Apo E return back to HDL**
- 3- Some TG are transferred from VLDL to HDL in exchange with cholesterol ester (By cholesterol ester transfer protein)**

VLDL → IDL (returns Apo E to HDL) → LDL



Lipid-Transfer Protein

VLDLs-Related Diseases

1- Hypolipoproteinemia

Abetalipoproteinemia

Defect in TG-transfer protein

Apo B-100 cannot be loaded with lipid

Accumulation of TG in liver

2- Fatty Liver (hepatic steatosis)

Imbalance between hepatic synthesis of TG and secretion of VLDLs.

Accumulation of TG in liver

VLDLs-Related Diseases, *continued...*

3- Hyperlipoproteinemia

Type I Hyperlipoproteinemia

- **Familial Lipoprotein lipase deficiency**
- **Due to deficiency of lipoprotein lipase or its cofactor (Apo C-II)**
- **Shows a dramatic accumulation (≥ 1000 mg/dl) of chylomicrons in plasma**
- **Usually associated with acute abdomen due to acute pancreatitis**
- **\uparrow plasma TG even in the fasted state**

Type III Hyperlipoproteinemia

- **- (Familial dysbetalipoproteinemia)**
- **- due to Apo E deficiency**
- **- Associated with hypercholesterolemia & premature atherosclerosis**

THANK YOU 😊