بسم الله الرحمن الرحيم

Lipoprotein Metabolism

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Everything in green is something I added from the lecture and extra-sources

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Introduction

Lipid compounds:

Relatively water insoluble **" which make s it difficult to move in the circulation"**

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

Why do we need lipid transport? "efficiency of transport"

1. **Different body tissues, at variable locations need lipids for different metabolic functions.**
2. **For efficient transport, then excretion of lipids.**

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….can be further Subdivided: Apo-B 100, Apo-C 2 …etc

Functions:

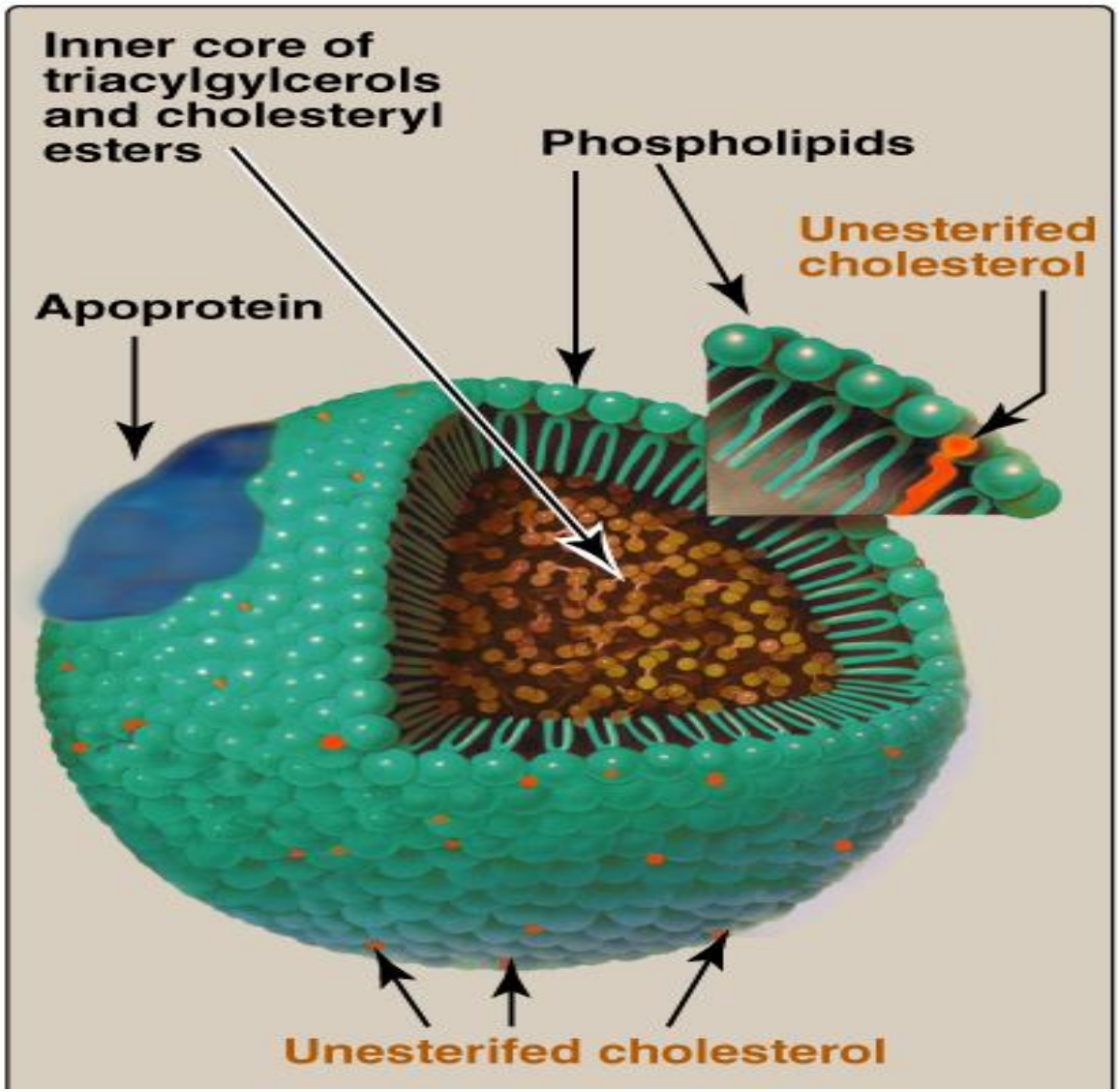
- Structural and transport function (most important)
- Enzymatic function (activation of enzymes)
- Ligands for receptors (for recognition)

Lipid part:

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

Apo=protein part (coat)

Spherical molecules of lipids and proteins (apoproteins)



Outer coat:

- Apoproteins
- Phospholipids
- Cholesterol (free, unesterfied)

Inner core:

- TG(triacyl glycerol)
- Cholesterol ester

Lipoprotein Structure

Types of Lipoproteins

- **Why do we have different types of lipoproteins?**

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

  Size and density

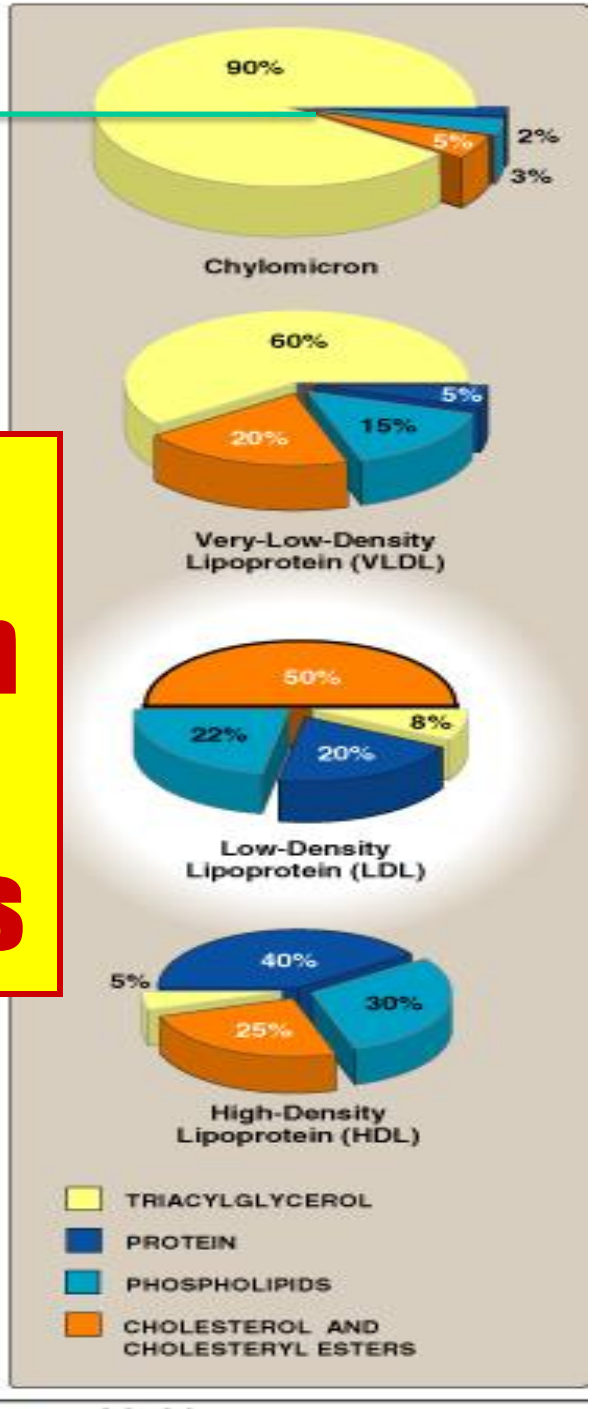
  Electrophoretic mobility

Density of lipoproteins can be measured through the use of ultra-centrifuge . The density of lipoproteins is determined through the percentage of lipid content to protein content.

Note: lipids are lighter(less dense) than proteins.

Mostly lipid, little protein, therefore has the lowest density

Types and Composition of Lipoproteins

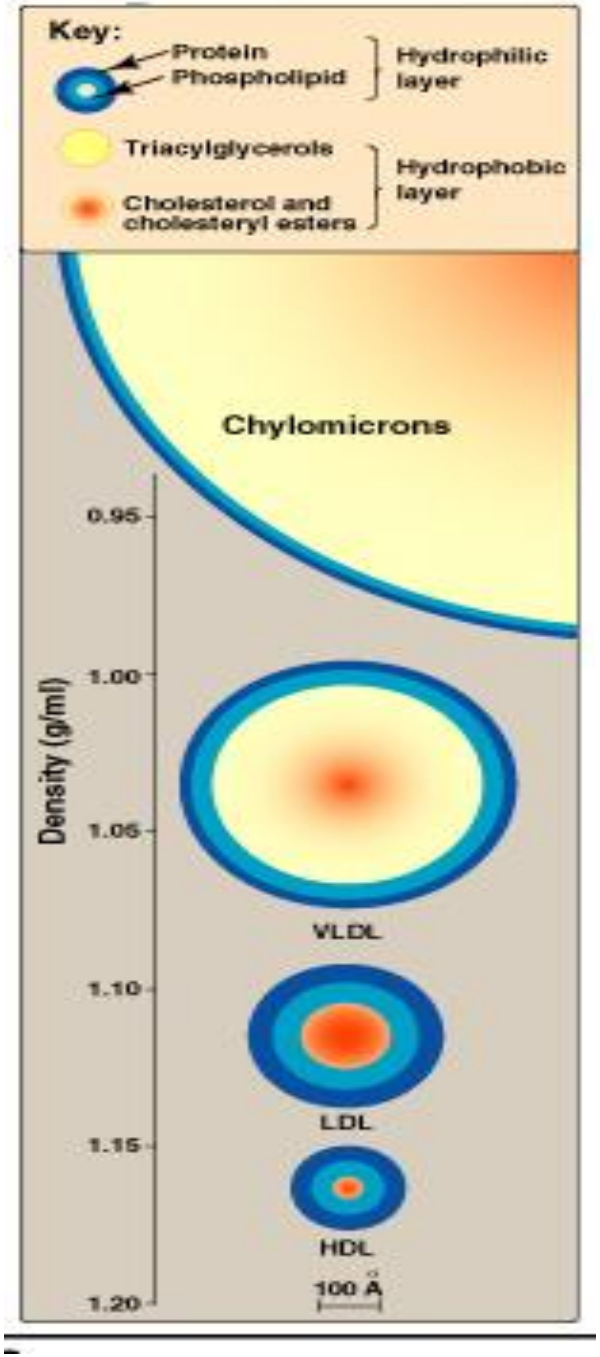


Chylomicrons

Very low density Lipoprotein (VLDL)

Low density Lipoprotein (LDL)

High density Lipoprotein (HDL)



Ultracentrifugation of Lipoproteins

Not used clinically, only for research use

Lipoprotein Electrophoresis

- Clinically used.

- different lipoproteins with different electro negativity are separated from the serum.

- the most electro-negative(HDL), will be the closest (nearest) to the anode(+).

- when the band size increase, it could indicate

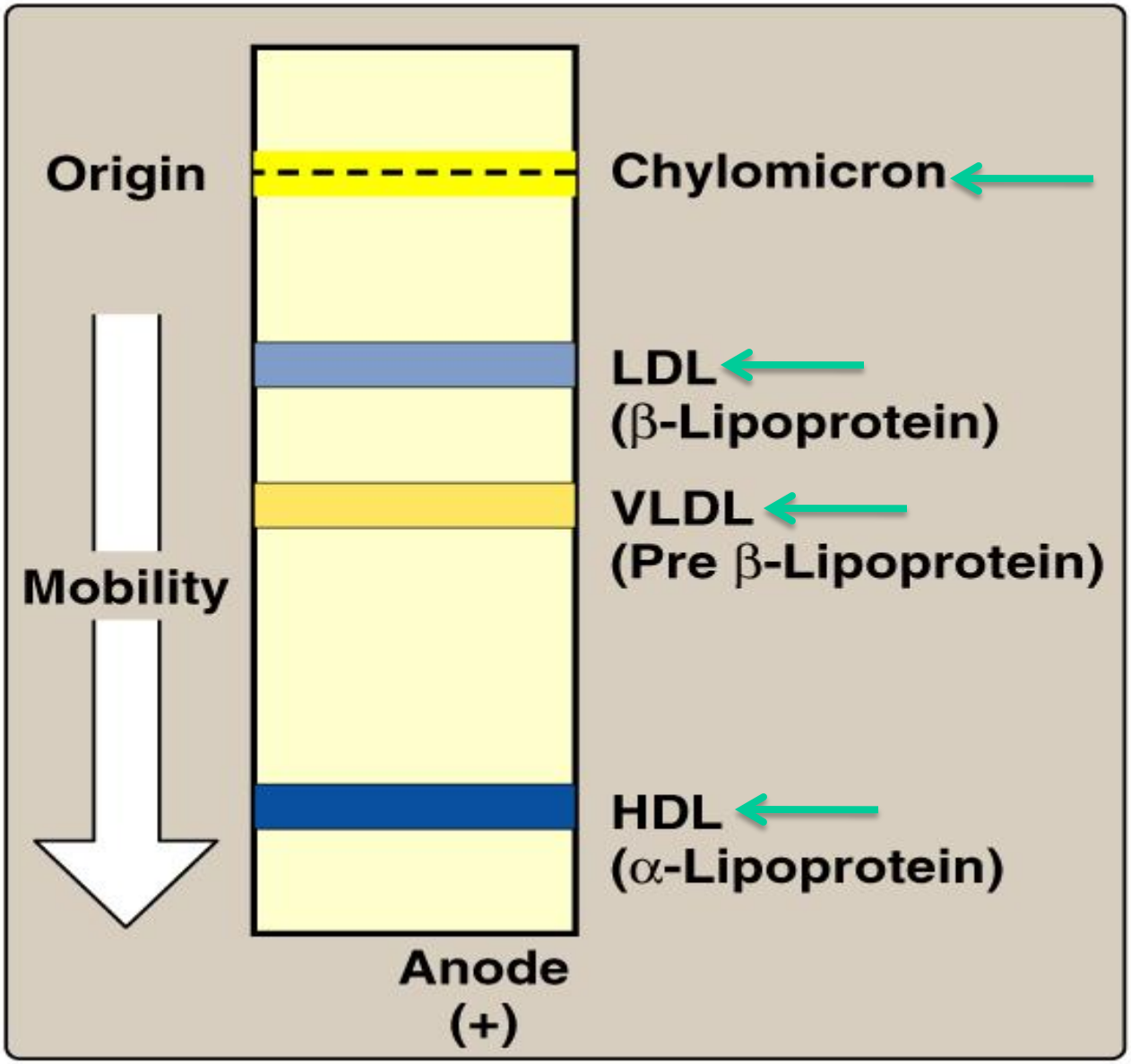


Figure 18.15

Plasma Lipoproteins

For triacylglycerol transport (TG-rich):

Chylomicrons: **TG of dietary origin** **"exogenous, absorbed in the intestinal mucosa"**

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

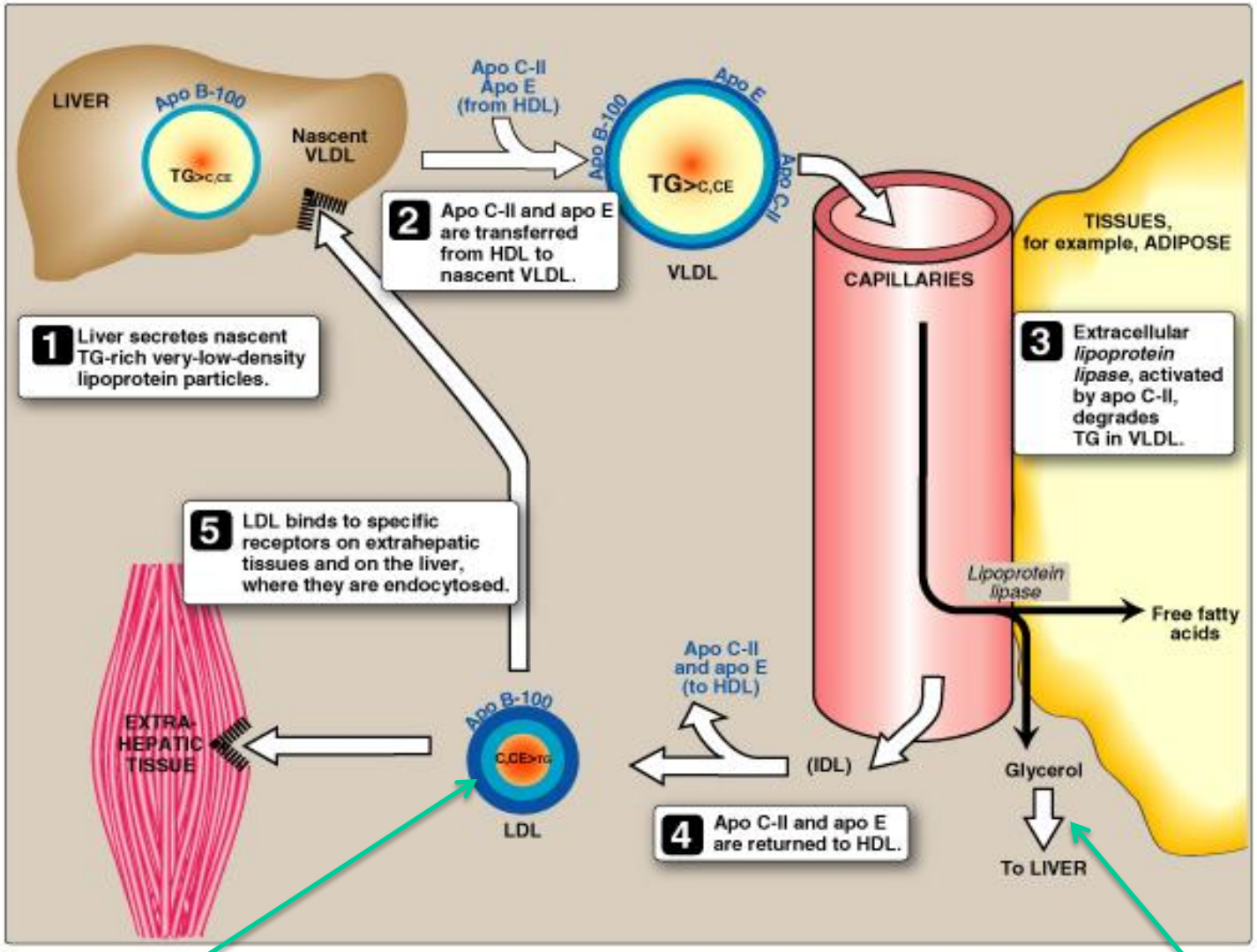
- Assembled and secreted by liver
- Mature VLDLs in blood
- Modifications of circulating VLDLs
- End products: IDL and LDL
- Related diseases:

  Hypolipoproteinemia: Abetalipoproteinemia

  Hyperlipoproteinemias:

    Type I hyperlipoproteinemia

    Familial type III hyperlipoproteinemia



At that stage, lipid content is lowered → density inceases

VLDL Metabolism

Glycerol undergo gluconeogenesis through the use of non-carbohydrate

Metabolism of VLDLs: Mature VLDLs

- **Assembled and secreted by liver directly into blood as nascent form** **"functionally in-active. NOT yet bonded to Apo c-2 or ApoE"**

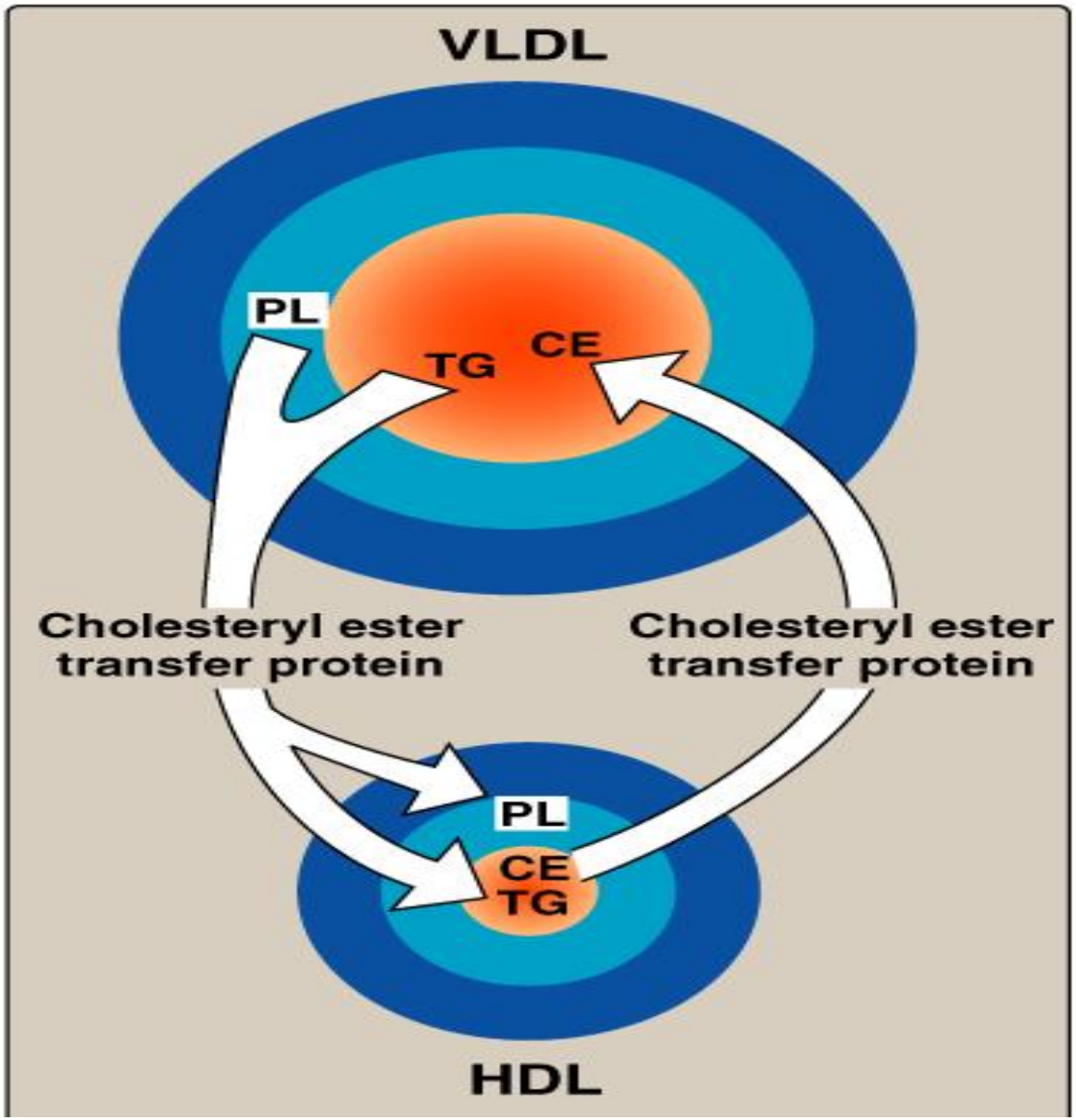
- **Mature VLDLs: contain Apo B-100 plus Apo C-II and Apo E. ApoC-II is required for activation of lipoprotein lipase**

- **Lipoprotein lipase is required to degrade TG into glycerol and fatty acids**

Modifications of Circulating VLDLs

- As TG is degraded, VLDLs become
  - Smaller in size
  - More dense
  - Apo C back to HDL
  - Exchange of TG with cholesterol ester (HDL) by cholesterol ester transfer protein
- Production of LDL in plasma

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



Lipid-Transfer Protein

VLDLs-Related Diseases

Hypolipoproteinemia

Abetalipoproteinemia

Defect in TG-transfer protein

Apo B-100 cannot be loaded with lipid

Accumulation of TG in liver

Fatty Liver (hepatic steatosis)

Imbalance between hepatic synthesis of TG and secretion of VLDLs.

Accumulation of TG in liver

VLDLs-Related Diseases

Hyperlipoproteinemia

Type I Hyperlipoproteinemia

Familial Lipoprotein lipase deficiency
or Apo C-II deficiency
Usually associated with acute abdomen
due to acute pancreatitis

Type III Hyperlipoproteinemia

Familial dysbetalipoproteinemia
Apo E deficiency
Hypercholesterolemia and atherosclerosis

Chylomicron Clinically

If blood was taken from someone two hours after he/she had a meal. The blood then was left for some time to separate it's component. In that condition the serum would usually look milky (yellow white and turbid*). This is caused by the high amount of chylomicron in the blood that was absorbed by the intestinal mucosa. The milky appearance would usually not appear if blood was taken few hours later in healthy individuals.

However, if the milky appearance persist for more than two hours, it is usually a pathological condition. The pathology in that case is type 1 hyperlipoproteinemia or familial lipoprotein lipase deficiency, due to lipoprotein lipase or apo C2 deficiency. This pathology is manifested by the dramatic accumulation of chylomicrons in the plasma.

*This appearance of turbidity is caused by the large chylomicron molecules (chilomycron has the largest size).