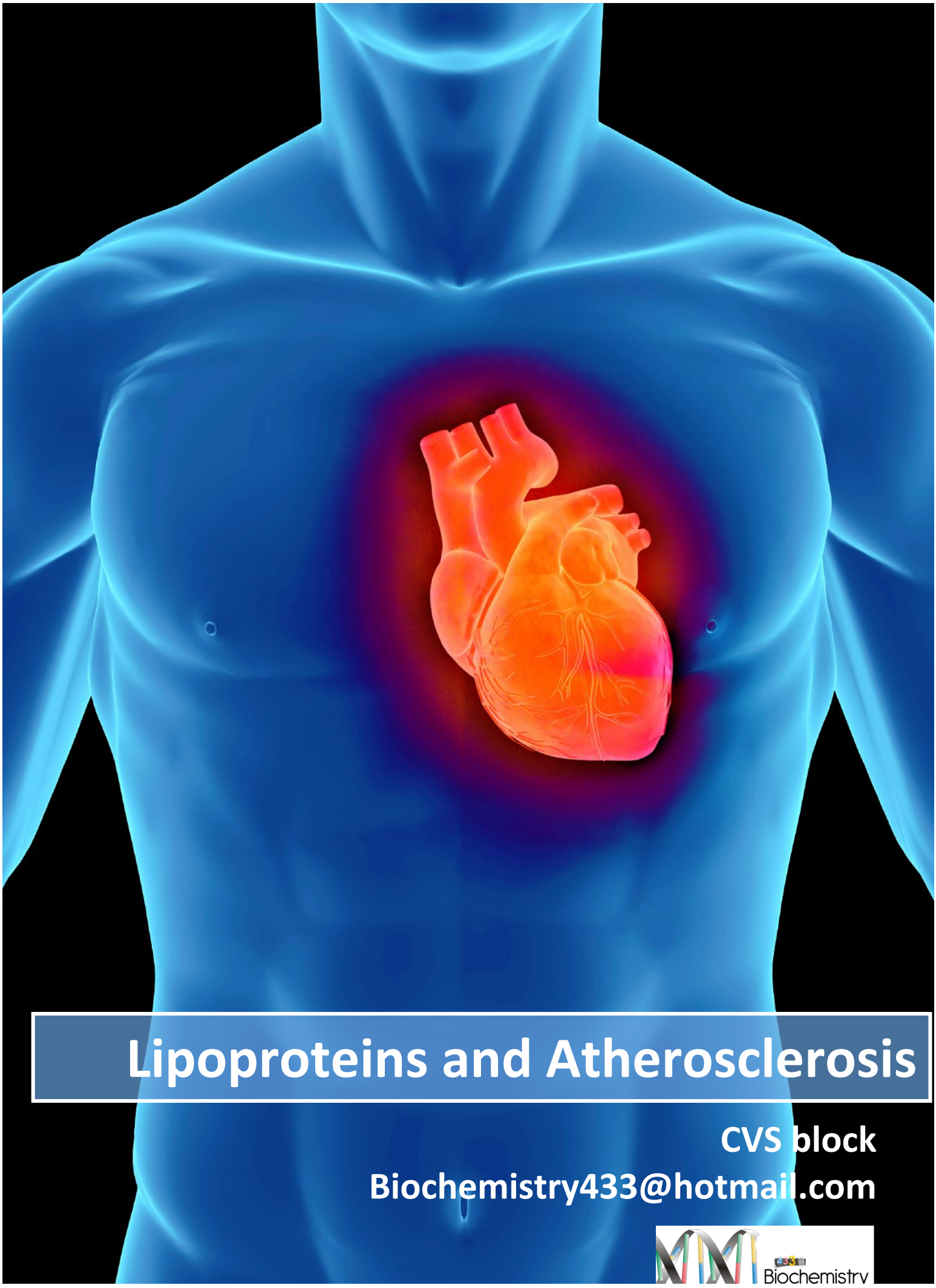


Lipoproteins and Atherosclerosis

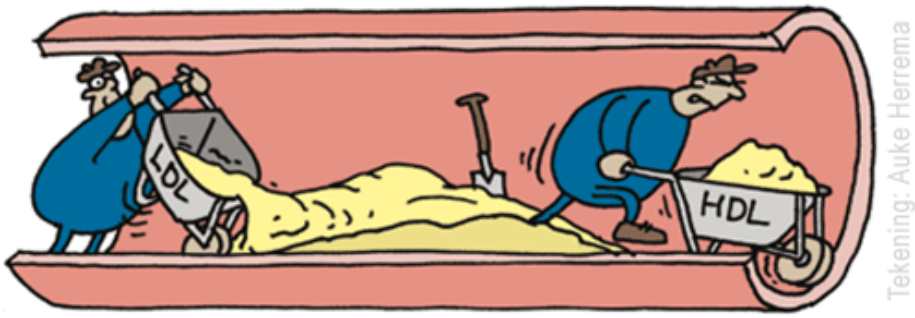
CVS block

Biochemistry433@hotmail.com

Biochemistry

Always remember:

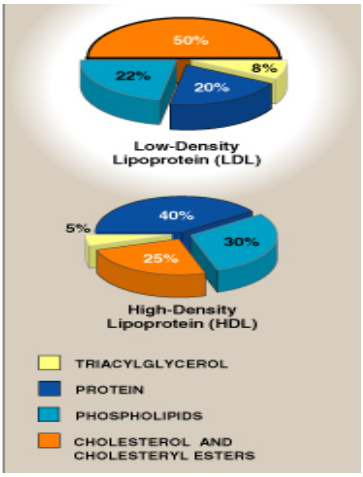
Transporting of cholesterol is from liver to peripheral tissue (done by LDL Bad carrier)
Reverse cholesterol transport is from Peripheral tissue to liver (done by HDL Good carrier)



Imbalance results in **cholesterol deposition** in the wall of blood vessels, thickening of the wall and narrowing of the lumen "Atherosclerosis"

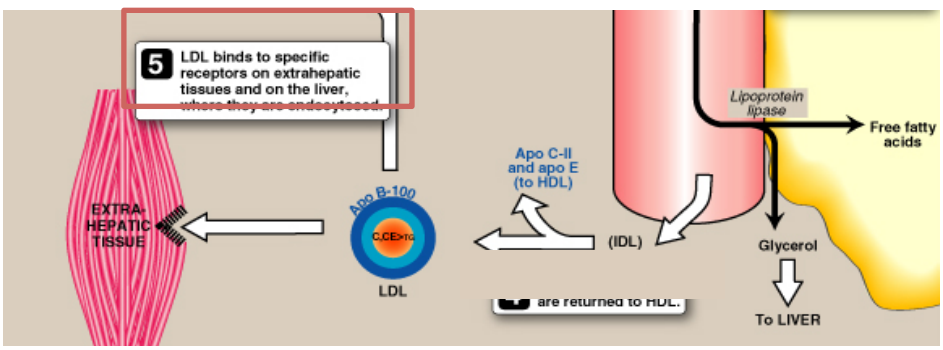
COMPOSTION OF LDL & HDL

- **(LDL):** Mostly free cholesterol
- **(HDL)** Mostly cholesterol ester + More % protein + More % phospholipids



LDL

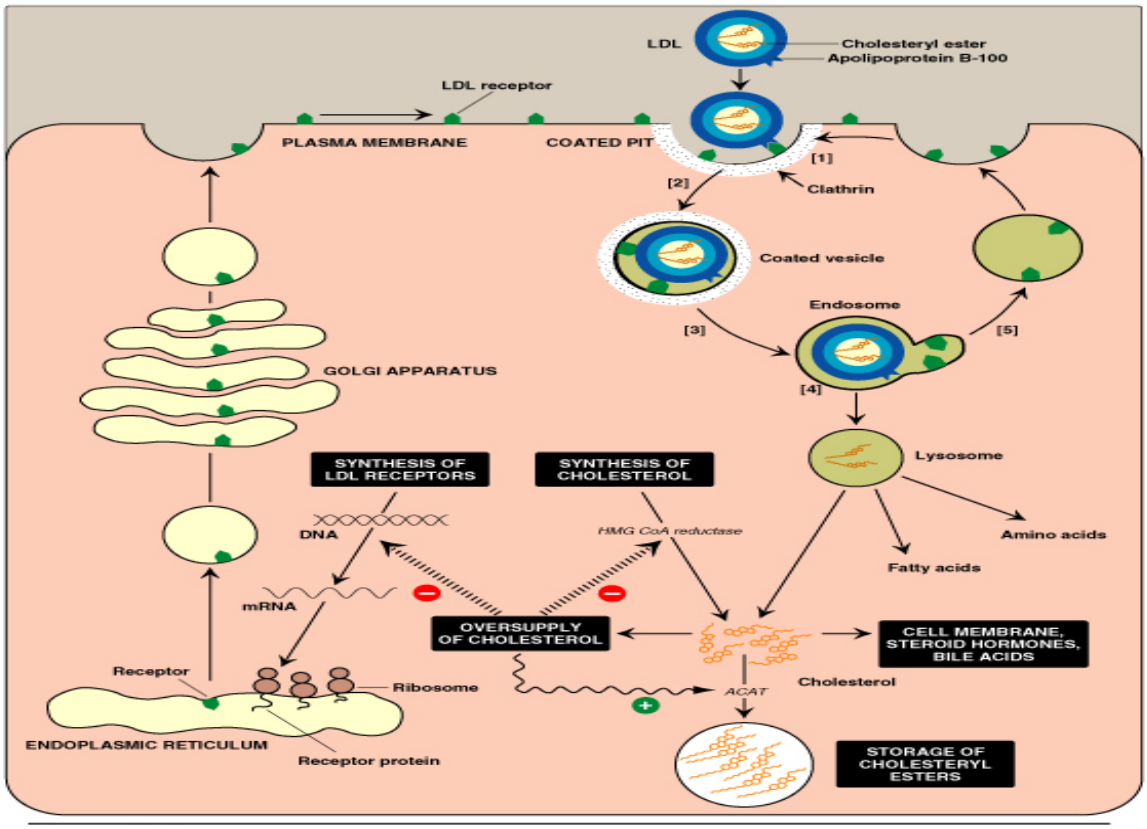
- Produced in the circulation as the end product of VLDLs
- Compared to VLDLs:
  1. It contains *ONLY* apo B-100
  2. Smaller size and more dense
  3. Less TG
  4. More cholesterol & cholesterol ester
- Transport cholesterol from liver to peripheral tissues
- Uptake of LDL at tissue level by LDL receptor-mediated endocytosis (will be discussed) and it is **Recognized by apo B-100**



- For LDL there are two types of receptors:
    - **LDL receptor:** Cell surface glycoprotein, High-affinity & tightly regulated
    - **Scavenger type A:** Pathological receptors cause atherosclerosis

RECEPTOR-MEDIATED ENDOCYTOSIS

- Is done By LDL receptors.
- LDL/Receptor binding and internalization of the complex by endocytosis
- Release of cholesterol inside the cells for:
    - Utilization (As in using it in forming steroid hormones or as a part of cell membrane)
    - Storage as cholesterol ester
    - Excretion (As in bile acids)



Degradation of LDL: into
1. **amino acids**
2. **phospholipids**
3. **fatty acids**

LDL receptor could be **degraded** of **recycled**

Additional note:
Cholesterol is converted to cholesteryl esters inside the cell by ***ACAT*** enzyme.
ACAT (acetyl-CoA cholesterol acyltransferase)

Down-regulation:

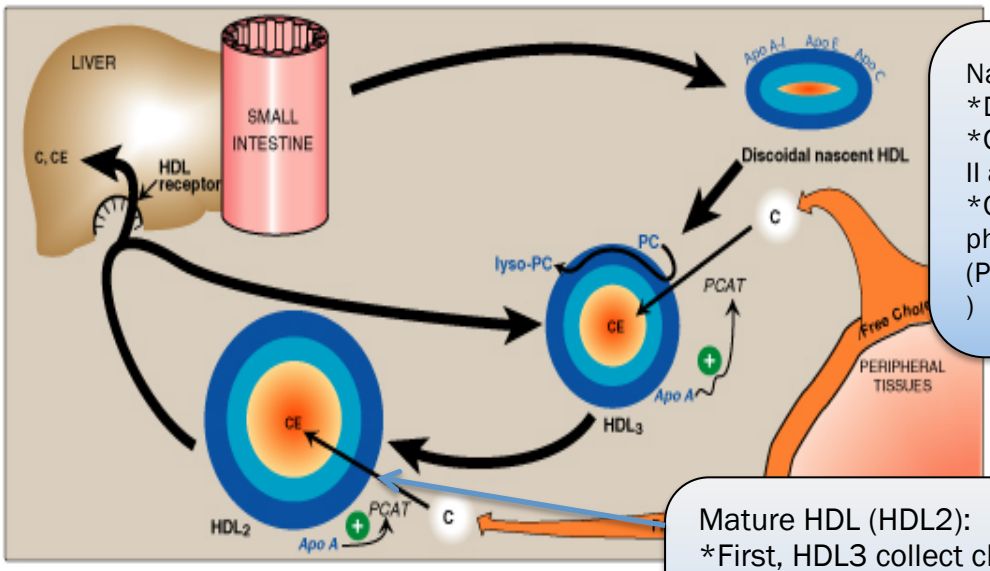
1. High intracellular cholesterol content
2. Degradation of LDL receptors
3. Inhibition of receptor synthesis at gene level
4. Decrease No. of receptor at cell surface
5. Decrease further uptake of LDL
6. Decrease de novo (from beginning) synthesis of cholesterol

Up-regulation:

1. Low intracellular cholesterol content
2. Recycling of LDL receptors
3. Stimulation of receptor synthesis at gene level
4. Increase No. of receptor at cell surface
5. Increase further uptake of LDL
6. Increase de novo synthesis of cholesterol

HIGH DENSITY LIPOPROTEINS (HDL)

HDL is produced by intestine + liver



Nascent HDL:
*Disk-shaped
*Contains apo A-I, C-II and E
*Contains primarily phospholipid (Phosphatidylcholine)

Mature HDL (HDL2):
*First, HDL3 collect cholesterol by LCAT or PCAT enzyme.
* then PCAT converts cholesterol to cholesterol ester
*Spherical mature particle HDL2

* LCAT/PCAT: Lecithin or phosphatidylcholine cholesterol acyltransferase (the are both the same enzyme)
* HDL has Apo-D, which is lipid transfer protein
* There is no deference in protein between nascent and mature HDL.

FUNCTION OF HDL

1. Reservoir of apoproteins e.g., Apo C-II and E to VLDL
2. Uptake of cholesterol: From other lipoproteins & cell membranes (HDL is suitable for uptake of cholesterol because of high content of phosphatidylcholine that can both solubilizes cholesterol and acts as a source of fatty acid for cholesterol esterification)
3. Esterification of cholesterol:
    a. Enzyme: PCAT/LCAT
    b. Activator: Apo A-I
    c. Substrate: Cholesterol
    d. Co-substrate: Phosphatidylcholine/Lecithin
    e. Product: Cholesterol ester & Lyso-PC (Lyso-PC: is a phosphatidylcholine minus the fatty acid)

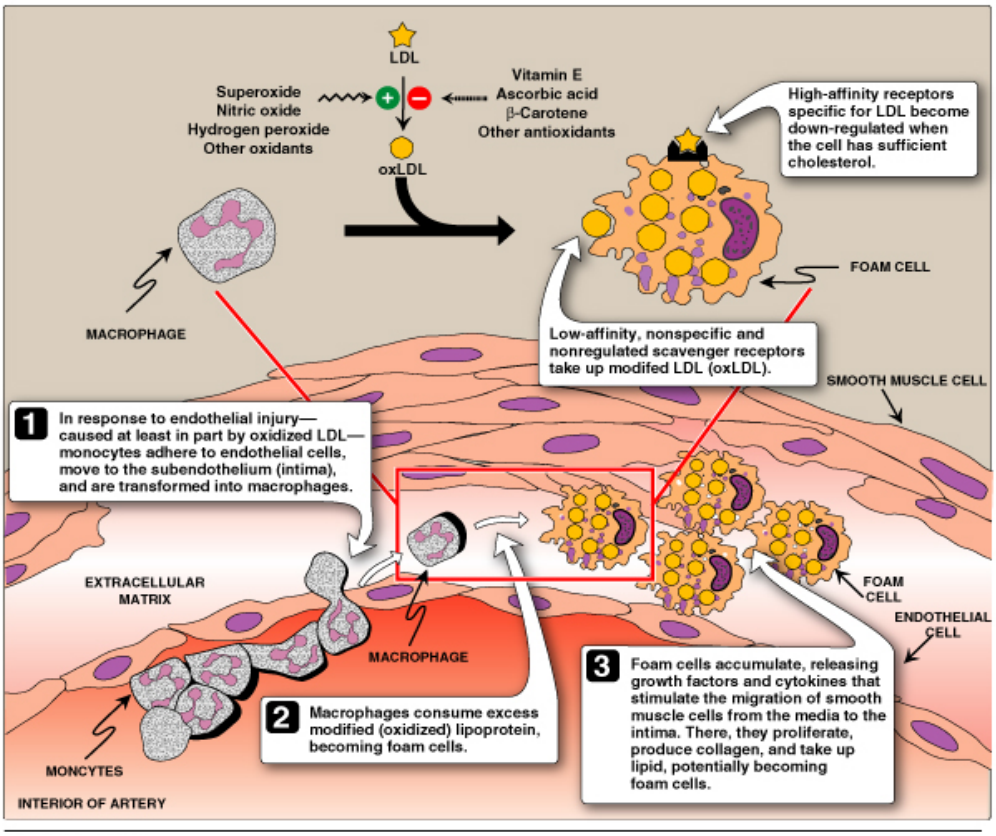
WHY IS HDL A GOOD CHOLESTEROL CARRIER

Inverse relationship between plasma HDL levels and atherosclerosis.

Reverse cholesterol transport involves:

1. Efflux of cholesterol from peripheral tissues and other lipoproteins to HDL3
2. Esterification of cholesterol & binding of HDL2 to liver and stroidogenic cells by scavenger receptor class B (SR-B1)
3. Selective transfer of cholesterol ester into these cells
4. Release of lipid-depleted HDL3

ATHEROSCLEROSIS



Modified (oxidized) LDL (Oxidative stress next lecture)
1) Uptake of oxLDL by macrophage scavenger receptor:
Scavenger receptor class A (SR-A) which is: Low-affinity, non-specific receptor Un-regulated receptor
2) Then the macrophages transform to Foam cell
3) Atherosclerotic plaque formation

Just try to read the details of the picture. It's related to pathology and pharmacology anyway ☺

LABORATORY INVESTIGATION OF ATHEROSCLEROSIS

Serum lipid profile: 10-12 hours (O/N) fasting

Measurement of

1. Serum triglyceride level: (reflect chylomicron and VLDL levels)
2. Serum total cholesterol level (reflect LDL and HDL levels)
3. Serum HDL-cholesterol level
4. Serum LDL-cholesterol level

Others, Serum lipoprotein electrophoresis
Serum apoprotein levels e.g., apo-B

Type IIa Hyperlipoproteinemia

(Familial hypercholestrolemia)

Functional defect of LDL-receptor
Increase plasma LDL level & therefore, plasma cholesterol level
Pre-mature atherosclerosis and increased risk for early-onset ischemic heart diseases
Associated with the presence of tendon xanthomas on hands and ankles

MCQs

Q1) If there is an up regulation a lipoprotein there will be :
a) Inhibition of receptor synthesis
b) increase metabolic activity
c) Increase number of the receptors
d) Decrease numbers of the receptors

Q2) Cholesterol ester is the form of cholesterol that is found in:
a) Blood stream
b) Inside the cell.
c) Outer surface of the cell.
d) LDL

Q3) which one of these is a good cholesterol carrier:
a) HDL
b) VLDL
c) LDL
d) Chylomicrons

Q4) LDL/receptor binding and internalization of the complex is done by:
a) Endocytosis
b) Exocytosis
c) Engulfment
d) Utilization

Q5) HDL is produced by:
a) Intestine
b) Liver
c) Spleen
d) ANS(1+2)

Q6) which one of the following isn't true about scavenger receptor class A:
a) Low affinity
b) Causes Atherosclerosis
c) Tightly regulated
d) None of the above

Answers: 1-C 2-B 3-A 4-A 5-D 6-C

Good luck 

From our team members:

Sara alDokhayel	**Ahmed Al-Hussien**
Maha AlRajhi	**Meshal Al-Ohali**
Lamees alMezaini	**Abdulrahman alharbi**
Batoul Al-Suhaibani	**Faisl Alghamdi**
Jowaher alabdulkarim	**Ziyad Alajlan**
Maram alaqil	**Ahmed Alqhtani**
Ghada AlHindi	**Mojahed Otef**
Amjad AlBatili	

433 Biochemistry Team

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