## Cholesterol anabolism and lipoproteins

## Introduction, overview, and structure of cholesterol

Cholesterol has an important function on cellular structure and also in its function. It's an important component of mammalian cells, we can find cholesterol in the membrane. This increases its fluidity because it's rich in phospholipids and sphingolipids with saturated fatty acids. It will be found in the lipid bilayer, where there will be an interaction between steroid ring and the fatty acid chains. The absence of covalent bonding can be easily transferred in and out of the membrane. If the membrane is very fluid, it will also be more permeable. The synthesis of cholesterol will be regulated on a transitional and post transitional level. Cholesterol can be transported to the liver and also to peripheral tissues. The molecule has 27 carbons, 4 fused rings that contain 17 carbons. 2 further carbons will be found as methyl groups and as junctions of rings AB and CD. It will have 8 carbons as a side chain. There will be a hydrogen group on carbon 3. Almost all of them are saturated except for the double bond found between carbon 5 and 6. Cholesterol is poorly water soluble. We can find cholesterol as free or as esterified cholesterol (CE). CE are less soluble in water, we can find them in the plasma, and they are stored in lipid droplets in the endoplasmic reticulum.

# Synthesis of cholesterol

The synthesis of cholesterol requires a source of carbon atoms, a source of reducing power and energy. Acetyl-CoA will provide the high energy, the reducing power will be NADPH and ATP will be the energy provided. To start of the synthesis, acetyl-CoA will be transformed to Acetoacetyl-CoA by acetoacetyl-CoA thiolase and later on to 3-hydroxy-3-methylglutaryl-CoA and finally to mevalonate by the enzyme HMG-CoA reductase. This last reaction will be called the rate limiting reaction since it leads to an irreversible product. It uses 2 NADPH to do this reaction. Then, 3 molecules of mevalonic acid will phosphorylate in two reactions, isopentenyl pyrophotomate and dimethylallyl pyrophosphate. This two will generate geranyl pyrophosphate and Dopontenyl pyrophosphate will lead to farnesyl pyrophosphate. Two molecules of fas will be condensed by squalene synthase to form squalene, a 30 caroned molecule.

# Regulation of cholesterol synthes

At an organism level, includely or cholesterol is either through diet or through de novo synthesis. There is an inverse velationship betweener network ingest of cholesterol and its biosynthesis. The cell acquires cholesterol from both de novo synthesis and the external supply.

Regulation of intracellular cholesterol concentration involves HMG-CoA reductase, LDL receptor,  $7\alpha$ -hydroxylase and a network of nuclear receptors. The intracellular (intramembrane) cholesterol concentration is a key factor regulating both cellular cholesterol synthesis and the expression of LDL receptors.

Activators Inhibitors Low sterols Abundant sterols Dephosphorylation Phosphorylation by AMPK Insulin Glucagon Tri-iodothyronine Cortisol

#### Regulation by HMG-CoA reductase

Sterol regulatory element-binding proteins (SREBPs) regulate the genes coding for enzymes involved in cholesterol synthesis. SREBPs are cleaved by a protease, releasing the active transcription factors, which in turn translocate to the nucleus and activate all the genes in the