Lecture 29

Cholesterol

Function

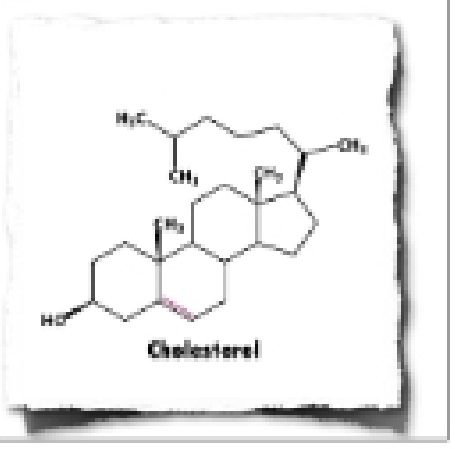
Synthesis

Regulation

Cholesterol Derivatives

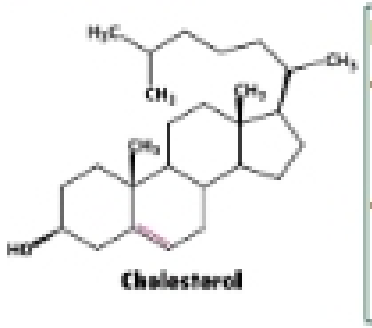
Function

Synthesis



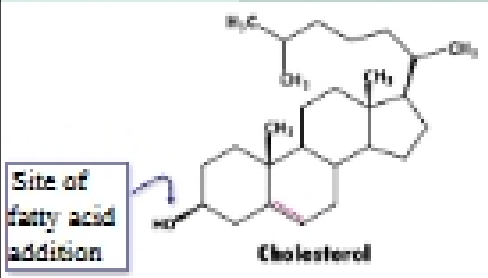
Cholesterol Structure & Function

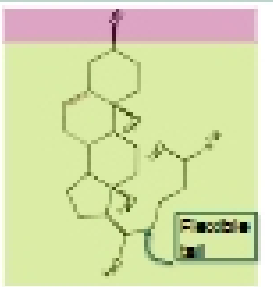
Structure: Sterold - 4 rings, Hydrophobic Tail
- Planar
- Hydrophobic



Function:
- Membrane Lipid
  - Modulates Membrane fluidity
  - Found in Lipid Rafts
- Precursor for Synthesis of:
  - Sterold Hormones
  - Bile Salts
  - Vitamin D

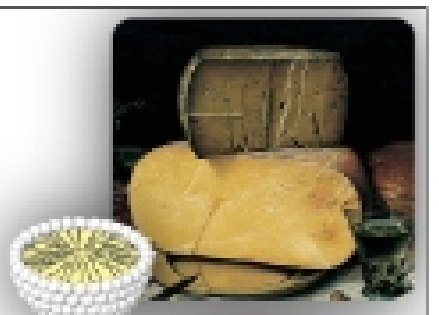
Cholesterol Structure & Function





- For transport in lipoproteins and for storage in the cell, polar OH can be esterified to a fatty acid to increase hydrophobicity
- In membranes, the polar hydroxyl group is oriented towards the aqueous environment and interacts with polar head groups of membrane lipids.

Two Sources of Cholesterol



Dietary Cholesterol
Ingested
Packaged in Intestines
Chylomicrons

Endogenous Cholesterol
Synthesized *de novo*,
Packaged in liver

Cholesterol Synthesis Counting by 5s

5 Important Steps in Cholesterol Synthesis:

Step 1
Condensation of 3 activated acetyl units to form 6C HMG CoA

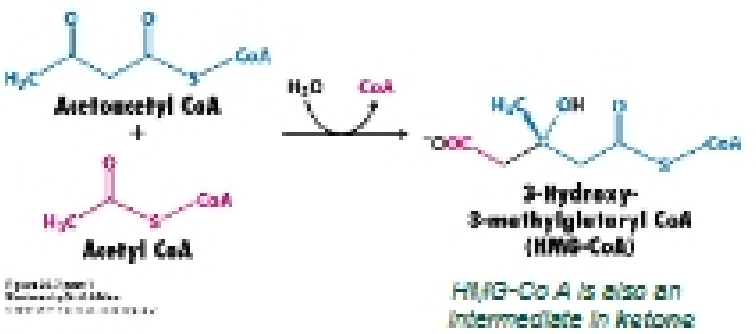
Step 2 Reduction of HMG CoA to **mevalonate**

Step 3
Decarboxylation to 5C activated isoprene, *isopentenyl pyrophosphate*

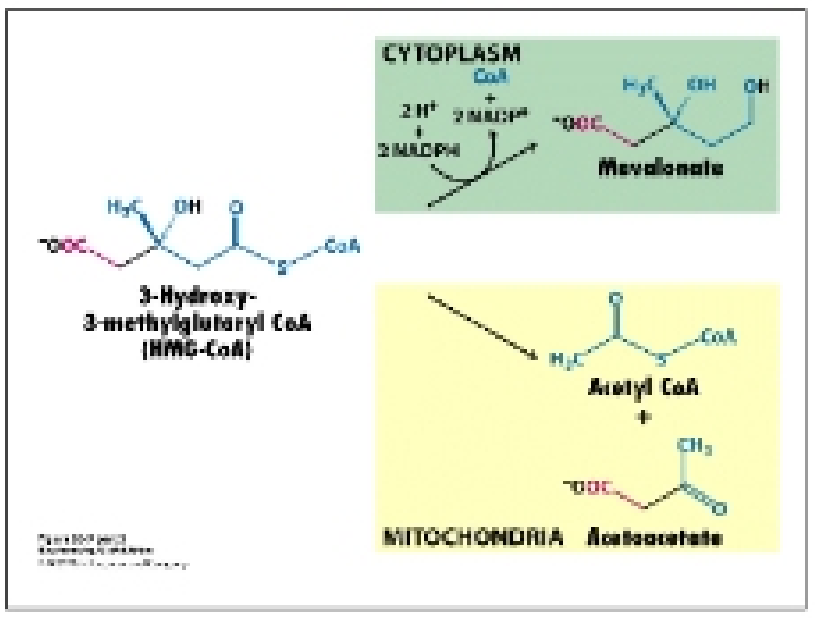
Step 4
Condensations of 6 activated isoprenes (*isopentenyl pyrophosphate, dimethylallyl pyrophosphate*, to form 30-carbon squalene
- formation of *geranyl pyrophosphate* (5 + 5 = 10 carbons)
- formation of *farnesyl pyrophosphate* (10 + 5 = 15 carbons)
- formation of squalene from 2 farnesyl-PP groups (15+15 = 30)

Step 5
Cyclization to lanosterol
Modification, in several steps, to form cholesterol

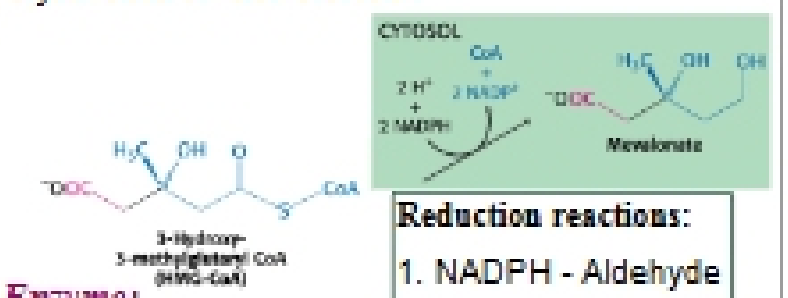
Enzyme:
HMG-CoA Synthase
Condensation reaction



HMG-CoA is also an intermediate in ketone body synthesis.



Synthesis of Mevalonate



Reduction reactions:

1. NADPH - Aldehyde
2. NADPH - Alcohol

Enzyme:

HMG Co A Reductase

Integral membrane protein

Catalyzes the rate-limiting step

The next step uses 3 molecules of ATP

Activity is highly regulated

One monomer of the tetrameric enzyme