**Biochemistry Notes for Lec #23** Jumana kussad

**Cholesterol**

- Chol > gallbladder stero>steroid ol>alcohol
- Cholesterol was first extracted from the gallbladder
- Steroid is made of 3 six-carbon rings and 1 five-carbon ring (i.e: 17 carbons)
- Cholesterol has a steroid nucleus, an -OH group at Carbon-3, a hydrocarbon tail at Carbon-17 and a double bond at Carbon-5.
- the only non-carbon & non-hydrogen atom in Cholesterol is the Oxygen in
the -OH at carbon number 3.
- Cholesterol is very hydrophobic
- Gallbladder stones are made from cholesterol
- To maintain cholesterol in its soluble form in the gallbladder, there must be sufficient amounts of bile acid and bile salts available, otherwise it won't dissolve and gallbladder stones would be formed
- Cholesterol ester: cholesterol forms an ester bond with Fatty acids
 (more hydrophobic)
- All cells have the capability to form cholesterol. **This means that its essential for all cells**. YET, not all cells do synthesize it, since they get it in the ready form (from diet for example)
- To lower the cholesterol levels in body, minimize the intake of food from animal origin.
- Food of plant origin has no Cholesterol (they can't synthesize it)
Example: vegetable oil has no cholesterol
- It's not that easy to eliminate cholesterol from diet, because almost all foods from animal origin contains cholesterol (Ex: one Egg has 250 mg of cholesterol)
\*Liver has the highest concentration of Cholesterol as a dietary component
- Cholesterol can't be degraded to give energy, the only way its eliminated is through bile.

**Cholesterol Synthesis**
- Acetyl CoA is the source of all carbon atoms in cholesterol synthesis
- Cholesterol synthesis also requires an energy source (ATP), and a reducing power (NADPH), and Oxygen.
-6 Isoprene molecules (5 carbons each) give one Squalene (30 carbons)
\*\* You must know the names and carbon numbers of cholesterol synthesis intermediates.
- First two steps in cholesterol synthesis (till the production of HMG coA) are similar to steps in ketone bodies synthesis. These steps for cholesterol synthesis take place in the cytosol, yet in ketone bodies synthesis they take place in the mitochondria.
- 2 NADH are needed per mevalonate (6C). \*for reduction of carboxyl group to aldehyde and then to alcohol\*
 - active form of isoprene is isopentonyl pyrophosphate ( 5C)
- Three isopentonyl pyrophosphates (5C each) are needed to form
 Farnesyl pyrophosphate (FPP) (15 C).
- Two Farnesyl Pyrophosphate condensation gives Squalene (30 C) with the release of two pyrophoshates.
-Squalene is a polyisoprene compound (6 Isoprenes)
-Fat soluble vitamins contain Isoprenes
- Rubber trees produce Isoprenes and cholesterol in the same matter as humans.
Addition of Oxygen to Squalene at Carbons 2 and 3 gives Squalene 2,3 epoxide (the only reaction requiring Oxygen in cholesterol synthesis)
- Squalene epoxide is unstabe.
- By Cyclase enzyme the steroid nucleus is formed by ring closure forming Lanosterol (the first Steroid intermediate)
- It's important to know the structure of 7-hydrocholesterol.
This compound is needed to produce the active form on Vitamin D
 (UV light/sunlight requiring reaction)
-The step in which HMG CoA is changed into Mevalonate at the beginning of the pathway is the rate limiting step in the cholesterol synthesis
(a reduction reaction that requires NADPH, catalyzed by HMG CoA reductase)
- To prevent the synthesis of cholesterol, inhibit this step by inhibiting the reductase enzyme.
- Statin drugs (ex: Lipitor) are given to people with high cholesterol levels to lower them.