**Ch21**

**1. Pathway of Carbon in Fatty Acid synthesis**

(a) In this experiment, without malonyl- CoA, the enzyme must convert acetyl-CoA to malonyl-CoA first, so the malonyl-CoA is also C-1 and C-2 labeled. Then in the process of fatty acid synthesis, the labeled malonyl-CoA is used to elongation the fatty acid chain. Therefore, the 14C appears uniformly in the palmitate.

(b) Except first acetyl-CoA, all of the acetyl-CoA need to be activated to form malonyl-CoA. As excess unlabeled malonyl-CoA in the soluble liver fraction, the labeled acetyl-CoA can just be the last two carbons in the palmitate, so only C-15 and C-16 is labeled.

**2. Synthesis of Fatty Acids from Glucose**

1 mol glucose can produce 2 mol **acetyl-CoA** through glycolysis and pyruvate dehydrogenase. In the glycolysis and citric acid cycle, **ATP** is directly generated by substrate-level phosphorylation and indirectly generated by NADH and FADH2 through oxidative phosphorylation. Also, 1 glucose can generate 2 pentose and 2 **NADPH** through pentose phosphate pathway.

**6. Modulation of Acetyl-CoA Carboxylase**

First, high amount of citrate indicates the excess of energy, so cell needs to storage the energy in the form of fatty acid. In this case, acetyl-CoA carboxylase is activated by citrate to synthesis more fatty acid.

Second, for citrate and isocitrate is bind preferentially to the filamentous form, they drive the equilibrium to the filamentous state and therefore stimulate the reaction. In contrast, the final product palmitoyl-CoA drive the equilibrium to the promoter form. Palmitoyl-CoA indicate that there has already been enough fatty acid. So, the rate of fatty acid synthesis should slow down.

**16. Regulation of Cholesterol Biosynthesis**

The central regulatory enzyme in cholesterol *de novo* synthesis is HMG-CoA reductase that catalyze HMG-CoA converting to mevalonate. Cholesterol is the negative regulator of this enzyme, so high concentration of cholesterol lowers the rate of cholesterol *de novo* synthesis. Also, the cholesterol inhibits the expression of HMG-CoA reductase gene.

**19. Potential Side Effects of Treatment with Statins**

Statin is the inhibitor of HMG-CoA, which lower the synthesis of mevalonate, the precursor of terpene. Coenzyme Q is a kind of terpene synthesis from mevalonate, so statin reduce the synthesis of Q at the same time.

**Extra question:**

High levels of cholesterol in the blood have been positively correlated with the incidence of atherosclerosis. Recently, the LDL:HDL ratio has been shown to be a better indicator. Explain why this ratio might be a predictor of coronary artery obstruction.

In human body, LDL is the dominant lipoprotein to distribute cholesterol from liver to body whereas HDL could recycle cholesterol from tissue. In this case, high rate of LDL/HDL ratio indicate large amount of cholesterol in the blood that brings high incidence of atherosclerosis like coronary artery obstruction.