Summary of Chapter 19

1. Lipid hydrolysis
   - Fatty acids in phospholipids are hydrolytically cleaved by various phospholipases.
   - Triacylglycerol in adipose cells is hydrolyzed to fatty acids and glycerol by triacylglycerol lipase which is activated by a phosphorylation through the hormone-trans-signal cascade.
   - Phospholipase A2 contains Ca²⁺ ion, which stabilizes the oxyanion transition state.

2. Fatty acid oxidation (β-oxidation).
   - Occurs in mitochondrion.
   - Acyl-CoA is transferred from cytosol to mitochondrion via carnitine carrier protein.

3. Fatty acid synthesis.
   - Occurs in cytoplasm in liver cells.
   - Fatty acyl is attached to acyl-carrier protein (ACP).
   - Precursor is malonyl-CoA, which is produced from acetyl-CoA + CO₂ with an ATP expense.
   - Fatty acid synthase is a multi-functional enzyme which has 8 different activities.
   - One malonyl-CoA attachment requires 2 NADPH.

4. Transport of acetyl-CoA
   - No specific transport from mitochondrion to cytosol --- therefore tricarboxylate transport system is used.

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Modification</th>
<th>Product</th>
<th>Enzyme</th>
<th>Energy mol.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Oxidation</td>
<td>-HCβ=CαH-</td>
<td>trans-Δ²-enoyl-CoA</td>
<td>acyl-CoA dehydrogenase</td>
<td>FADH₂</td>
</tr>
<tr>
<td>2. Hydration</td>
<td>-H(OH)Cβ- CαH₂-</td>
<td>3-L-hydroxyacyl-CoA</td>
<td>enoyl-CoA hydratase</td>
<td></td>
</tr>
<tr>
<td>3. Oxidation</td>
<td>-(O)Cβ-CαH₂-</td>
<td>β-ketoacyl-CoA</td>
<td>3-L-hydroxyacyl-CoA dehydrogenase</td>
<td>NADH</td>
</tr>
<tr>
<td>4. Cleavage</td>
<td>Rₙ-2-C(O)-SCoA</td>
<td>Fatty acyl-CoA (2 C atoms shorter)</td>
<td>β-ketoacyl-CoA thiolase</td>
<td>Acetyl-CoA</td>
</tr>
</tbody>
</table>

- ATP production by fatty acid oxidation (Can you calculate ATP production?)
  - Even carbon fatty acids
  - Odd carbon fatty acids
  - Unsaturated fatty acids
- Exchange rate: 1 NADH = 3 ATP; 1 FADH₂ = 2 ATP; 1 Acetyl-CoA = 12 ATP; 1 Propionyl-CoA = 20 ATP
- Odd carbon fatty acid oxidation produces propionyl-CoA, which is converted to succinyl-CoA. In the conversion, B₁₂ cofactor enzyme, methylmalonyl-CoA mutase rearranges the carbon skeleton.
- Excess of acetyl-CoA is converted to ketone bodies (acetoacetate + β-hydroxybutyrate) in mitochondria of liver cells. Ketone bodies are used as energy source.
- 3 Acetyl-CoA are condensed to β-hydroxyl-β-methylglutaryl-CoA (HMG-CoA), and then break down to acetoacetate & acetyl-CoA by HMG-CoA lyase.
• Acetyl-CoA in mitochondrion is converted to citrate with oxaloacetate.
• Citrate is transported to cytosol through \textit{tricarboxylate transport system}.
• Citrate is converted to acetyl-CoA and oxaloacetate.

5. Regulation of fatty acid metabolism
• Glucagon & epinephrine stimulate fatty acid oxidation.
• Insulin stimulates fatty acid synthesis.

6. Cholesterol metabolism
• Occurs in cytosol.
• Acetyl-CoA (C₂) → HMG-CoA (C₆) → Mevalonate (C₆) → Isopentenyl-PP₁ (C₅) → Geranyl-PP₁ (C₁₀) → Farnesyl-PP₁ (C₁₅) → Squalene (C₃₀) → Cholesterol (C₂₇)
• β-hydroxyl-β-methylglutaryl-CoA (HMG-CoA) is a key cholesterol precursor.
• HMG-CoA is reduced to mevalonate by \textbf{HMG-CoA reductase} in cytosol.
• Cholesterol synthesized in liver is converted to cholesterol ester, and then put into VLDL.
• VLDL, IDL, and LDL deliver cholesterol to tissues through bloodstream, whereas HDL delivers cholesterol to liver.
• LDL recognizes LDL receptors and enters into cells through endocytosis.
• Cholesterol level is regulated by \textbf{HMG-CoA reductase} activity.
  • Hormones regulate HMG-CoA reductase activity by enzyme cascade.
  • Phosphorylated HMG-CoA reductase is inactive, whereas dephosphorylated enzyme is active.
  • Insulin activates HMG-CoA reductase, whereas glucagon inactivates HMG-CoA reductase.
  • HMG-CoA reductase activity is regulated by synthesis of HMG-CoA reductase mRNA and degradation of HMG-CoA reductase.
• High cholesterol level in blood is called \textbf{Familial hypercholesterolemia}.

7. Complexed lipids
• Glycerophospholipids:
  • Head groups are activated by attaching CDP, such as CDP-choline, CDP-ethanoamine, and then are connected to 1,2-diacylglycerol.
  • Diacylglycerol portion is activated by attaching CDP, and then is connected to inositol, etc.
• Sphingolipids:
  • Basic fragments, sphingosine and ceramide are synthesized from palmitoyl-CoA, serine and acyl-CoA.
  • Sphingomyelin is synthesized from ceramide and phosphatidylcholine.
  • Cerebrosides are synthesized from ceramide and UDP-sugar, UDP-glucose, UDP-galactose.