Lipids and Fatty Acids

Objectives:

1. What are Lipids?
   - properties
   - glycerolipids vs. isoprenoids
   - glycerolipid structure
   - glycerolipid nomenclature

2. Fatty acid biosynthesis
   - Cellular localization
   - Substrate and its origin
   - Enzymes of de novo fatty acid synthesis
   - De novo fatty acid elongation (C2->C18)

References:

What are lipids?

TAG

Vitamin D2
What are lipids?

1. Heteropolymers consisting of different subunits

2. Macromolecules defined on the basis of their physical properties:
   - Insoluble in water
   - Soluble in non-polar organic solvents
Lipids are chemically heterogeneous

TAG

Originate from different biosynthetic pathways
Glycerolipids

Fats and oils

Triacylglycerol (TAG)
Triacylglycerols form oil droplets

[Diagram of triacylglycerol molecule]

Oilseed embryo
Glycerolipids

Membrane lipids

Glycerol backbone

Fatty acyl group

Head group

Monogalactosyldiacylglycerol (MGDG)
Glycerolipid nomenclature

1. Glycerol backbone

2. Fatty acyl groups on $sn$-1 and $sn$-2 positions
   - Saturated – no double bonds
   - Unsaturated – one or multiple double bonds

3. Head group on $sn$-3 position
   - Sugar moiety -> Glycolipids
   - Phosphate + alcohol -> Phospholipids
   - No head group -> Acyl glycerols
Fatty acid nomenclature

- **Oleic acid 18:1**

  - **Number of Carbon atoms:** 18
  - **Number of Double bonds:** 1
  - **Double bond position (counting from carboxyl end):** \( \Delta^9 \)
  - **Trivial name:** Oleic acid
  - **cis configuration unless indicated**

- **Z configuration**

- **trans double bond**

- **E configuration**

- **Methyl end**

- **Carboxyl end**

- **cis double bond**
## Common Eukaryotic Fatty Acids

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Systematic name</th>
<th>Trivial name</th>
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<tbody>
<tr>
<td>16:0</td>
<td>Hexadecanoic acid</td>
<td>Palmitic acid</td>
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<tr>
<td>18:0</td>
<td>Octadecanoic acid</td>
<td>Stearic acid</td>
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<td>16:1</td>
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<td>$\Delta^9\Delta^{12}\Delta^{15}$</td>
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Characteristics of Common Fatty Acids

• 16 or 18-carbon unbranched acyl chain  (even number)
• Zero to 3 double bonds
• Double bonds are methylene interrupted (Allylic)
• Components of membrane and storage lipids
De novo Fatty Acid Synthesis

Site: PLASTID
Substrate: acetyl-CoA

Fig. 10-9
De novo Fatty Acid Synthesis

Acetyl-CoA Carboxylase reaction
1st committed step in fatty acid synthesis

Fig. 10-11
FAS Enzymes

Enzymes:

1. ACCase = Acetyl-CoA Carboxylase

2. Malonyl-CoA:ACP transacylase

3. CONDENSING ENZYMES – key enzymes of FAS involved in C-C bond formation (CO₂ release – IRREVERSIBLE!)
   - different substrate specificities:
     - KAS III – C₂
     - KAS I – C₄–C₁₄
     - KAS II – C₁₆

4. KR = 3-ketoacyl-ACP reductase

5. DH = 3-hydroxyacyl-ACP dehydratase

6. ER = 2-3 trans enoyl-ACP reductase

ACP = Acyl Carrier Protein – primer for FAS, carries the fatty acyl chain
Organization of FAS Enzymes

**TYPE I (Animals and Fungi)**

Location: **Cytosol**

Organization: A complex of 2 large subunits (250 kDa each) catalyzing all the reactions of FAS

**TYPE II (Plants and Bacteria)**

Location: **Plastid stroma**

Organization: Enzyme activities reside on individual proteins – this reflects prokaryotic origin of plastids
Fatty Acid Synthesis

Main products of FAS are 16:0 and 18:1

FAS = fatty acid synthesis
FAT = acyl-ACP thioesterase
LACS = acyl-CoA synthetase
AT = acyl transferase
DES = stearoyl-ACP desaturase
Main products of FAS are 16:0 and 18:1

How do we know that?

Acetate labeling of isolated plastids \textit{in vitro} \Rightarrow C16 and C18 fatty acyl chains get labeled

What happens when we add isolated microsomes to the labeled C16 and C18 fatty acids?

Very long chain fatty acids (>C18) get made