Fatty Acids and Triglyceride Structure

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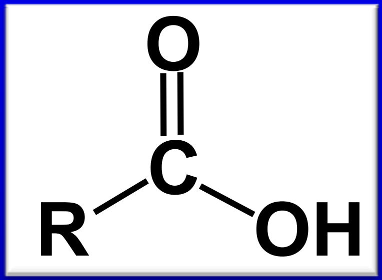
Fatty Acids

Fatty Acids

- Fatty acids are **carboxylic acids** with mostly long hydrocarbon unbranched alipahtic (non-aromatic) chains ranging from 4 to 36 carbons.
  - Carboxylic acids are organic acids characterized by the presence of a carboxyl group, which has the formula C(=O)OH, usually written -COOH or -CO_2H.



  - The chain can be saturated meaning a saturated compound has no double or triple bonds. In saturated linear hydrocarbons, every carbon atom is attached to two hydrogen atoms, except those at the ends of the chain, which bear three hydrogen atoms.
  - The chain can be unsaturated meaning a carbon structure contains double or occasionally triple bonds. Many vegetable oils contain fatty acids with one (*monounsaturated*) or more (*polyunsaturated*) double bonds in them.

Fatty Acid Characteristics

- Where double bonds are formed, hydrogen atoms are eliminated. Thus, a saturated fat is "saturated" with hydrogen atoms.
- In cellular metabolism hydrogen-carbon bonds are broken down – or ozidized – to produce energy, thus an unsaturated fat molecule contains somewhat less energy (i.e fewer calories) than a comparable sized saturated fat.
- The greater the degree of unsaturation in a fatty acid (ie, the more double bonds in the fatty acid), the more vulnerable it is to lipid peroxidation (rancidity).

Fatty Acid Nomenclature

- A ***cis*** configuration means that adjacent hydrogen atoms are on the same side of the double bond. The rigidity of the double bond freezes its conformation and, in the case of the *cis* isomer, causes the chain to bend and restricts the conformational freedom of the FA.
- A *trans* configuration, by contrast, means that the next two hydrogen atoms are bound to *opposite* sides of the double bond. As a result, they do not cause the chain to bend much, and their shape is similar to straight saturated fatty acids.
    - Most fatty acids in the *trans* configuration (trans fats) are not found in nature and are the result of human processing (e.g., hydrogenation).

Fatty Acids

- **Nomenclature**
- **Trivial:** Common name
  - Stearic, Palmitoleic, Oleic, Linolenic, Linoleic acids
- **Systematic Nomenclature:** Counting begins from the carboxylic acid end with double bonds labeled cis/trans or E/Z
  - (9Z)-octdec-9-enoic acid
- **Δ^X Nomenclature:** Each double bond is indicated by Δ^X, where the double bond is located on the xth carbon-carbon bond counting from the carboxylic acid end. Each double bond is preceded by a cis or trans prefix
  - Linoleic acid is cis,cis- Δ^9, Δ^{12}

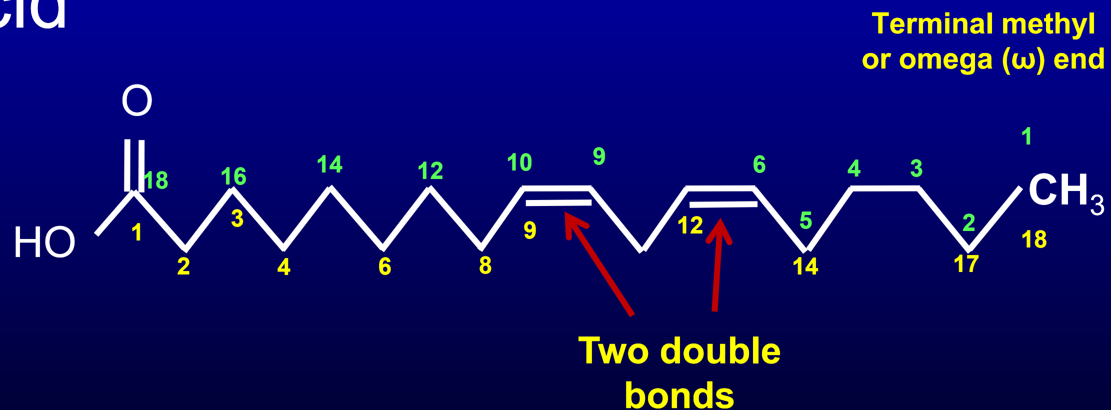
Fatty Acid Nomenclature

- **n-x nomenclature:** n minus (-) x; also omega-x or ω-x
  - Does not provide the name but is a shorthand way to categorize FA by properties. A double bond is located at the xth carbon-carbon bond counting from the terminal methyl carbon (designated as n or ω toward the carbonyl carbon
  - Example: Omega-3 or n-3 fatty acids
- **Lipid numbers:** take the form of C:D where C is the number of carbon atoms in the fatty acid and D is the number of double bonds in the FA. If ambiguous, it can be paired with Δ^X, or n-x term
  - Examples:
    - 18:3 18:3, n-6
    - 18;3, cis,cis,cis, Δ^9, Δ^{12} Δ^{15}

Fatty Acid Nomenclature

- Flax Seed Oil (Greek word for flax is linon)
- An unsaturated (polyunsaturated) omega-6 FA
  - Is a carboxylic acid with 18 carbons and two cis double bonds, with the first double bond at the 6th carbon from the methyl (omega) end.
  - Linoleic Acid : an essential FA
  - Octadecanoic acid
  - cis,cis Δ^9, Δ^{12}
  - 18;2
  - 18:2 n-6

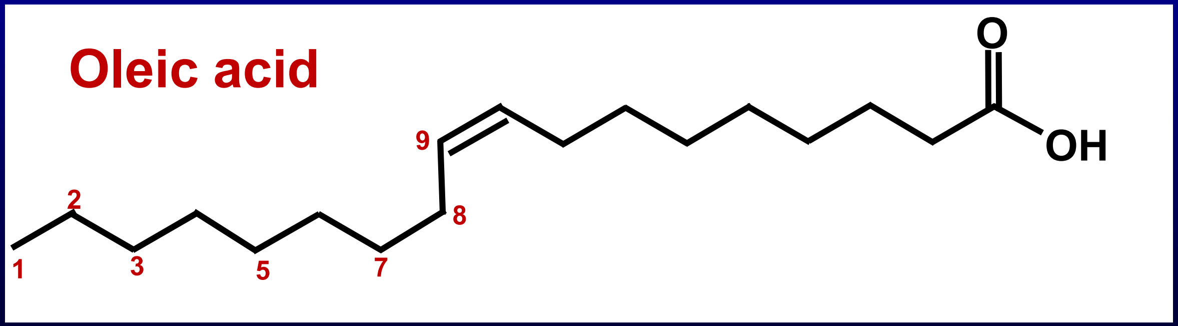
Omega (ω) is the last letter in the Greek alphabet



$C_{18}H_{32}O_2$

Fatty Acid Characteristics

- **Monounsaturated fatty acids:** Examples
  - Palmitoleic acid(16:1 n−7) which has 16 carbon atoms with the first double bond occurring 7 carbon atoms away from the methyl group (and 9 carbons from the carboxyl end).
  - cis-Vaccenic acid (18:1 n−7)
  - Oleic acid (18:1 n−9) has 18 carbon atoms with the first double bond occurring 9 carbon atoms away from the methyl group.



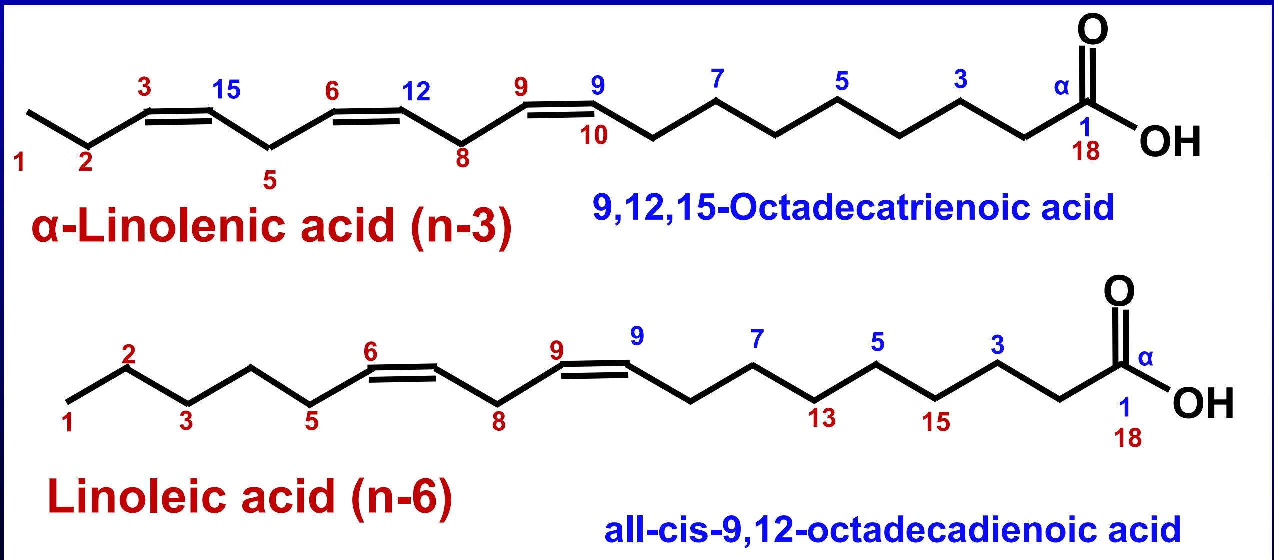
Fatty Acid Characteristics

✦ **Polyunsaturated fatty acids (PUFA):** examples

- Methylene-Interrupted Polyenes: These fatty acids have 2 or more double bonds that are separated from each other by a single methylene group(a carbon atom is bonded to two hydrogen atoms).

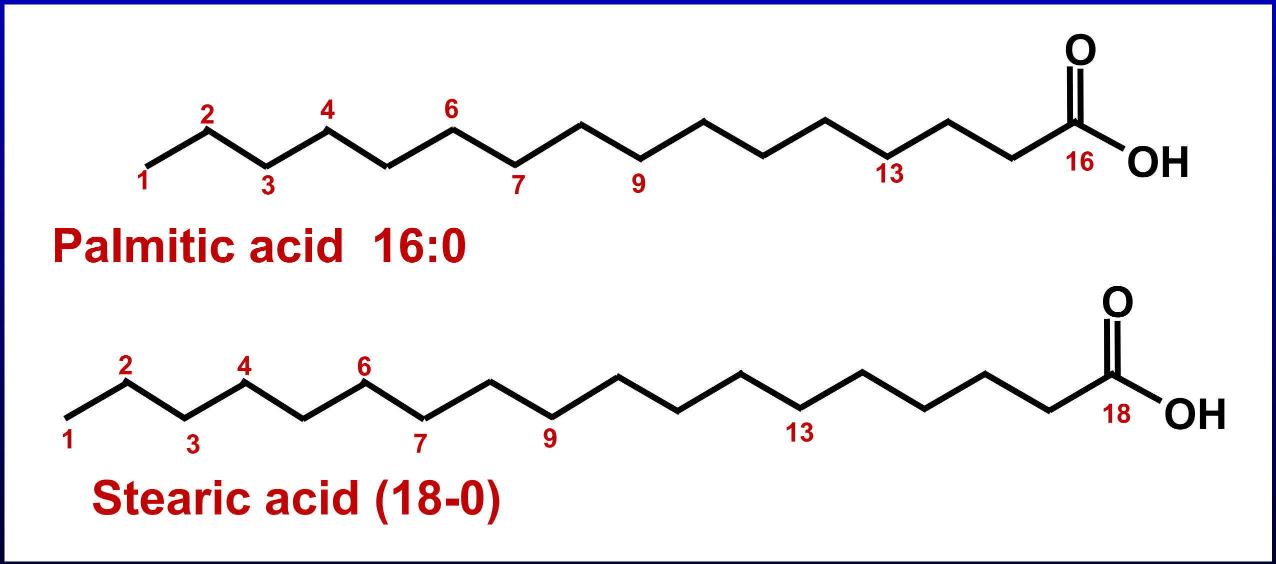
Methylene-interrupted double bond **-C-C=C-C-C=C-**

- Examples are certain omega-3 (n-3) like alpha-Linolenic acid
- Or certain Omega-6 (n-6) like Linoleic acid

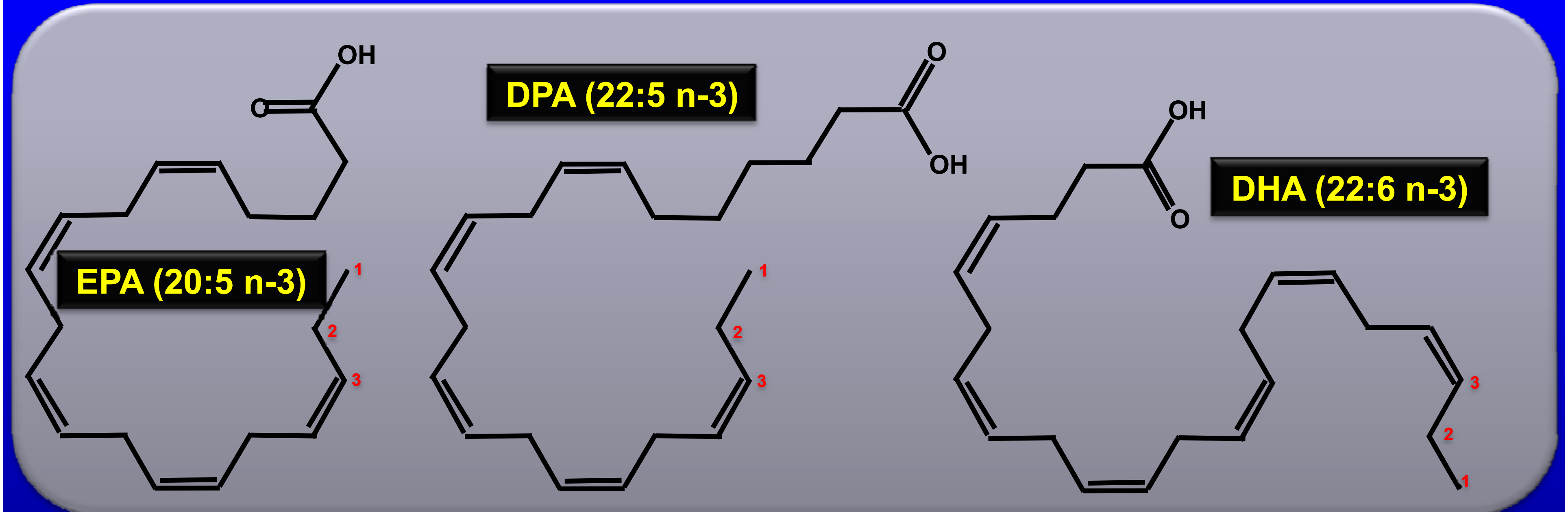


Fatty Acid Characteristics

- **Saturated fatty acids (PUFA):** examples
  - Lauric acid with 12 carbon atoms (contained in coconut & palm oil and breast milk).
  - Myristic acid with 14 carbon atoms (contained in cow's milk and dairy products)
  - Palmitic with 16 carbon atoms (contained in palm oil and meat)
  - Stearic acid with 18 carbon atoms (also contained in meat and cocoa butter)



Chemical structure of Marine N-3 FA

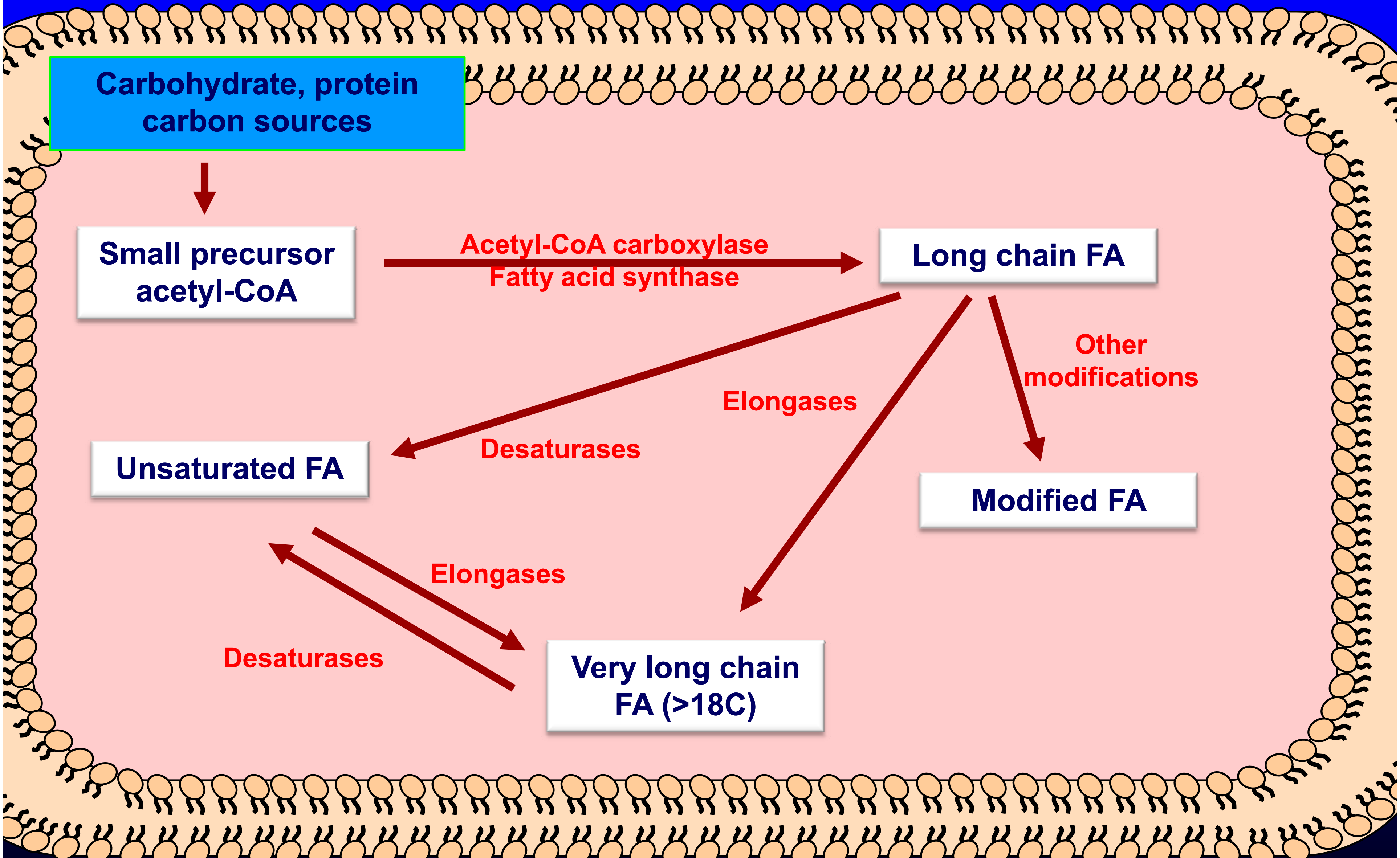


Chemically, they are chains of 20 (EPA) or 22 (DPA and DHA) carbon atoms with 5 (EPA and DPA) or 6 (DHA) double bonds in the chain. EPA (20:5), DPA (22:5), and DHA (22:6) are found almost exclusively in seafood even though fish do not produce them.

In fact, EPA, DPA, and DHA are produced by single-celled marine organisms (phytoplankton) that are eaten by fish and they are essential fatty acids for fish and humans.

de Leiris J et al. J Cardiovasc Pharmacol 2009

De Novo Fatty Acid Synthesis



Gurr MI et al. Lipid Biochemistry 5th Ed 2002 Blackwell Science Malden, MA

Beta Oxidation of Fatty Acids

► **Beta oxidation** is the process by which fatty acids, in the form of Acyl-CoA molecules, are broken down in mitochondria and/or in peroxisomes to generate Acetyl-CoA, the entry molecule for the Krebs cycle or cholesterol synthesis

► The fatty acid reacts with ATP to give a fatty acyl adenylate, plus inorganic pyrophosphate. This reactive acyl adenylate then reacts with free coenzymeA to give a fatty acyl-CoA ester plus AMP

► Once inside the mitochondria, the β-oxidation of fatty acids occurs

http://en.wikipedia.org/wiki/Beta_oxidation

Beta Oxidation of Fatty Acids

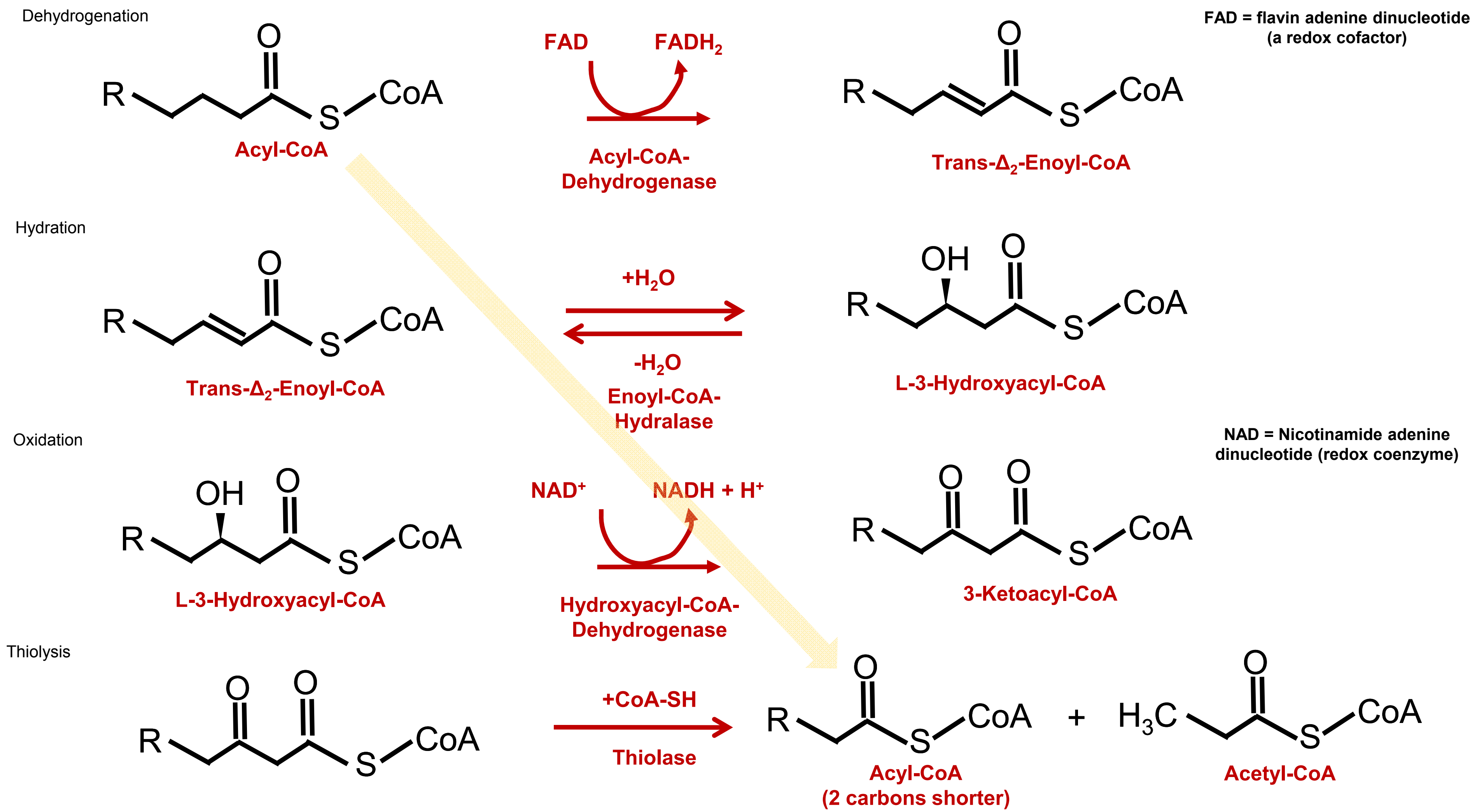
► Fatty acid oxidation also occurs in peroxisomes, when the fatty acid chains are too long to be handled by the mitochondria.

- ► However, the oxidation ceases at octanyl CoA.

► It is believed that very long chain (greater than C-22) fatty acids undergo initial oxidation in peroxisomes which is followed by mitochondrial oxidation.

http://en.wikipedia.org/wiki/Beta_oxidation

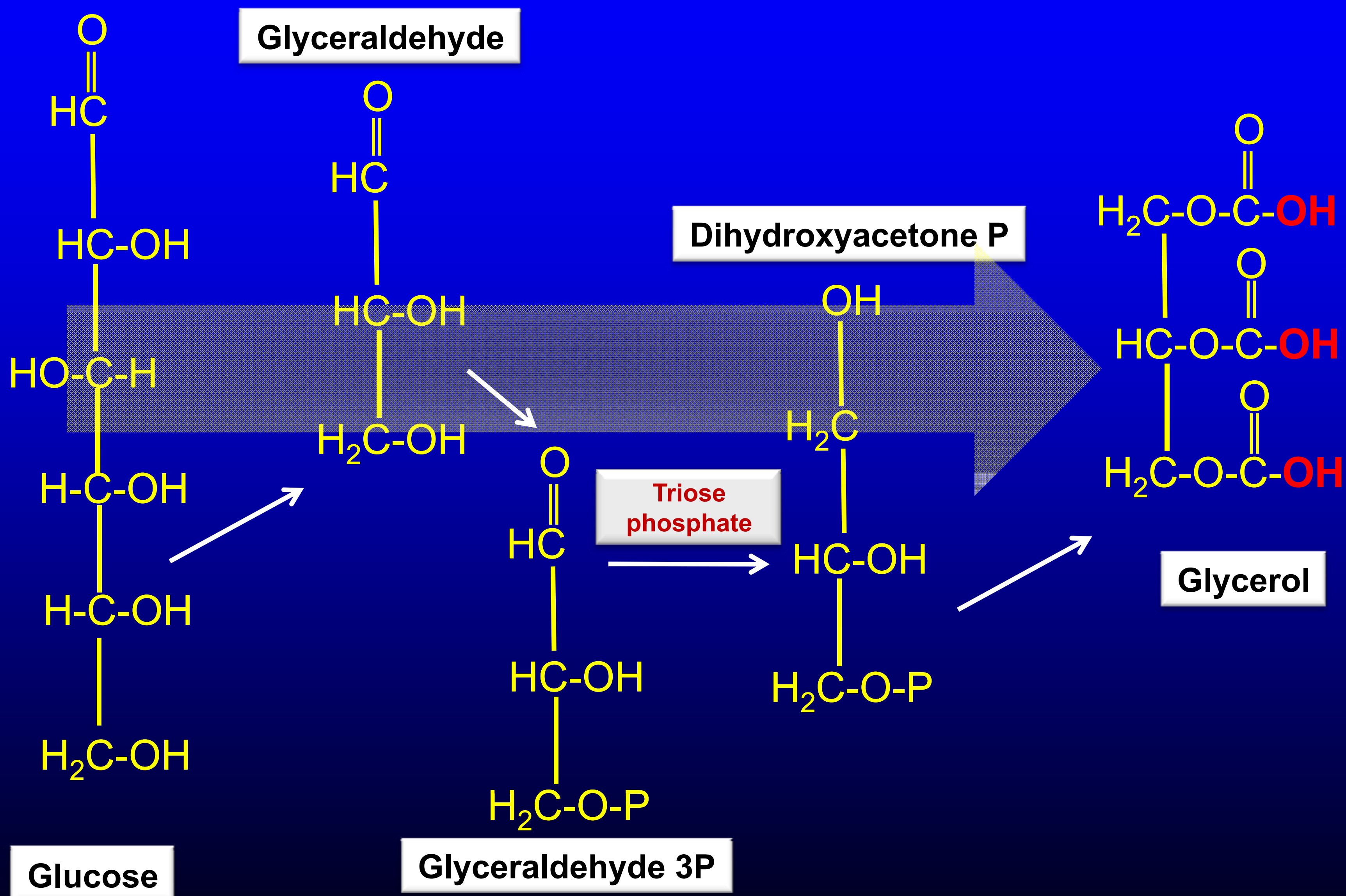
Beta Oxidation of Fatty Acids



This process continues until the entire chain is cleaved into acetyl CoA units. The final cycle produces two separate acetyl CoA's, instead of one acyl CoA and one acetyl CoA. For every cycle, the Acyl CoA unit is shortened by two carbon atoms. Concomitantly, one molecule of $FADH_2$, NADH and acetyl CoA are formed.

Lipids: Triglycerides

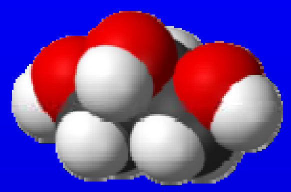
Glucose - Glycerol

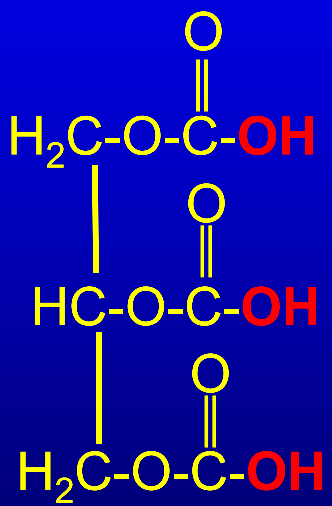


Parks EJ et al. J. Lipid Res. 2006;47:1651–1660

Glycerol

- **Glycerol** is classified by the FDA among the sugar alcohols as a caloric macronutrient. Glycerol has three hydrophilic **hydroxyl** groups that are responsible for its solubility in water and its hygroscopic nature.
- The glycerol substructure is a central component of many lipids including TG and phospholipids.
  - Glycerol is currently categorized by the American Dietetic Association as a carbohydrate.

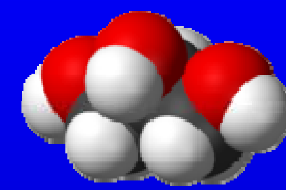


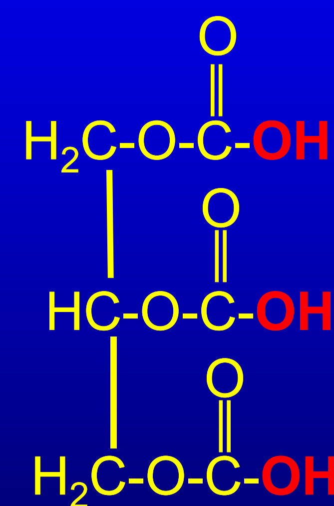


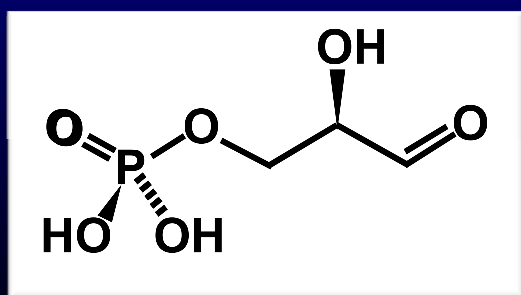
http://en.wikipedia.org/wiki/Glycerol

Glycerol

- Glycerol is a precursor for synthesis of triacylglycerols and of phospholipids in the liver and adipose tissue.
- When the body uses stored fat as a source of energy, glycerol and fatty acids are released into the bloodstream. The glycerol component can be converted to glucose by the liver and provides energy for cellular metabolism.
- Before glycerol can enter the pathway of glycolysis or gluconeogenesis (depending on physiological conditions), it must be converted to their intermediate glyceraldehyde 3-phosphate



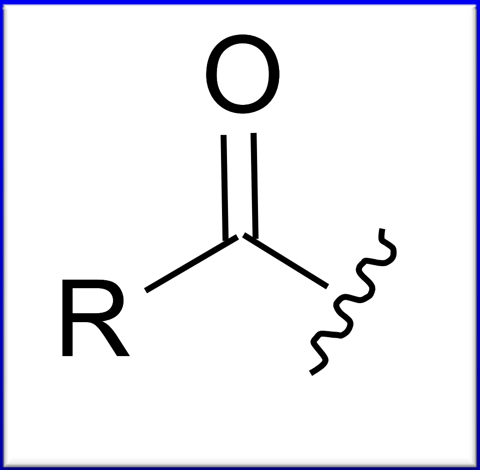




http://en.wikipedia.org/wiki/Glycerol

Acyl Groups

- An **acyl group** is a functional group derived by beta oxidation of FA or the removal of one or more hydroxyl groups from an oxoacid (an acid containing oxygen).
- The acyl group is usually derived from a carboxylic acid of the form RC-O-OH. It therefore has the formula RC(=O)- , with a double bond between the carbon and oxygen atoms (i.e. a carbonyl group), and a single bond between R moiety and the carbon.



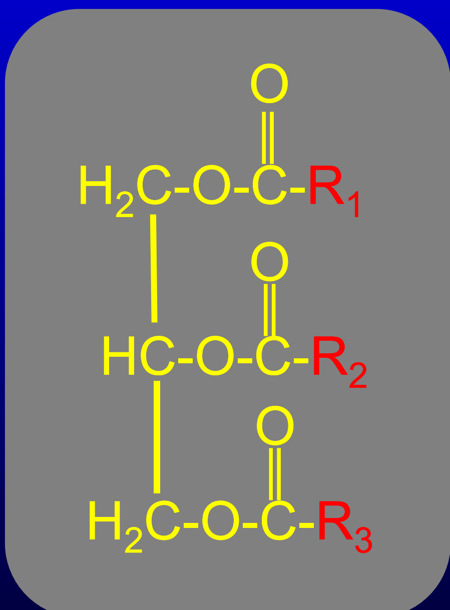
- Acyl groups can also be derived from other types of acids such as sulfonic acids and phosphonic acids.
- Acyl CoAs are derivates of fatty acid metabolism, with acetyl CoA as an example.

http://en.wikipedia.org/wiki/acyl

Triacylglycerol or Triglycerides

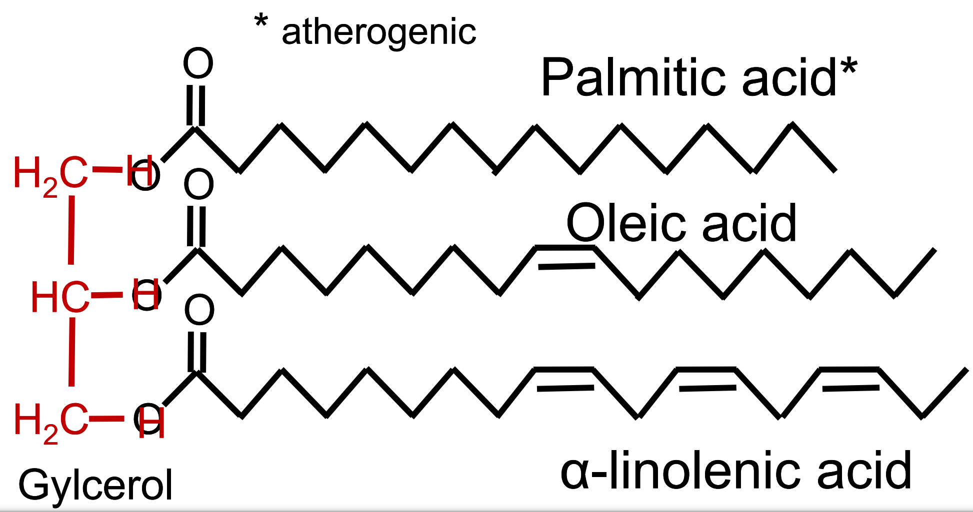
► Triglycerides or triacylglycerols are water-insoluble lipids consisting of three fatty acids (acyl group) linked to one glycerol molecule.

- ► They represent a concentrated source of metabolic energy contributing 9 kcal/gm.



R = Fatty acid chain

Most common saturated fats in TG are Lauric and Myristic* acids (the tropical oils) and Palmitic* and Stearic (from meats)

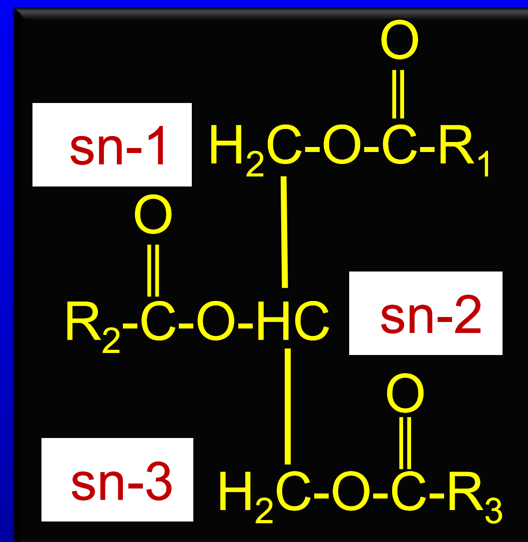


Rafai, N et al. Handbook of Lipoprotein Testing AACC Press Washington DC 2nd Ed 2000

Triacylglycerol Nomenclature

- Each TAG may contain a mixture of different fatty acids or may contain three of the same fatty acids. These fatty acids are esterified to three distinct positions on the glycerol which is described by a stereospecific numbering system (sn);
  - **sn-1, sn-2 and sn-3.**

R = Fatty acid chain



- The sn refers to the position of the carbon atoms on the glycerol; the carbon atom that is at the top of the Fischer projection that has a vertical carbon chain with the hydroxyl group at carbon-2 orientated to the left is referred to as sn-1 (outer position). sn-2 Refers to the position at carbon-2 (middle position) and sn-3 (outer position) refers to the position below sn-2.

Berry SEE. Nutrition Research Reviews (2009), 22, 3–17

Triacylglycerol Composition

- The term molecular species describes the specific make-up of the TAG.
- For example, a TAG with palmitic acid at sn-1, oleic acid (18 : 1n-9) at sn-2 and stearic acid at sn-3 is referred to as the molecular species 1-palmitoyl 2-oleoyl 3-stearoylglcerol or in short-hand POS (where P is palmitic acid, O is oleic acid and S is stearic acid).
- ATAG mixture with just five different fatty acids can therefore exist as 105 different TAG molecular species (TAG-MS) according to differences in positional composition.
- SFA are found predominantly in the external sn-1 and sn-3 positions and unsaturated fatty acids in the sn-2 position of the TAG. Conversely, in animal fats, the sn-2 position of the TAG contains a high proportion of SFA

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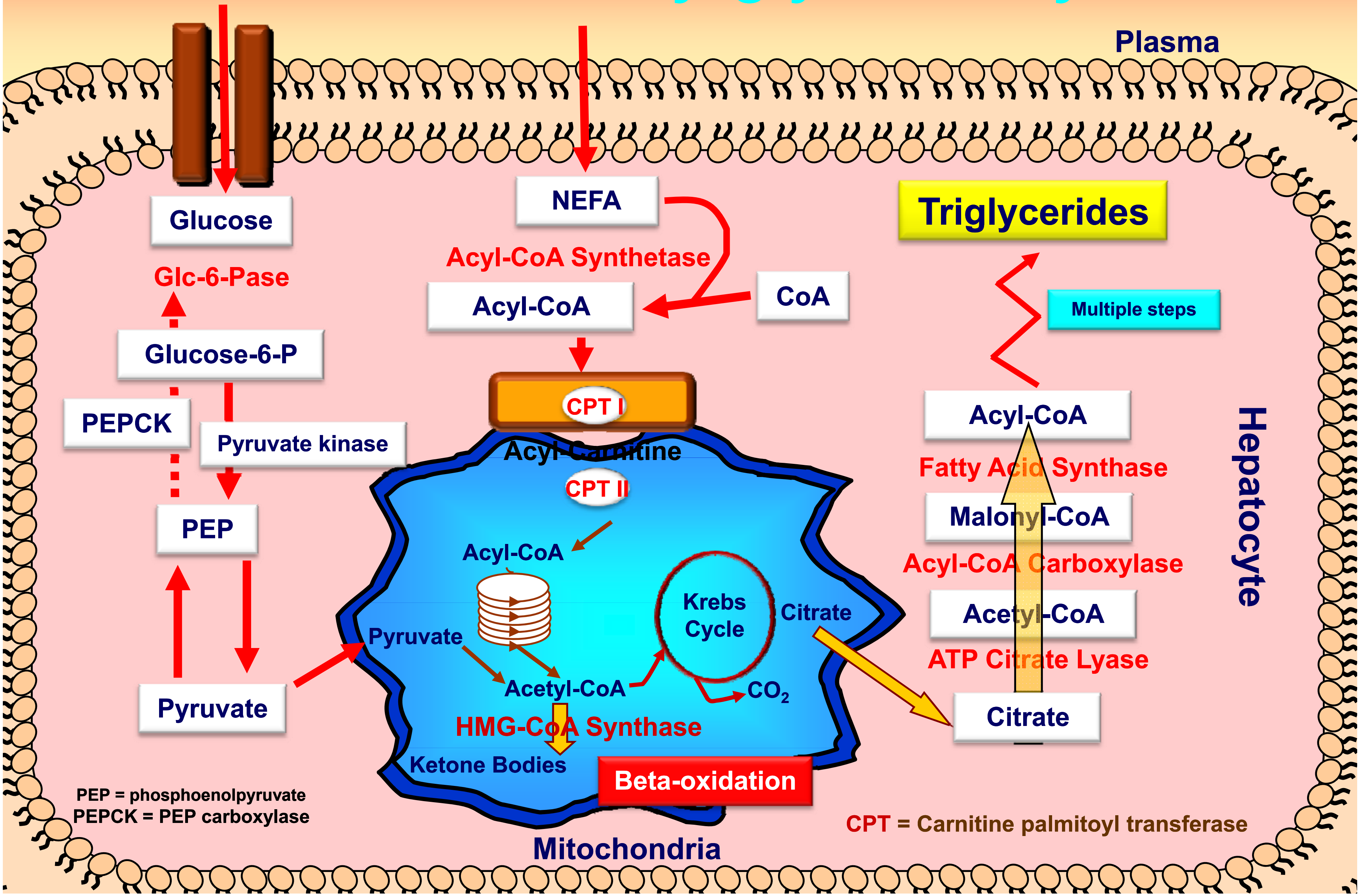
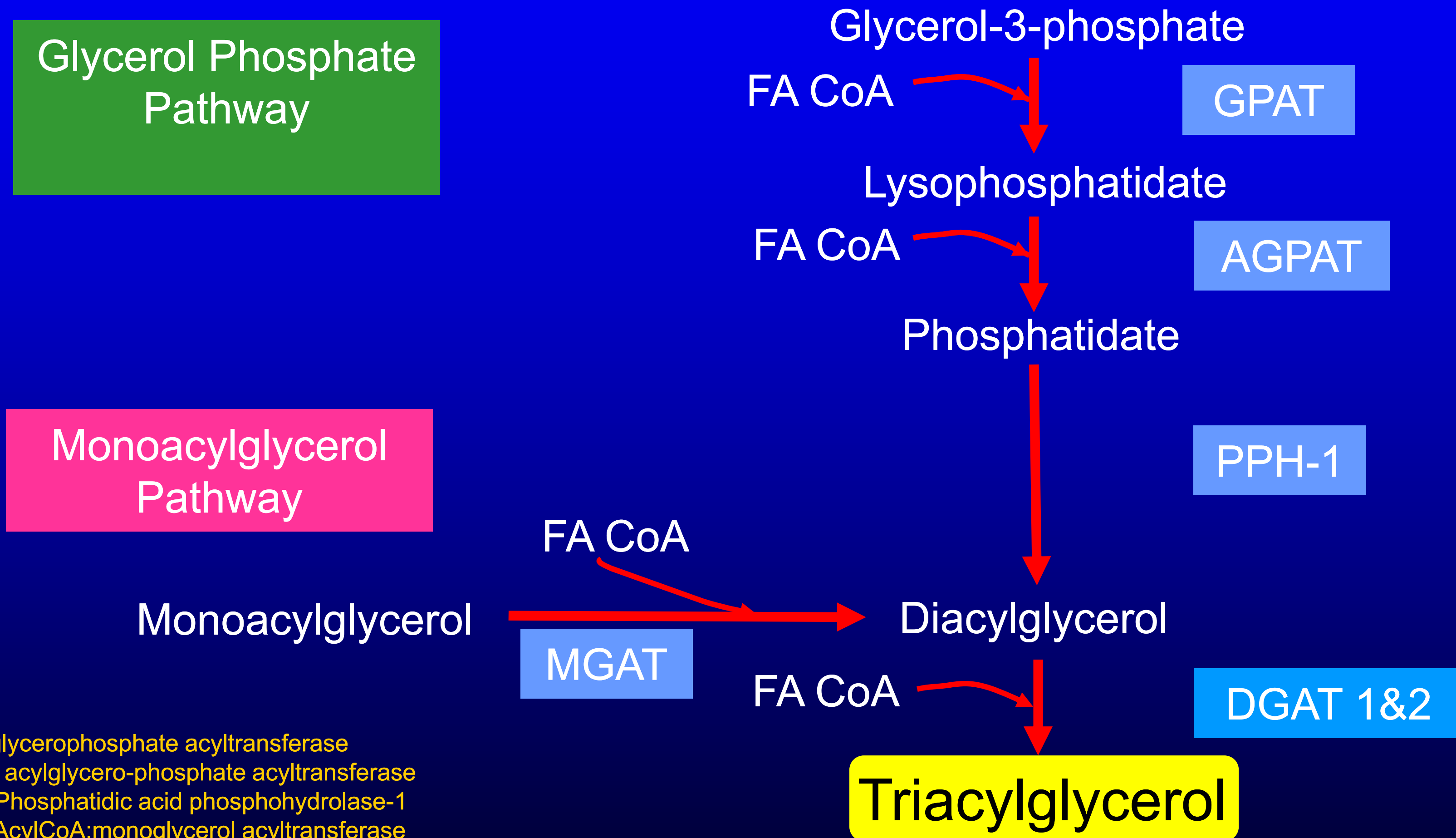
Substrates for Triacylglycerol Synthesis



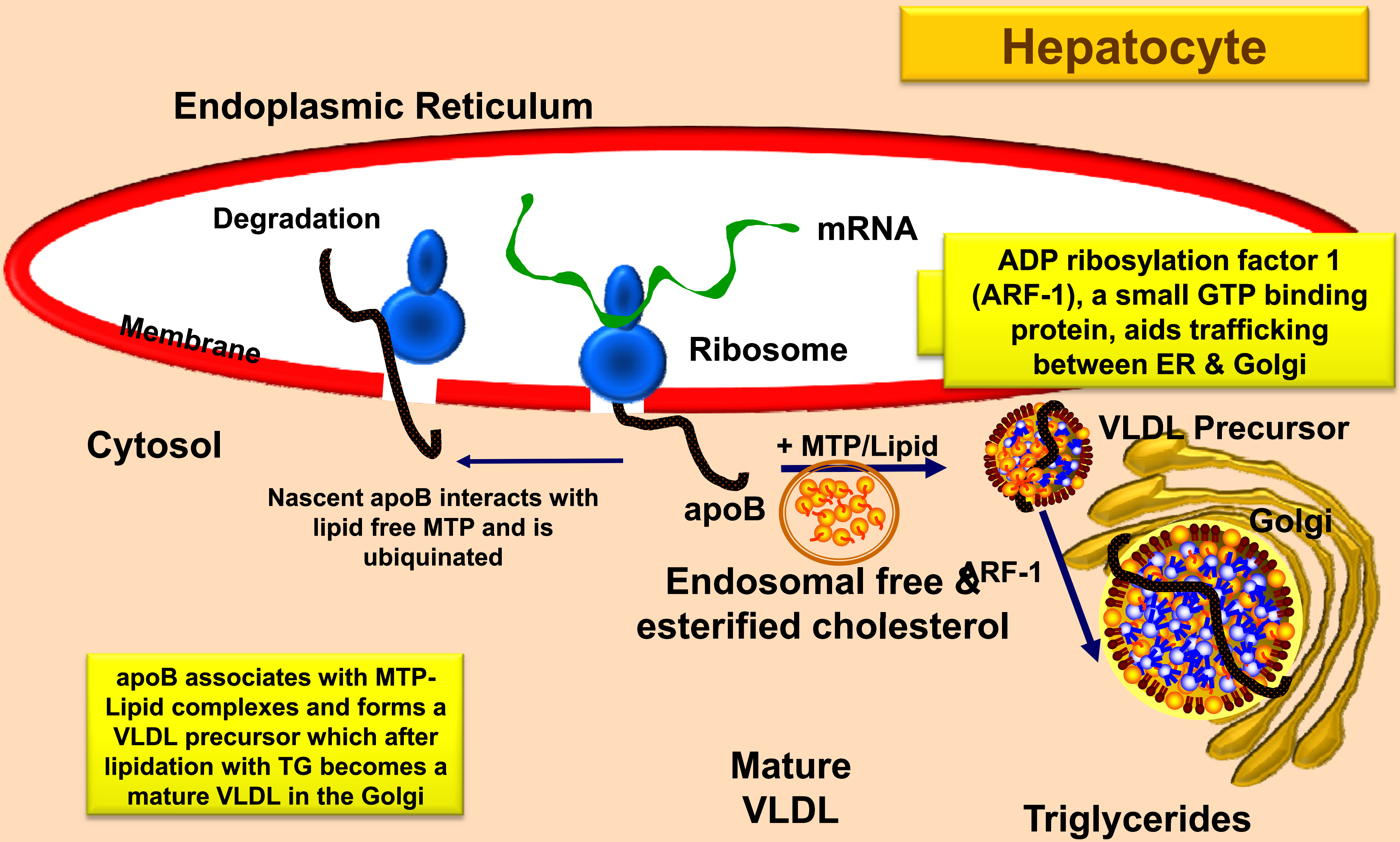
Enzymatic Regulation of Triacylglycerol (Triglyceride) Synthesis



GPAT = glycerophosphate acyltransferase
AGPAT = acylglycero-phosphate acyltransferase
PPH-1 = Phosphatidic acid phosphohydrolase-1
MGAT = AcylCoA:monoglycerol acyltransferase
DGAT Diacylglycerol acyltransferase

Hubert C. Chen, Robert V. Farese, Jr ATVB 2005;25:482-486.

Lipidation of Apolipoprotein B



Adiels M et al. Cur Opin Lipidol 2006;17:238-246

Whitfield AJ et al. Clin Chem 2004;50:1725-1732