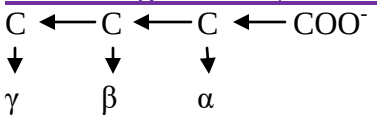
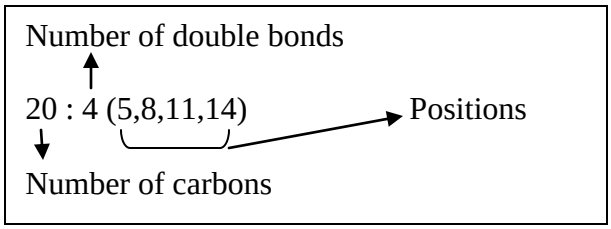
Unit II – Problem 3 – Biochemistry: Fatty Acids and TAG Metabolism

- **Free fattry acids are oxidized in:**
  - Liver.
  - Muscles.
    Notice that fatty acids oxidation provides energy to the body (especially when fasting).
- **Fatty acids are considered as components of cell membranes**: forming phospholipids and glycolipids. In addition, they are precursors used for prostaglandin synthesis.
- **Structure of fatty acids:**
  - They are composed of a hydrophobic hydrocarbon chain with a terminal hydrophilic carboxyl group (this is known as amphipathic nature).
  - **Therefore, fatty acids are transported through:**
    - ✓ Lipoprotein particles.
    - ✓ Albumin (in case of fatty acid esters).
- **Saturation o fatty acids:**
  - Saturated fatty acids contain single bonds only while unsaturated fatty acids contain one (mono) or more (poly) double bonds in cis-configuration. Notice that unsaturated fatty acids have decreased melting temperature.
- **Chain length of fatty acids:**

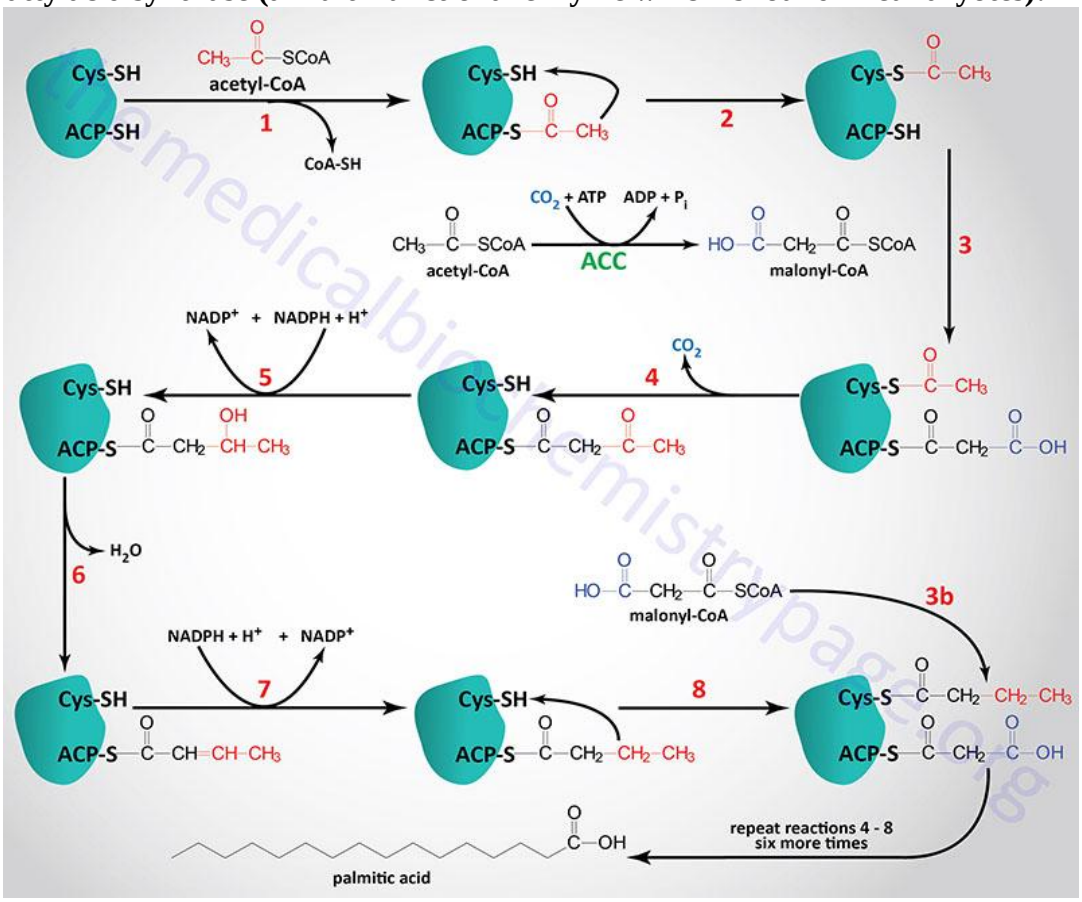




- **Essential fatty acids (obtained from diet):**
  - **Linoleic**: for prostaglandin synthesis.
  - **Linolenic**: required for growth and development.
- **De Novo synthesis of fatty acids:**
  - It occurs mainly in the liver and also in lactating mammary glands and adipose tissues.
  - Excess carbohydrates and protein can be converted to fatty acids and stored in the body.
  - Synthesis of fatty acids is represented by cytosolic reactions in which acety CoA is added with the use of energy (in the form of ATP) and NADPH (which is obtained from Pentose Phosphate Pathway).
  - **What are the sources of acetyl CoA?**
    - ✓ Oxidation of pyruvate.
    - ✓ Catabolism of fatty acids.
    - ✓ Catabolism of ketone bodies.
    - ✓ Catabolism of certain amino acids.
  - **Production of cytosolic acetyl CoA:**
    - ✓ Acetyl CoA in mitochondria → via oxalozcetate and citrate synthase → citrate → via ATP-citrate lyase (releasing oxaloacetate) → acetyl CoA in cytosol.
  - **Carboxylation of fatty acids to malonyl CoA:**
    - ✓ This reaction is catalyzed by acetyl CoA carboxylase (ACC) which uses CO_2, ATP and biotin (as a cofactor).
    - ✓ Short term regulation of (ACC):
      - ❖ Citrate enhances the activity.
      - ❖ (ACC) is inactivated by phosphorylation via AMPK.
      - ❖ Epinephrine and glucagon inactivate (ACC).
      - ❖ Insulin activates (ACC).

- ✓ Long term regulation of (ACC):
  - ❖ Prolonged consumption of high calories food.
  - ❖ SREBP.

- **Fatty acid synthase (a multi-functional enzyme which is found in eukaryotes):**



- **Further elongation of fatty acids chains:**
  - ✓ Needs: malonyl CoA and ATP.
  - ✓ Location: SER (Smooth Endomplasmic Reticulum).
  - ✓ Note: VLCFA (>22) are produced in the brain.
- **Desaturation of fatty acids occurs by the enzyme desaturase (which adds cis double bonds).**
- **Storage of fatty acids as components of Tri-Acyl Glycerol (TAG):**
  - ✓ Glycerol binds to fatty acids through ester bonds.
  - ✓ Three fatty acids will attach to glycerol. The first one will be saturated, the second is unsaturated while the third fatty acids is either saturated or unsaturated.

- **TAG:**

- **Synthesis of glycerol phosphate:**
  - ✓ In the liver:
    - ❖ Glucose → through glycolysis → DHAP → reduced to → glycerol phosphate.
    - ❖ Gylcerol → through glycerol kinase → glycerol phosphate.
  - ✓ In adipose tissues:
    - ❖ Glucose → through glycolysis → DHAP → reduced to → glycerol phosphate.
- **Conversion of free fatty acids to their active form:**
  - ✓ Fatty acids → through fatty acyl CoA synthetase → fatty acid CoA
- **Synthesis of a molecule of TAG from glycerol phosphate and fatty acyl CoA:**
  - ✓ Glycerol phosphate → acyltransferase → lysophosphatidic acid → acyltransferase → phosphatidic acid → removal of phosphate → diacylglycerol → acyl transferase → TAG