Tutorial 27: Metabolism, Krebs Cycle and the Electron Transport Chain

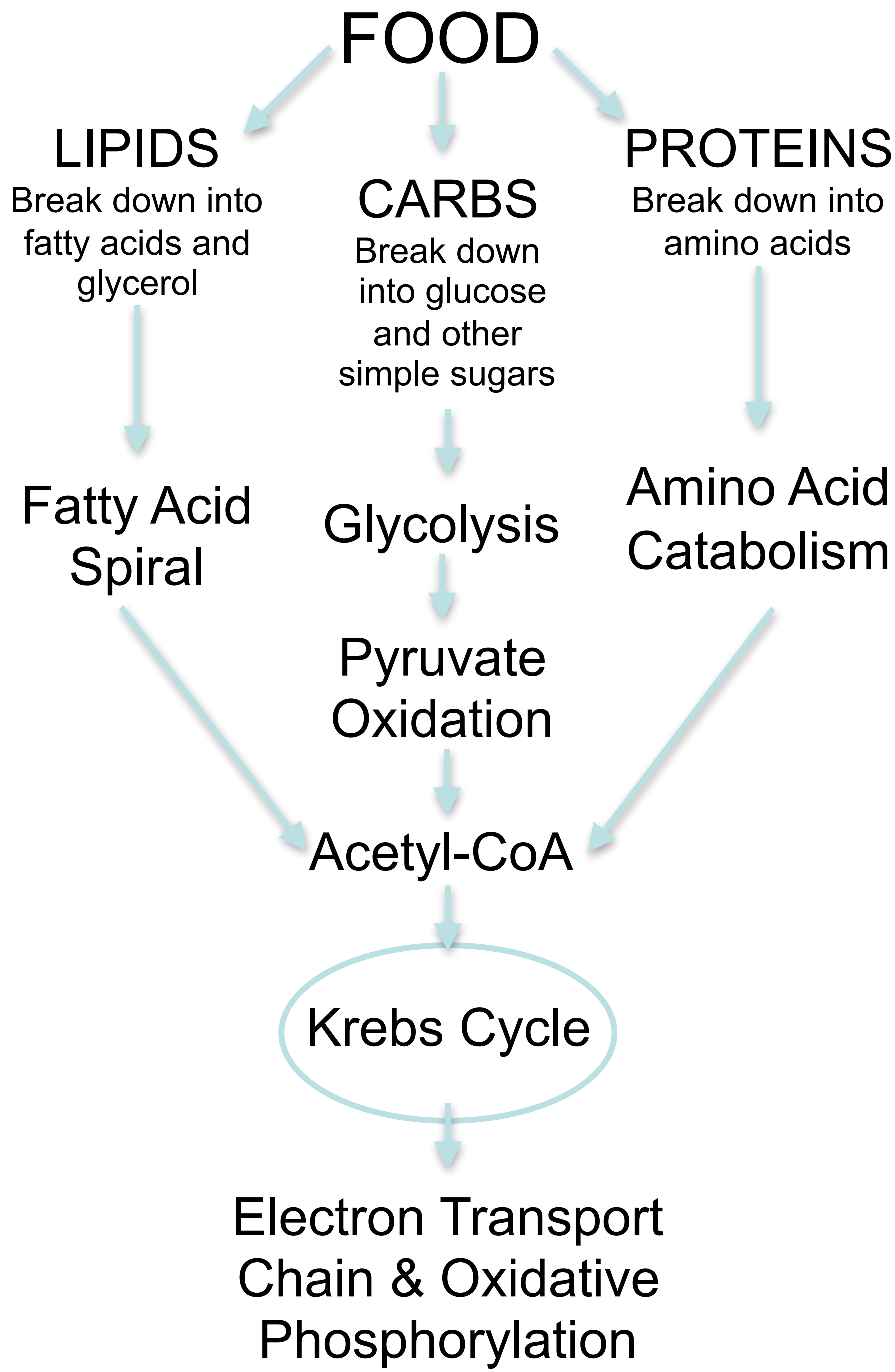
Goals:

- ✓ To be able to describe the overall catabolic pathways for food molecules.
- ✓ To understand what bonds are hydrolyzed in the digestion of carbohydrates, lipids and proteins, and to know what molecules are absorbed from the digestion process.
- ✓ To be able to describe the catabolic processes that carbon skeletons from all food sources share: the Krebs cycle (aka the citric acid cycle), electron transport chain, and oxidative phosphorylation.
- ✓ To be able to calculate the ATP yield for each acetyl-CoA oxidized in the Krebs cycle, electron transport chain and oxidative phosphorylation.

Metabolism

- **Metabolism:** refers to all the chemical reactions that provide energy and the substances required for continued cell growth.
  - **Catabolism**: The metabolic reactions in which molecules are broken apart. Overall, these reactions are exergonic and provide energy.
  - **Anabolism**: The metabolic reactions in which molecules are built up from smaller pieces. These reactions are endergonic and require energy (usually from ATP).

Overview of Catabolism



Krebs Cycle

- **Overview of the Krebs Cycle:** The Krebs Cycle is an eight step cyclical process in which carbon from food is oxidized into carbon dioxide. In the first half of the cycle (steps 1-4), two carbons from food enter as acetyl-CoA and exit as carbon dioxide. In the second half of the cycle (steps 5-8), the reactant for step 1 (oxaloacetate) is regenerated. Each oxidation step requires a coenzyme to be reduced, thus 3 NADH/H+ and 1 $FADH_2$ are produced in each turn of the Krebs Cycle.

- **Details of the Krebs Cycle:**
  - In step 1, two carbons from food enter as acetyl-CoA and attach to the 4 carbon molecule oxaloacetate to make the 6 carbon molecule citrate.
  - In step 2, citrate undergoes isomerization to isocitrate.
  - Steps 3 and 4 are both oxidations with NAD+ as the oxidizing agent, and both steps result in a carbon lost as carbon dioxide.
  - Step 5 is an exergonic reaction that is coupled to the synthesis of GTP from GDP.
  - In step 6, two hydrogen atoms are removed to create the double bond in fumarate. This requires a dehydrogenase enzyme, and the coenzyme FAD as the oxidizing agent.
  - In step 7, the double bond of fumarate is hydrated to form malate.
  - In step 8, malate is oxidized to reform oxaloacetate with NAD+ acting as the oxidizing agent.

- **Net Result from the Krebs Cycle:**

3 reduced coenzymes NADH/H+, which yields 9 ATP

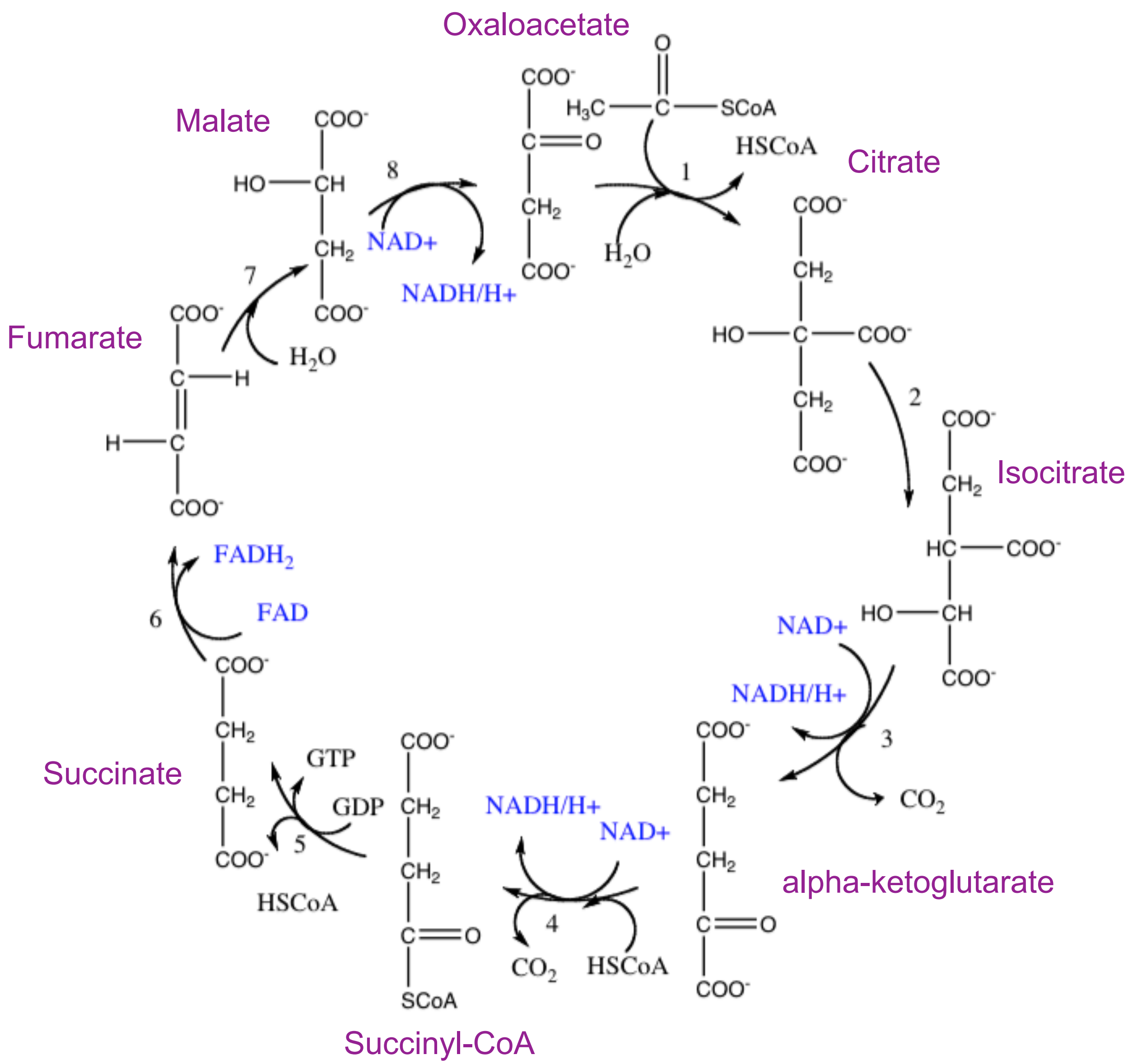
1 reduced coenzyme $FADH_2$, which yields 2 ATP

<u>1 energy rich molecule of GTP, which yields 1 ATP</u>

TOTAL ATP = 12*

*ATP yields are based on NADH/H+ yield of 3 and $FADH_2$ yield of 2 in the electron transport chain.

Krebs Cycle Continued



Step	Enzyme
1	Citrate Synthase
2	Aconitase
3	Isocitrate Dehydrogenase Complex
4	alpha-Ketoglutarate Dehydrogenase Complex
5	Succinyl CoA Synthetase
6	Succinate Dehydrogenase
7	Fumarase
8	Malate Dehydrogenase

Electron Transport Chain (ETC) and Oxidative Phosphorylation

- **Overview of the ETC and Oxidative Phosphorylation:**
  - The reduced coenzymes (NADH and $FADH_2$) are reoxidized when they pass electrons to the ETC. The ETC refers to a series of oxidation-reduction reactions where each successive oxidizing agent is stronger than the last. The electrons ultimately combine with H+ ions and oxygen from the air we breath to form water.

$$O_2 + 4\ e^- + 4\ H^+ \rightarrow 2H_2O$$

  - Energy is released as the electrons are passed to stronger and stronger oxidizing agents. This energy is harnessed to move H+ ions from the mitochondiral matrix and into the intermembrane space. This creates potential energy.
  - In oxidative phosphorylation, the H+ ions pass through ATP synthase enzymes (embedded in the inner mitochondrial membrane) and re-establish equal concentration on both sides of the membrane. This movement through ATP synthase facilitates the formation of ATP from ADP.
  - Recall that reoxidation of 1 NAD+ results in formation of 3 ATP during the ETC and oxidative phosphorylation, and reoxidation of 1 FAD results in formation of 2 ATP during the ETC and oxidative phosphorylation.