

### Overview of Oxidative Phosphorylation

1. Energy-rich molecules, such as glucose, are metabolized by a series of oxidation reactions ultimately yielding what! CO<sub>2</sub> and water
2. The metabolic intermediates of these oxidation reactions donate electrons to specific coenzymes which are... Nicotinamide Adenine Dinucleotide (NAD<sup>+</sup>) and Flavin Adenine Dinucleotide (FAD)
3. What do NAD<sup>+</sup> and FAD form due to the oxidation reactions? the energy-rich reduced forms, NADH and FADH<sub>2</sub>.
4. These reduced coenzymes NADH and FADH<sub>2</sub> can each donate a pair of electrons to a specialized set of electron carriers, collectively called ... the electron transport chain (ETC).
5. As electrons are passed down the ETC, they lose what? much of their free energy.
6. The coupling of electron transport with ATP synthesis is called ... oxidative phosphorylation
7. What's OXPHOS? Oxidative phosphorylation.

### Mitochondrial Machinery

1. The Inner membrane of the mitochondria is impermeable to...most small ions, small and large molecules.
2. Matrix you have TCA cycle enzymes, Fatty acid oxidation enzymes, mtDNA, mtRNA and mitochondrial ribosomes.

### Electron Transport Chain

1. There are 4 Complexes in ETC
2. NADH electrons first comes into complex I and gets transfer to complex III and then Complex IV.
3. FADH<sub>2</sub> electrons go to Complex II and then gets transfer to Complex III and then Complex IV.
4. Complex I: We have NADH that comes from the mitochondria and its the substrate that will be oxidized by dehydrogenases.
5. The name of Complex I is NADH Dehydrogenase
6. Dehydrogenases remove the electrons from NADH and transfer to FMN (flavin mononucleotide) also inside in the Complex I.
7. Succinate dehydrogenase: At Complex II, electrons from the succinate dehydrogenase-catalyzed oxidation of succinate to fumarate move from the coenzyme, FADH<sub>2</sub>, to an iron-sulfur protein, and then to coenzyme Q.
8. Coenzyme Q (CoQ) is a quinone derivative with a long, hydrophobic isoprenoid tail.
9. CoQ is a mobile electron carrier and can accept hydrogen atoms from NADH dehydrogenase (**Complex I**), from succinate dehydrogenase (**Complex II**), and from other mitochondrial dehydrogenases: glycerophosphate dehydrogenase and acyl CoA dehydrogenase.

10. CoQ transfers electrons to **Complex III** (cytochrome bc<sub>1</sub>) and then, links the flavoprotein dehydrogenases to the cytochromes.
11. Cytochromes: The remaining members of the ETC are cytochrome proteins. Each contains a heme group .
12. Cytochrome C is not a complex it just carries electrons from Complex II to Complex IV.
13. Electrons are passed along the chain from cytochrome bc<sub>1</sub> (**Complex III**), to cytochrome c, and then to cytochromes a + a<sub>3</sub> (**Complex IV**)
14. Complex IV is called cytochrome c oxidase because its being oxidized.
15. At Complex IV, the transported electrons, O<sub>2</sub>, and free protons are brought together, and O<sub>2</sub> is reduced to water.
16. Complex II is Succinate dehydrogenase.
17. The TCA cycle is Complex II, its embedded in the membrane.
18. Complex III and Complex IV can only do one electron at the time
19. Why would electrons go through all these Complexes to form at the end water? That's electro chemistry

### Energetic Coupling

1. Blocking electron transfer by any one of these inhibitors stops electron flow from substrate to oxygen because the reactions of the electron transport chain are tightly coupled like meshed gears.
2. There are compounds or antibiotics that specifically blocks oxidative phosphorylation and without them we would have never been able to figured this stuff out.
3. Electron Transfer Chain reaction occurs from compounds with high negative to compounds more positive.
4. The more negative the E<sub>o</sub> of a redox pair, the greater the tendency of the reductant member of that pair to lose electrons.
5. The more positive the E<sub>o</sub>, the greater the tendency of the oxidant member of that pair to accept electrons.
6. Electrons flow from the pair with the more negative E<sub>o</sub> to that with the more positive E<sub>o</sub>.
7. ½ O<sub>2</sub>/H<sub>2</sub>O is the most oxidant and the stronger oxidizing agent that can accept electrons.
8. NAD<sup>+</sup>/NADH is the strongest reducing agents that is that they have stronger tendency to lose electrons.

### ATP Synthase

1. Electron transport is coupled to the phosphorylation of ADP by the pumping of protons across the inner mitochondrial membrane, from the matrix to the intermembrane space, at Complexes I, III, and IV.

2. When NADH flows through Complexes I, III and IV, it gives you three NADH protons.
3. When FADH<sub>2</sub> flows through Complex II, which is not a pump, but since electrons will go after this through Complex III and IV we will get two protons.
4. This process creates an electrical gradient and a pH gradient.
5. The energy generated by this proton gradient is sufficient to drive ATP synthesis.
6. The proton gradient serves as the common intermediate that couples oxidation to phosphorylation.
7. The multi-subunit enzyme ATP synthase (Complex V) catalyzes formation of ATP from ADP+P<sub>i</sub>.
8. The ATP synthase contains a domain (F<sub>0</sub>), and an extra-membranous domain (F<sub>1</sub>)
9. The F<sub>0</sub> domain spans the inner mitochondrial membrane.
10. The F<sub>1</sub> domain appears as a sphere that protrudes into the mitochondrial matrix.
11. F<sub>0</sub> rotation causes conformational changes in the β subunits of the F<sub>1</sub> domain that allow them to bind ADP + P<sub>i</sub>, phosphorylate ADP to ATP, and release ATP.
12. The ATP/ADP transporter is able to move ADP to the matrix so it can react with the ATP synthase and all the ATP that will be formed moved to the outside.

### Uncoupling Proteins

1. Uncoupling proteins form channels that allow protons to reenter the mitochondrial matrix without energy being captured as ATP.
2. The energy is released as heat, and the process is called nonshivering thermogenesis.

### Glycerol 3-P and Malate

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2. The inner mitochondrial membrane lacks an NADH transporter, and NADH produced in the cytosol cannot directly enter the mitochondrial matrix.
3. However, two electrons of NADH are transported from the cytosol into the matrix using substrate shuttles.
4. In the glycerophosphate shuttle two electrons are transferred from NADH to dihydroxyacetone phosphate by cytosolic glycerophosphate dehydrogenase.
5. The glycerol 3-phosphate produced is oxidized by the mitochondrial isozyme glycerol 3-phosphate as FAD is reduced to FADH<sub>2</sub>.
6. CoQ of the ETC oxidizes the FADH<sub>2</sub>.
7. The glycerophosphate shuttle, therefore, results in the synthesis of **two ATPs** for each cytosolic NADH oxidized.