Lecture 30: Electron Transport & ATP Synthesis

Electron transport

Location: Inner mitochondrial membrane

Input: NADH, FADH₂

Output: Proton gradient across inner membrane, higher proton concentration between the two membranes.

Overview:
- The energy captured by oxidation steps in glycolysis and the TCA cycle are stored on NADH and FADH₂.
- These compounds are oxidized in the electron transport chain, releasing additional energy as electrons are removed from them.
- This energy is stored in a proton gradient across the inner mitochondrial membrane.
- The energy stored in this gradient is used to produce ATP.
- Final electron acceptor is oxygen.

Addition of electrons to oxygen releases energy:

\[ 	ext{O}_2 + 4 \text{H}^+ + 4e^- = \text{O}_2 + 2 \text{H}_2 \rightarrow 2 \text{H}_2\text{O} + \text{lots of energy} \]

Energy Changes in Electron Transport

Oxidation of NADH

**Complex I:** NADH → NAD⁺
- NADH is oxidized back to NAD⁺.
- The electrons from NADH are transferred to coenzyme Q, a non-polar electron carrier. The membrane must be fluid for it to diffuse from one complex to the next.
- **Four protons** are pumped from the inside (matrix) to the intermembrane space for each pair of electrons processed.

**Complex III:**
- Electrons from CoQH₂ passed to cytochrome c.
- **Four protons** are pumped for each pair of electrons processed.

**Cytochrome C:** A small iron containing protein that shuttles electrons, one at a time, from III to IV.

**Complex IV:** Cytochrome c oxidase
- Donates a total of four electrons to O₂.
- Pumps an additional two protons for each pair of electrons that are processed.
Oxidation of FADH$_2$

**Complex II: FADH$_2$ → FAD**
- Two electrons from FADH$_2$ are transferred to CoQ.
- Does not pump any protons.
- CoQ goes to complex III.
- Remaining path is the same as NADH oxidation:
  - Complex III → 4 protons pumped/pair of electrons.
  - Complex IV → 2 protons pumped/pair of electrons.

Let's count how many protons are pumped by the oxidation of one NADH:

\[ 10 \text{ H}^+ \]

Let's count how many protons are pumped by the oxidation of one FADH$_2$:

\[ 6 \text{ H}^+ \]

**ATP Synthesis (Oxidative phosphorylation):**

ATP synthesis is attained by coupling the energy stored in the proton gradient to the chemical synthesis of ATP.

The enzyme that accomplishes this coupling is called ATP-synthase. This is called oxidative phosphorylation since the generation of ATP is coupled to oxidation.

\[ 9 \text{ H}^+ = 3 \text{ ATP synthesized} \]
Structural Features:
1. The $F_o$ Complex
   - Membrane-spanning, multi-protein complex.
   - Responsible for coupling the movement of three protons to $120^\circ$ rotations of the $\gamma$-subunit.
2. The $F_1$ Complex
   - Attached to $F_o$, it protrudes into the mitochondrial matrix.
   - Composed of five different subunits: $\alpha_3\beta_3\gamma\delta\varepsilon$
   - The $\gamma$ subunit is the shaft at the center of the $\alpha_3\beta_3$ disk. $\gamma$ rotates $120^\circ/3$ protons.
   - The $\beta$ subunits are asymmetric due to their interactions with the $\gamma$-subunit (allosteric effects).
     1. One conformation of the $\beta$ subunit has very low affinity for both ADP and ATP.
     2. One conformation of the $\beta$ subunit has high affinity for ADP and $P_i$.
     3. One conformation of the $\beta$ subunit has high affinity for ATP.

How the motor works:
- Every time three proton move through the complex, the $\gamma$ subunit rotates $120^\circ$.
- The rotation of $\gamma$ subunit changes the conformation of the $\beta$-subunits such that the Gibbs energy of the bound ADP + $P_i$ becomes higher than the energy of ATP, thus ATP forms spontaneously from the bound ADP and $P_i$.
- The newly-formed ATP is released with the transport of three additional protons.
- The actual synthesis, or formation of the bond between ADP and $P_i$, is catalyzed by conformational changes of the $\beta$-subunit that occur as a consequence of the rotation.
- Since all three $\beta$ subunits are functioning at the same time, the transport of 9 protons in a complete cycle produces 3 ATP.

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<thead>
<tr>
<th>NADH</th>
<th>~10 protons pumped</th>
<th>~3 ATP</th>
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</thead>
<tbody>
<tr>
<td>FADH$_2$</td>
<td>~6 protons pumped</td>
<td>~2 ATP</td>
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