Electron Transport System

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What did We learn so far?

• Glucose is converted to **pyruvate** in glycolysis. The process generates **two** ATPs.

• Pyruvate is taken into the mitochondria and is further oxidized in the TCA cycle.

• First PDHc converts pyruvate to **Acetyl-CoA** which enters TCA-cycle. Here energy is captured as **NADH**.

• Series of eight oxidation reactions resulted in production of **two** CO₂ while the energy was collected in the form of NADH and FADH₂. **One** ATP was produced in the process.
Review of the TCA-cycle

Acetyl CoA ➔ Citrate Synthase ➔ Citrate ➔ Aconitase ➔ Isocitrate ➔ Isocitrate dehydrogenase ➔ α-Ketoglutarate ➔ α-Ketoglutarate dehydrogenase ➔ Succinyl CoA synthetase ➔ Succinyl CoA ➔ Succinate dehydrogenase ➔ Fumarate ➔ Fumarase ➔ Malate ➔ Malate dehydrogenase ➔ NADH ➔ GTP ➔ FADH2

http://tru-wealth.blogspot.com/2013/05/your-bodys-chemistry-pyruvate-for.html
The electron transport chain is the final stage of aerobic respiration leading to the forming of ATP.

Now finally we are about to obtain the ATP necessary for survival by using the reduced cofactors, NADH and FADH$_2$, formed in the TCA-cycle.

Note that there is a difference between the way ATPs were generated so far and the way ETC makes ATP.
Substrate Level Phosphorylation VS Oxidative Phosphorylation

- **Substrate Level Phosphorylation:**
  - results in the formation of ATP by the direct enzymatic transfer of phosphate group to ADP.

\[
\text{ADP} \to \text{ATP} \\
R-\text{OPO}_3^{2-} \to R-\text{OH}
\]

- **Oxidative Phosphorylation:**
  - uses an electrochemical or chemiosmotic gradient of protons (H\(^+\)) across the inner mitochondrial membrane to generate ATP from ADP.
Reaction 5: Oxidation Reaction

Succinyl CoA synthetase

Succinyl CoA

GDP → GTP

Succinate
Molecular Species Involved

- Flavoproteins
- Ubiquinone
- Succinate dehydrogenase
- Cytochromes
- Iron-sulfur proteins
- Protein bound copper
The Overall Picture of ETC

Oxidation steps

- NADH
- FADH$_2$

Protein complex I
Protein complex II
Protein complex III
Protein complex IV

Purpose
- Use the released energy to pump protons.

Electrons move along the electron transport chain going from donor to acceptor until they reach Oxygen.

$O_2$ → $H_2O$
Reduction potential is a measure of the tendency of a chemical species to acquire electrons and thereby be reduced.

Molecules with a more positive Standard Reduction Potential will pull electrons away from molecules with a more negative Standard Reduction Potential.
The flow of electrons through the cell's electron transport chain is strictly in the direction of molecules with increasing Standard Reduction Potentials.
Key point:
The electrons lose energy as they pass down the electron transport system. Some of this energy is used to pump protons (hydrogen ions) into the outer compartment of the mitochondrion.
The relationship between Standard Free Energy change ($\Delta G^o'$) and $\Delta Eo'$ is:

$$\Delta G^o' = -nF \Delta Eo'$$

Standard reduction potential difference:

$$\Delta Eo' = Eo' (e \text{ acceptor}) - Eo' (e \text{ donor})$$

REMEMBER

NADH and FADH$_2$ are the first electron donors.  
$O_2$ is the last electron acceptor.
**O₂ reduction by NADH: Overall Reaction**

\[
\frac{1}{2} \text{O}_2 + \text{NADH} + \text{H}^+ \rightarrow \text{H}_2\text{O} + \text{NAD}^+
\]

\[
\frac{1}{2} \text{O}_2 + 2\text{H}^+ + 2\text{e}^- \rightarrow \text{H}_2\text{O} \quad \text{E}_\text{o}' = +0.815 \text{ V}
\]

\[
\text{NAD}^+ + \text{H}^+ + 2\text{e}^- \rightarrow \text{NADH} \quad \text{E}_\text{o}' = -0.315 \text{ V}
\]

\[
\Delta\text{E}_\text{o}' = \text{E}_\text{o}' (\text{e acceptor}) - \text{E}_\text{o}' (\text{e donor})
\]

\[
\Delta\text{E}_\text{o}' = 0.815 - (-0.315) = 1.130 \text{ V}
\]

\[
\Delta\text{G}_\text{o}' = -nF \Delta\text{E}_\text{o}' = -218 \text{ KJ/mole}
\]
• Oxidation of $O_2$ (2e$^-$ transfer) under standard biochemical conditions releases 218KJ of free energy.

• An ATP synthesis requires 30.5 KJ/mole free energy.

• Therefore several moles of ATP can be synthesized.
ETC is carried out by 4 complexes.

1. **Complex I**: also known as the NADH-coenzyme Q reductase or NADH dehydrogenase.

2. **Complex II**: also known as succinate-coenzyme Q reductase or succinate dehydrogenase.

3. **Complex III**: also known as coenzyme Q reductase.

4. **Complex IV**: also known as cytochrome c reductase.

Each complex contains several different electron carriers.
Complex I is also called NADH-Coenzyme Q reductase because this large protein complex transfers 2 electrons from NADH to coenzyme Q. Complex I was formerly known as NADH dehydrogenase. Complex I is huge, 850,000 kD and is composed of more than thirty subunits. It contains a FMN prosthetic group and seven or more Fe-S clusters. This complex has between 20-26 iron atoms bound. The prosthetic group FMN is absolutely required for activity. Therefore this complex is a flavoprotein.

This complex binds NADH, transfers two electrons in the form of a hydride to FMN to produce NAD$^+$ and FMNH$_2$. The subsequent steps involve the transfer of electrons one at a time to a series of iron-sulfur complexes that includes both 2Fe-2S and 4Fe-4S clusters.

Note the importance of FMN. First it functions as a 2 electron acceptor in the hydride transfer from NADH. Second it functions as a 1 electron donor to the series of iron sulfur clusters. FMN and FAD often play crucial links between 2 electron transfer agents and 1 electron transfer agents.

The final step of this complex is the transfer of 2 electrons one at a time to coenzyme Q. CoQ like FMN and FAD can function as a 2 electron donor/acceptor and as a 1 electron donor/acceptor. CoQ is a mobile electron carrier because its isoprenoid tail makes it highly hydrophobic and lipophillic. It diffuses freely in the bilipid layer of the inner mitochondrial membrane.

The process of transferring electrons from NADH to CoQ by complex I results in the net transport of protons from the matrix side of the inner mitochondrial membrane to the inter membrane space where the H$^+$ ions accumulate generating a proton motive force. The intermembrane space side of the inner membrane is referred to as the P face (P standing for positive). The matrix side of the inner membrane is referred to as the the N face.

The transport of electrons from NADH to CoQ is coupled to the transport of protons across the membrane. This is an example of active transport. The stoichiometry is 4 H$^+$ transported per 2 electrons.

Coenzyme Q = Ubiquinone
Complex I is called **NADH-Coenzyme Q reductase**.

Transfers **two** electrons from **NADH** to coenzyme Q.

Electrons are transferred through Complex I using **FMN (flavin mononucleotide)** and a series of **Fe-S clusters**.

The process accomplishes the pumping of **four** protons across the **inner mitochondrial membrane** to the **intermembrane space**.

The **NAD^+** can now go back to the Krebs Cycle to pick up another pair of electrons.
Complex III
Coenzyme Q-cytochrome c reductase

(a) First half of Q cycle

Intermembrane space (P-phase)

UQH₂
UQ Pool

Matrix (N-phase)

Qp site

UQH₂
UQ

Qn site

2 H⁺

Cyt c

UQ⁻

UQ

Cyt c₁

FeS

Cyt b₁

Cyt b_H

First UQH₂ from pool

2e⁻ oxidation at Qp site

1e⁻

UQ to pool

UQ at Qn site

Synopsis

2H⁺ out

Cyt c

(b) Second half of Q cycle

Intermembrane space (P-phase)

UQH₂
UQ Pool

Matrix (N-phase)

Qp site

UQH₂
UQ

Qn site

2 H⁺

Cyt c

Net

UQH₂ + 2 H⁺_in + 2 Cyt cox → 2e⁻ → 4 H⁺ out + 2 Cyt c_red + UQ

2H⁺
IV. Complex I

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The prosthetic group FMN is absolutely required for activity. Therefore this complex is a flavoprotein. This complex binds NADH, transfers two electrons in the form of a hydride to FMN to produce NAD\(^+\) and FMNH\(_2\). The subsequent steps involve the transfer of electrons one at a time to a series of iron-sulfur complexes that includes both 2Fe-2S and 4Fe-4S clusters.

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Complex I: NADH-coenzyme Q reductase

Coenzyme Q = Ubiquinone
Summary

• This complex accomplishes the oxidation of ubiquinol and the reduction of two molecules of cytochrome-c.

Four hydrogens are pumped across the membrane to the intermembrane space.
Complex IV
Cytochrome c Oxidase

Intermembrane space (P-Phase)

Matrix (N-Phase)

$\frac{1}{2}O_2 + 2H^+ \rightarrow H_2O + 2H^+$
Summary

• This final complex in the electron transport chain accomplishes the final transfer of the electrons to oxygen.

• It pumps two protons across the membrane. This makes a total of ten protons across the membrane for one NADH into the electron transfer chain.
Oxygen loves electrons, but adding fewer than 4 electrons at a time makes oxygen unstable. So Cyt a3 holds them apart until 4 electrons accumulate.

When these four once energetic electrons have accumulated at Cyt a3, they are fed all at once to oxygen.
Complex II includes succinate dehydrogenase and serves as a direct link between the citric acid cycle and the electron transport chain.
Reaction 6: Oxidation Reaction

Oxidation of Succinate to Fumarate

Succinate Dehydrogenase (membrane bound)

\[
\begin{align*}
\text{Succinate} & : \quad O^- \quad C \quad CH_2 \quad CH_2 \quad C \quad O^- \\
\text{Fumarate} & : \quad O^- \quad C \quad CH \quad CH \quad C \quad O^-
\end{align*}
\]
No Protons pumped

\[ FADH_2 + UQ_{\text{oxidized}} \rightarrow FAD + UQ_{\text{reduced}} \]

\[ FAD + 2H^+ + 2e^- \rightarrow FADH_2 \quad E_o' = -0.22 \, V \]

\[ UQH_2 \rightarrow UQ + 2H^+ + 2e^- \quad E_o' = 0.06 \, V \]

\[ \Delta E^o' = E_o' (\text{e acceptor}) - E_o' (\text{e donor}) \]

\[ \Delta E^o' = 0.06 - (-0.22) = 0.028 \, V \]

\[ \Delta G^o' = -nF \Delta E_o' = -5.4 \, \text{KJ/mole} \]
This complex forms a second entry point into the electron transport chain using the succinate product of the TCA cycle. This is independent of NADH pathway.
The role of Oxygen

• The role of oxygen in cellular respiration is substantial. As a final electron receptor, it is responsible for removing electrons from the system.

• If oxygen were not available:
  – Electrons could not be passed among the coenzymes.
  – The energy in electrons could not be released.
  – The proton pump could not be established.
  – ATP could not be produced.
  – Without sufficient ATP, a cell depending upon mitochondrial ATP for energy will die.
  – When enough cells die, the entire organism will die.
Cyanide binds cytochrome oxidase so as to prevent the binding of oxygen.
Carbon Monoxide

- Carbon Monoxide binds tightly to Fe+2 form of cytochrome a3 (Complex VI).
THE END

More questions??
Please email me @
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