**Session 13 - The Q-Cycle - A Proton Pump**

-- Works by a redox-loop mechanism

**Players**

- **Quinone (Q)**
  - H$_3$CO$_2^-$
- **Semiquinone Radical (Q$^{\bullet\bullet}$)**
  - H$_3$CO$_2^-$
- **Semiquinone (QH$^{\bullet\bullet}$)**
  - H$_3$CO$_2^-$
- **Hydroquinone (QH$_2$)**
  - H$_3$CO$_2^-$

**Cycle 1**

1. IMS
2. Rieske Protein (Part of ISP)
3. 2 $\text{H}^\bullet$
4. $\text{Q}^{\bullet\bullet}$
5. $\text{b}_L$
6. $\text{b}_H$
7. 2 $\text{H}^\bullet$
8. $\text{X}$

- **Complex I**
- **Complex II**
- **Complex III**

- **Matrix**
- **ISP = Iron-sulfur protein**

**Cycle 2**

1. (Fe$^{3\bullet\bullet}$)
2. 2 $\text{H}^\bullet$
3. $\text{Q}^{\bullet\bullet}$
4. $\text{b}_L$
5. $\text{b}_H$
6. 2 $\text{H}^\bullet$
7. $\text{Q}^{\bullet\bullet}$

- **Complex III**

**So, for each QH$_2$ oxidized, you translocate 4 $\text{H}^\bullet$ -- and move two electrons via CytC(Fe$^{2\bullet\bullet}$) to Complex IV.**

**Restored**

- A second molecule is borrowed

**Net 1st half-reaction**

-- Two $\text{H}^\bullet$ translocated

-- One CytoC-(Fe$^{3\bullet\bullet}$) reduced

**Net 2nd half-reaction**

-- Another two $\text{H}^\bullet$ translocated (Step 3)

-- Another One CytoC-(Fe$^{3\bullet\bullet}$) reduced (Step 3)

**From Cycle 1 above. This semiquinone radical is derived from the first QH$_2$.**
Session 13 - Another way to look at the Q Cycle

We have converted the $e^\circ$ transfer potential of NADH/FADH$_2$ into a proton gradient -- Next we want to convert the proton gradient into the phosphate transfer potential of ATP $\rightarrow$ "oxidative phosphorylation"

Note: The previous 2-cycle presentation is more chemically accurate - but this way of looking at the cycle might help. Look at both versions but the previous page is the operative mechanism.

Coupling Proton Transport with ATP Synthesis

As drawn here:

-- The C-Ring and $\gamma$ spin when $H^\circ$ are pumped

-- This causes conformational change in $\beta$ subunit active site (☐) that favors ADP + P$_i$ $\rightarrow$ ATP

-- Three conformations at ☐:
  O = Open (nothing bound)
  L = Loose (ADP + P$_i$ bound)
  T = Tight (ATP bound)

Making ATP

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Key Point - flow of protons starts with binding of ADP
**Physiological Scenario**

1.) Stress-muscle intensive situation

2.) ATP $\rightarrow$ ADP + P_i in matrix

3.) ADP binds to protons flow

4.) ATP released and continuously made

5.) pH in Inner Membrane Space ↑ because of lost protons

6.) Electron Transport Chain responds by oxidizing NADH at elevated rate - trying to maintain $\Delta$pH across the mitochondrial IM

7.) Concentration of NADH drops in matrix

8.) Note that NADH "product inhibits" the TCA cycle + PDH steps that make it (there also is an allosteric component)

9.) The ↑ [NADH] boots up the TCA cycle to make more of it - letting you continue to make ATP

10.) It all starts with ADP production. This is called "acceptor control" where ADP is the "acceptor" of P_i

11.) Eventually with a persistent dog, you become O_2 limited

12.) Glycolysis boots up

13.) The Lactate-Pyruvate (homo-lactic fermentation) shuttle boots up

14.) Lactate acidifies the blood

15.) Bohr effect reduces affinity of Hb for O_2

16.) More O_2 delivered to tissues

17.) Respiration boots up again, because O_2 is available