# MITOCHONDRIAL RESPIRATORY CHAIN

- Mitochondrial respiratory chain complex genes in the mitochondrial respiratory chain complex gene group encodes proteins involved in oxidative phosphorylation, also called the respiratory chain. Oxidative phosphorylation is an important cellular process that uses oxygen and glucose to generate ATP.
- Five protein complexes, made up of several small proteins, are involved in this process. The complexes are named **complex I, complex II, complex III, complex IV, and complex V.**
- During oxidative phosphorylation, the protein complexes carry out chemical reactions that drive the production of ATP.
- Specifically, they create an electro-chemical gradient across the inner mitochondrial membrane through a step-by-step transfer of electrons, driven by proton motive force.
- This difference in electrical charge provides the energy for ATP production.
- The mitochondrial respiratory chain complex gene group are the combination of includes genes found in nuclear DNA as well as genes found in mtDNA

## Complex I - NADH: ubiquinone oxido-reductase, NADH-CoQ reductase, or NADH dehydrogenase

- In Complex I (NADH: ubiquinone oxido-reductase, NADH-CoQ reductase, or NADH dehydrogenase), two electrons are removed from NADH and ultimately transferred to a lipid-soluble carrier, ubiquinone (UQ).
- The reduced product, ubiquinol (UQH2), freely diffuses within the membrane, and Complex I translocates four protons (H+) across the membrane, thus producing a proton gradient.
- Complex I is one of the main sites at which premature electron leakage to oxygen occurs, thus being one of the main sites of production of superoxide.
- NADH is oxidized to NAD+, by reducing Flavin mononucleotide to FMNH2 in one two-electron step.
- FMNH2 is then oxidized in two one-electron steps, through a semiquinone intermediate.
- Each electron thus transfers from the FMNH2 to an Fe-S cluster, from the Fe-S cluster to ubiquinone (Q).
- Transfer of the first electron results in the free-radical (semiquinone) form of Q, and transfer of the second electron reduces the semiquinone form to the ubiquinol form, QH2.
- During this process, four protons are translocated from the mitochondrial matrix to the intermembrane space.
- As the electrons become continuously oxidized and reduced throughout the complex an electron current is produced along the 180 A width of the complex within the membrane.
- This current powers the active transport of four protons to the intermembrane space per two electrons from NADH.

## Complex II - Succinate dehydrogenase or Succinate-CoQ reductase

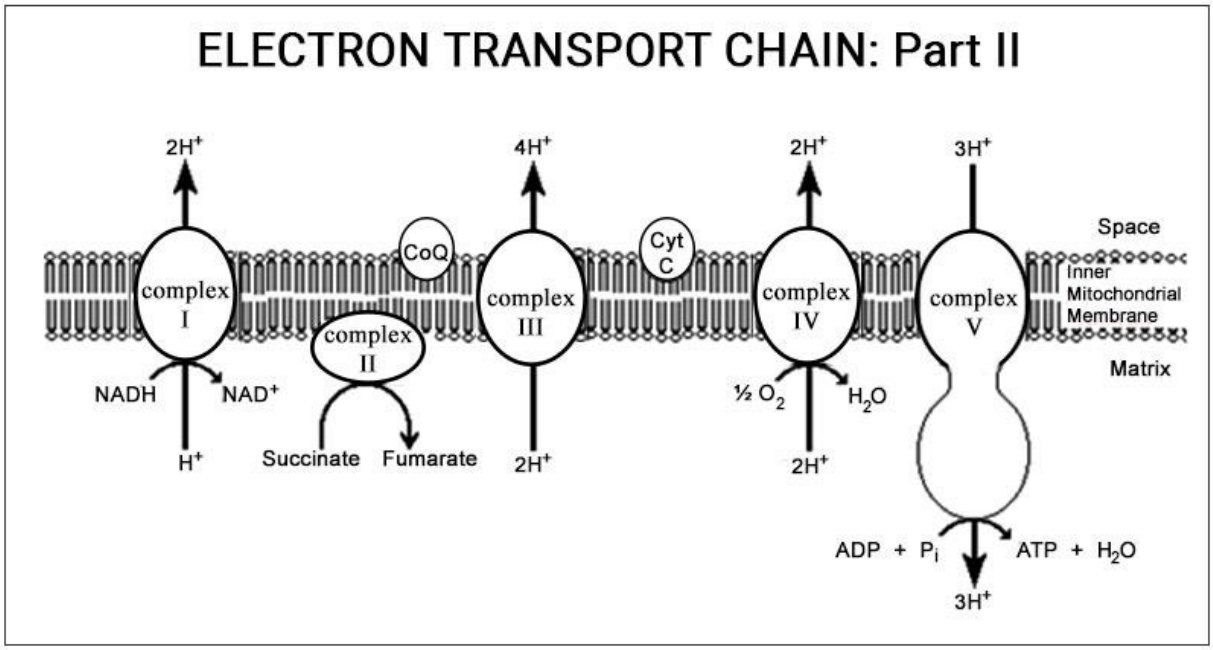
- In Complex II (Succinate dehydrogenase or Succinate-CoQ reductase) additional electrons are delivered into the quinone (Q) originating from Succinate and transferred (via flavin adenine dinucleotide (FAD)) to Q.
- Complex II consists of four protein subunits: *Succinate dehydrogenase; Succinate dehydrogenase (ubiquinone) iron-sulfur subunit, mitochondrial,; Succinate dehydrogenase complex subunit C, and Succinate dehydrogenase complex, subunit D.*
- Other electron donors (e.g., fatty acids and glycerol 3-phosphate) also direct electrons into Q (via FAD).
- Complex 2 is a parallel electron transport pathway to complex 1, but unlike complex 1, no protons are transported to the intermembrane space in this pathway. Therefore, the pathway through complex 2 contributes less energy to the overall electron transport chain process.

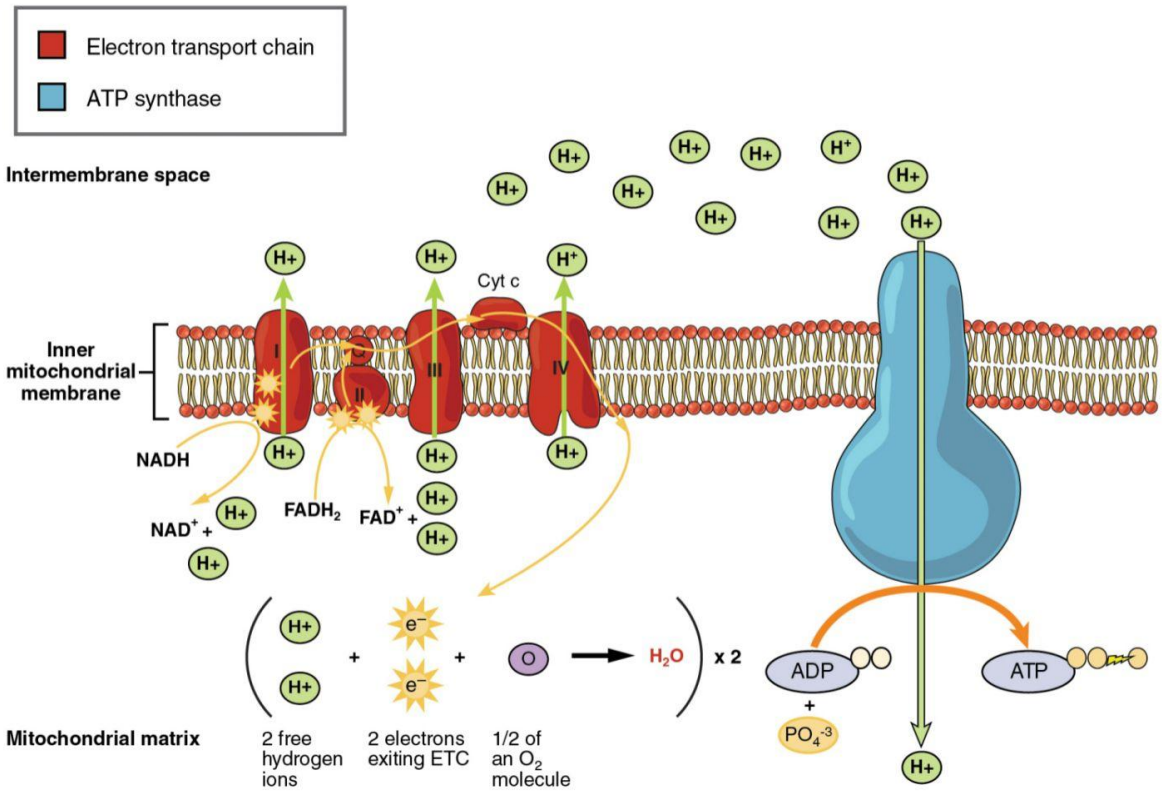
## Complex III - Cytochrome bc1 complex or CoQH2-cytochrome c reductase

- In Complex III (Cytochrome bc1 complex or CoQH2-cytochrome c reductase, the Q-cycle contributes to the proton gradient by an asymmetric absorption/release of protons.
- Two electrons are removed from QH2 at the QO site and sequentially transferred to two molecules of Cytochrome c, a water-soluble electron carrier located within the intermembrane space.
- The two other electrons sequentially pass across the protein to the Qi site where the quinone part of ubiquinone is reduced to quinol.
- Complex III may also leak electrons to molecular oxygen, resulting in superoxide formation.

## Complex IV - Cytochrome c oxidase, sometimes called Cytochrome AA3

- In Complex IV Cytochrome c oxidase, sometimes called Cytochrome AA3, four electrons are removed from four molecules of Cytochrome c and transferred to molecular oxygen (O2), producing two molecules of water.
- At the same time, eight protons are removed from the mitochondrial matrix (although only four are translocated across the membrane), contributing to the proton gradient.




Electron transport chain
ATP synthase
Intermembrane space
Inner mitochondrial membrane
Mitochondrial matrix
Cyt c
I
II
III
IV
NADH
NAD+ +
FADH2
FAD+ +
H+
e−
O
H2O
x 2
ADP
+
PO4-3
ATP
2 free hydrogen ions
2 electrons exiting ETC
1/2 of an O2 molecule