جامعة الملك سعود
King Saud University

Biochemistry437

# Respiratory chain

Biochemistry Team 437


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Respiratory block

**EDITING FILE**

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# Electron Transport Chain

"respiratory chain/ cellular respiration"

- A system of electron transport that uses respiratory O2 to produce ATP (Energy)

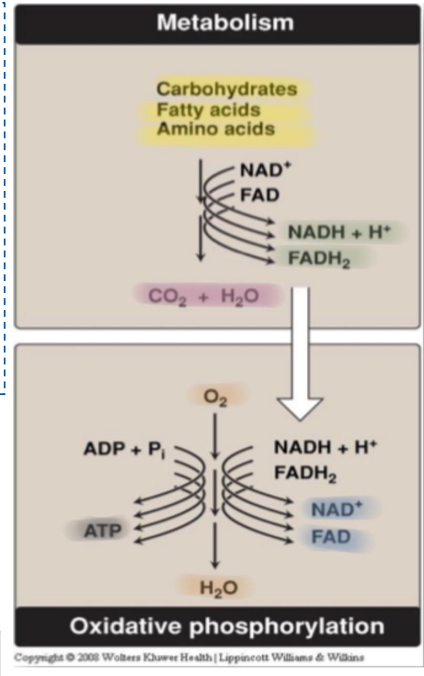
-**Located:** in the inner mitochondrial membrane, along with all of the other degradation pathways like Krebs cycle, B oxidation for fatty acids and protein degradation, all of which produce the reduced enzymes NADH and FADH

- **Final common pathway of metabolism**

- Electrons from food metabolism "Carbohydrates, Fat, Protein" are transported to O2 "final acceptor of electrons"

- Uses maximum amount of body's oxygen

-The metabolic breakdown of of different energy yielding molecules "Carbohydrates, Fat, Protein" Leads to the production of simple molecules CO2+H2O in the process they produced Energy Rich Reduced Coenzymes NADH+FADH2





*Electron (e-) lose their free energy
*Excess energy generates heat

- The majority of O2 we are inhaling is reduced to water, O2 is converted into H2O because it accepts the electrons "H" from the coenzymes. in this process it releases ATP -- NADH+FADH2 is oxidised again to NAD+FAD releasing energy which leads to further production of ATP

Remember that:

| Oxidation (Reducing agent) | Reduction (Oxidizing agent) |
|---|---|
| Lose electrons | Gain electrons |
| Loss hydrogen | Gain hydrogen |
| Gain oxygen | Lose oxygen |

# Structure of the mitochondria

- **Outer membrane:** Contains special channels (porin proteins) making it permeable to most ions & small molecules [not selective]

- **Inner membrane:** Specialized structure, **site of the ETC** rich in proteins, impermeable to most small ions & molecules. Bigger than the outer membrane because of CRISTAE [very selective]

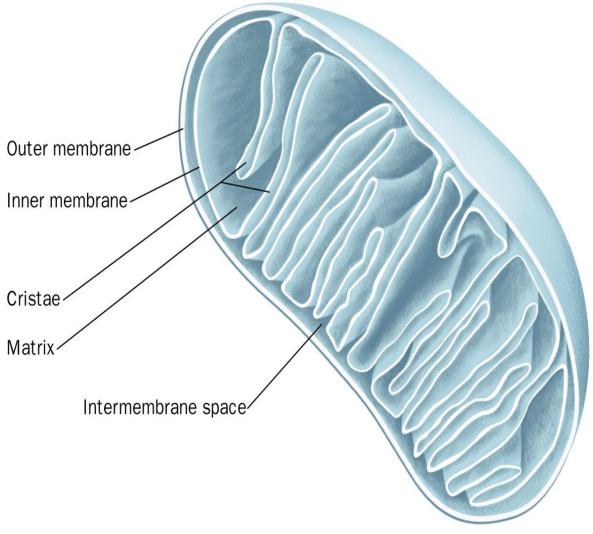
- **Cristae:** Folding of the inner membrane to increase the surface area.

- **Matrix**

- Gel like solution in the interior of the mitochondria.
- Contains TCA (tricarboxylic acid) cycle enzymes, fatty acid oxidation enzymes & MtDNA (mitochondria DNA) & mitochondrial ribosomes

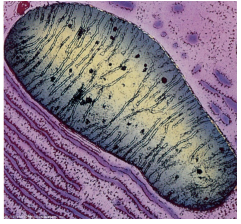
- **Intermembrane space:**

Space between outer membrane and inner membrane

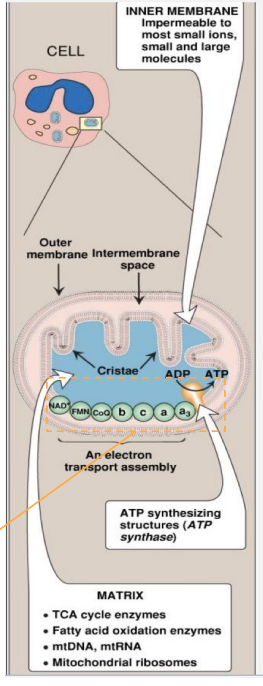



In the picture you can see:

- The components of the electron transport chain.
- All of the components are present on the inner membrane except cytochrome C is present in the intermembrane space.
- Along with the cytochromes we can see the ATP synthase, which is an ATP synthesizing structure. Everything is discussed later in more details



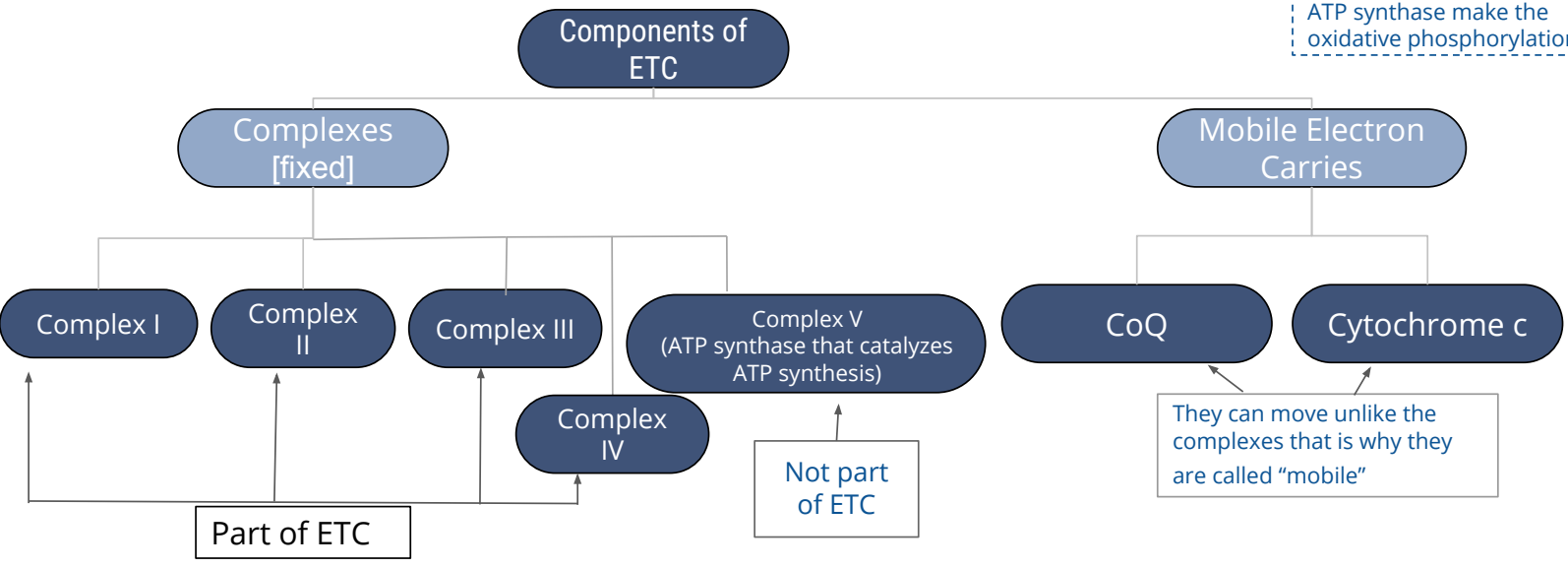
An electron micrograph of an animal mitochondrion



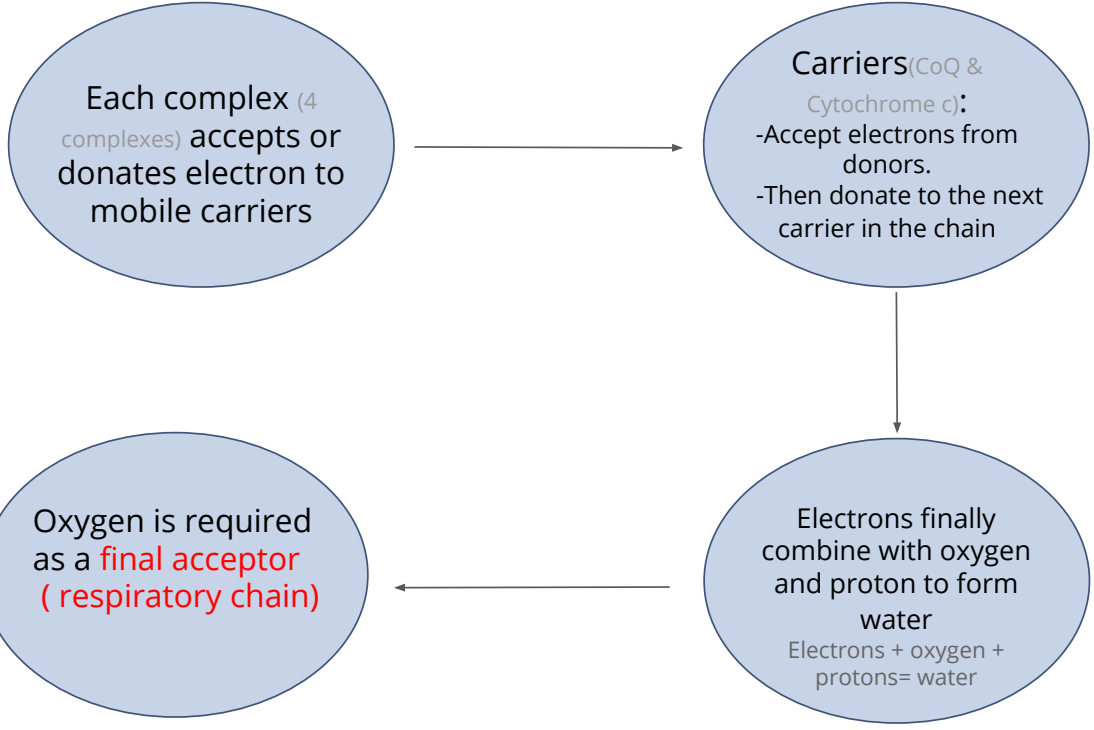
# Component of ETC

- All members/components are located in the inner mitochondrial membrane (IMM) (except cytochrome c which is located in the intermembrane space)

* Complexes are composed of more than one protein working together.
* the 4 complexes + the ATP synthase make the oxidative phosphorylation

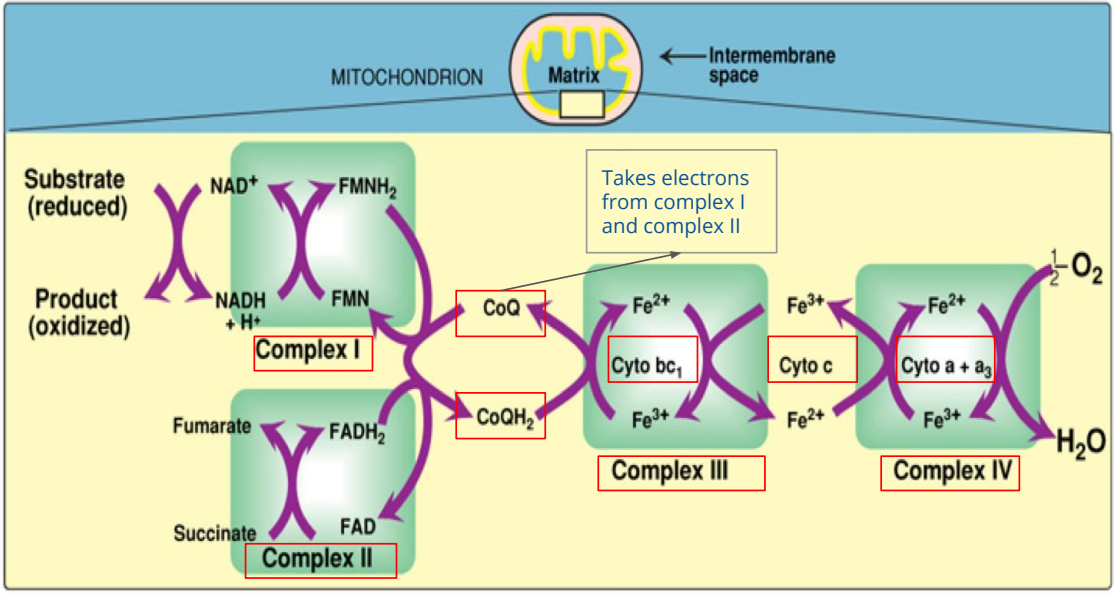


# Organization of ETC




- Complex 1 and complex II are sharing a mobile carrier , both give their electrons to coenzyme Q.
- It is a chain because it takes electron from one and give it to the other
- We have 4 complexes and 2 mobile carriers.

# Electron Transport Chain (ETC)






(focus on from whom is it taking the electron & to whom is it giving the electron basically all the red boxes)

Summary of the process:

1. CoQ receives an electron from complex 1 and complex 2, then it gets reduced and become CoQH2.
2. Then it gives the electron to cytobc1 "in complex III "then CoQ gets oxidized back to CoQ to do another round of taking the electron.
3. Complex III is a combination of two cytochromes cytochrome B and cytochrome C1, which Gives electrons to mobile carrier Cytochrome C.
4. Cytochrome C receives the electron and gives it to Cytochrome a + a3 " in complex IV"
5. Notice that no ATP has been generated yet from this process, the ATP generating step is discussed later in this lecture

# The Complexes and Co-Enzyme

| Complex I | Complex II | Co-Enzyme Q | Complex III | Complex IV |
|---|---|---|---|---|
| Complex I – NADH Dehydrogenase<br><br>• This complex collects the pair of electrons from NADH and passes them to CoQ | Complex II – Succinate dehydrogenase<br><br>• It is also a part of the TCA cycle<br><br>• Transfers electrons to CoQ from FADH2 | Also called ubiquinone (ubiquitous in biological systems)<br>"Meaning it is present in all biological systems"<br><br>• The only non-protein member of the ETC<br><br>• Lipid soluble and mobile | • Complex III:<br><br>Cytochrome **bc1** | • Complex IV:<br><br>Cytochrome **a** + **a3** |

Electrons flow from: • CoQ ⟶ Complex III ⟶ Cytochrome C⟶ Complex IV

# Cytochromes

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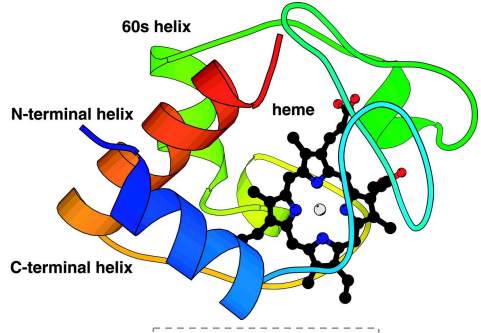
• Each cytochrome is a protein that contains

– Heme group (porphyrin ring + iron in Fe3+ “ferric” state)

“Don’t confuse this structure with the Heme in the hemoglobin structure!
Hemoglobin is composed of protoporphyrin and iron in the ferrous state Fe2+”




Extra picture

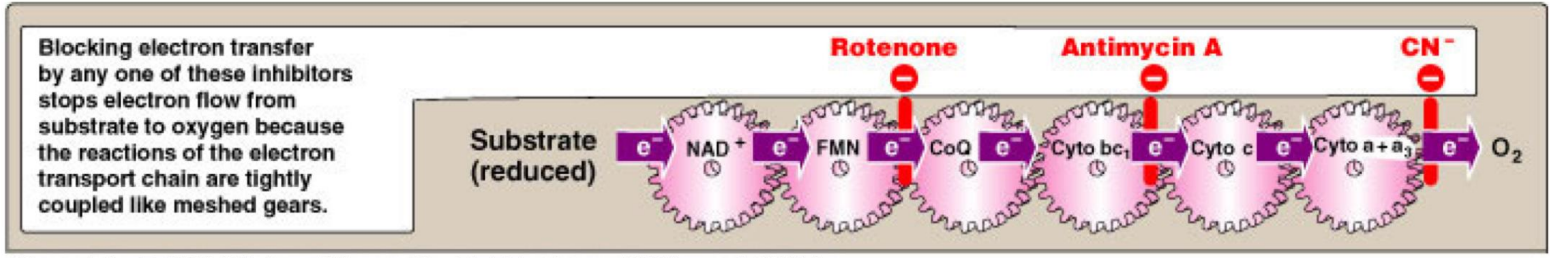
(A Cytochrome is comprised of two parts:)
a protein and a Heme Group

• When cytochromes accept electron:
– Fe3+ is converted to Fe2+
– Fe2+ is re-oxidized to Fe3+ when it donates electrons to the next carrier

Redox reactions

# Site-specific inhibitors of ETC

Certain molecules that can inhibit ETC and they have a particular site where they will inhibit If the transport is interpreted in the ETC at any site what will happen ?
-No production of ATP
-Energy dissipated as heat. known as non-shivering thermogenesis . when the ETC is inhibited it will increase the body temperature but not by shivering




Rotenone : inhibits between FMN(complex II)and CoQ
Antimycin A : poison which inhibits between cyto bc1 and cyto c
CN : When there is Carbon monoxide poisoning or cyanide poisoning poisoning or sodium azide poisoning they will inhibit the Cycle (oxidative phosphorylation) at the last step before the oxygen gets oxidized

# ETC is coupled to proton transport for ATP synthesis

How will the electron transport chain produce ATP?

- The energy of electron transfer is used to drive the protons out of the matrix
- It is done by complexes I,III and IV (proton pumps)
  Complex II doesn't transport any protons and it does not dissipate any energy
- This creates a proton gradient across the IMM to synthesize ATP

When the electron is transported some energy is released that energy helps the protons “H+” to go from the matrix into the intermembrane space

That creates a proton gradient which means there is a PH gradient and the PH in the intermembrane space will be lower than the matrix (because in the intermembrane space there is a lot of protons)

Protons have to come back inside the matrix .they Come Back by the help of the ATP synthase when they come back they release energy and that energy is used to convert adp to ATP

# ATP synthase

- ATP synthase (Complex V ) synthesizes ATP
- Consists of two domains:
  - F0 – membrane spanning domain (shaft )
  - F1 – extramembranous domain ( bulb like - in the matrix )

Protons come back to the inner membrane through the F0 domain of ATP synthase .

when they're coming back they releases Energy and create a conformational change in the ATP synthase which leads to rotating the shaft , Catalytic site opens and catalysis the conversion of ADP to ATP

ATP goes out the the mitochondria through ATP-ADP translocase ( antiporter transport system) it will take in ADP and takes out the ATP

"Explained again in steps in the next slide"

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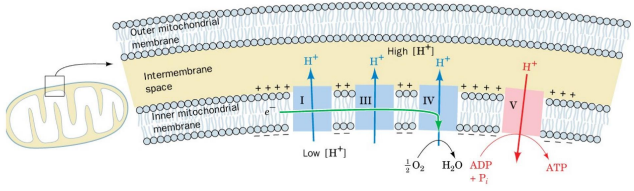
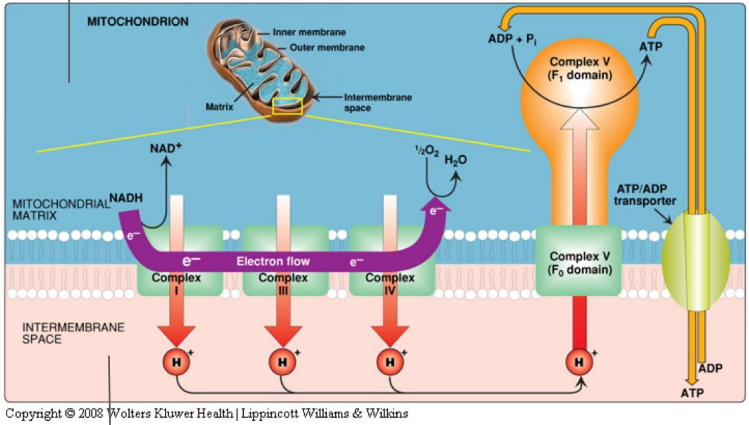



Coupling of electron transport (*green arrow*) and ATP synthesis

# Transport of Protons

Matrix





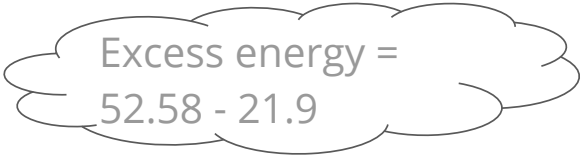
Intermembrane space

**Explanation:**

- IM space has a lot of protons and it is creating a gradient, protons have to go back into matrix.
- They go back through the F0 domain of ATP synthase in order to create ATP.
- When they enter F0 domain, they release energy→ energy creates conformational change in ATP synthase → open catalytic site → catalyzes conversion of ADP into ATP. ( 4 protons are required to make 1 ATP molecule)
- ATP leaves mitochondria through to ADP\ATP transporter.
- ADP\ATP transporter takes ATP out of matrix and ADP into matrix.

# Energetics of ATP Synthesis

- The energy required for phosphorylation of ADP to ATP = 7.3kcal/mol (energy released when breaking phosphate from ATP)
- Energy produced from the transport of a pair of electrons from NADH to $O_2$ = 52.58 kcal. (Energy produced from transporting electrons)
- No. of ATP molecules produced is 3 (NADH to $O_2$) = 21.9 Kcal
- Excess energy is used for other reactions or released as heat to maintain the body temperature.



# P:O ratio

"The number of ATP produced per 1 oxygen."

ATP made per oxygen atom reduced:

For NADH:

P:O = 3:1

For FADH2:

P:O = 2:1

# Inhibitors blocking ATP Synthesis

Inhibitors blocking **ATP Synthase.**

**Oligomycin**:

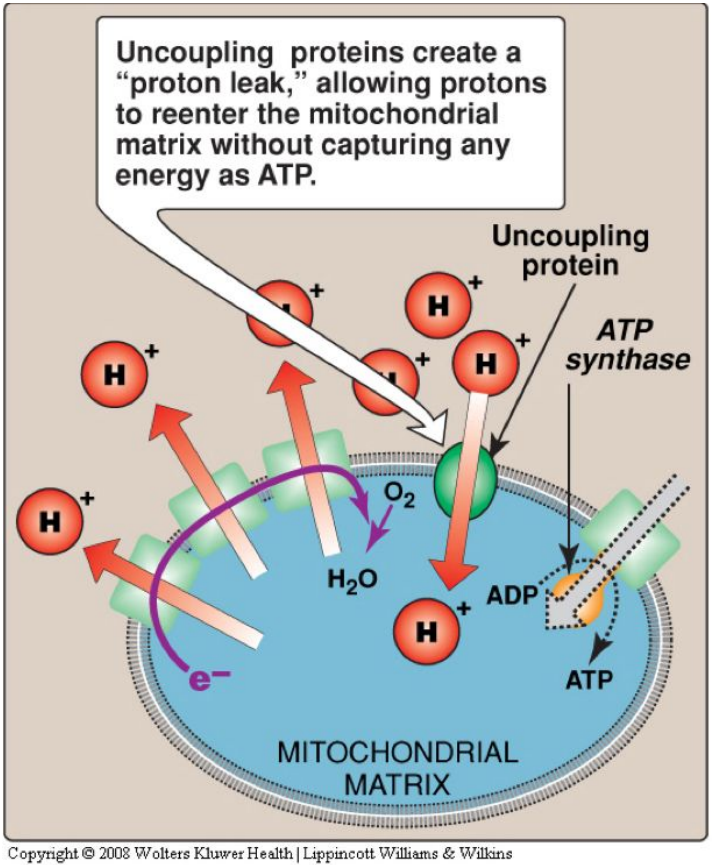
–Binds to $F_0$ domain of ATP synthase and closes the $H^+$ (proton)channel.

No protons going in ATP synthase → no synthesis of ATP.

**Uncoupling proteins (UCP):**

–Create proton leaks (holes in IMM) (allow protons to re-enter the matrix without ATP synthesis).

–Energy is released as heat (non-shivering thermogenesis).





If there are proton leaks→ protons will go back to the matrix without passing through the ATP synthase → no ATP will be synthesized → all the energy will be released as heat.

UCP is found in brown fat, which is found in newborn babies and animals, it helps protect them from cold because UCP generates heat.

# Summary

**Electron transport chain:**

•Final common pathway of metabolism It is a system of electron transport that uses respiratory O2 to finally produce ATP

•it's in the inner membrane of mitochondria

**Components of ETC**

• All members/components are located in the inner mitochondrial membrane (IMM) except cytochrome C .
•All members of the chain are proteins (with the exceptions of co-enzyme Q, which is a lipid-soluble quinone)

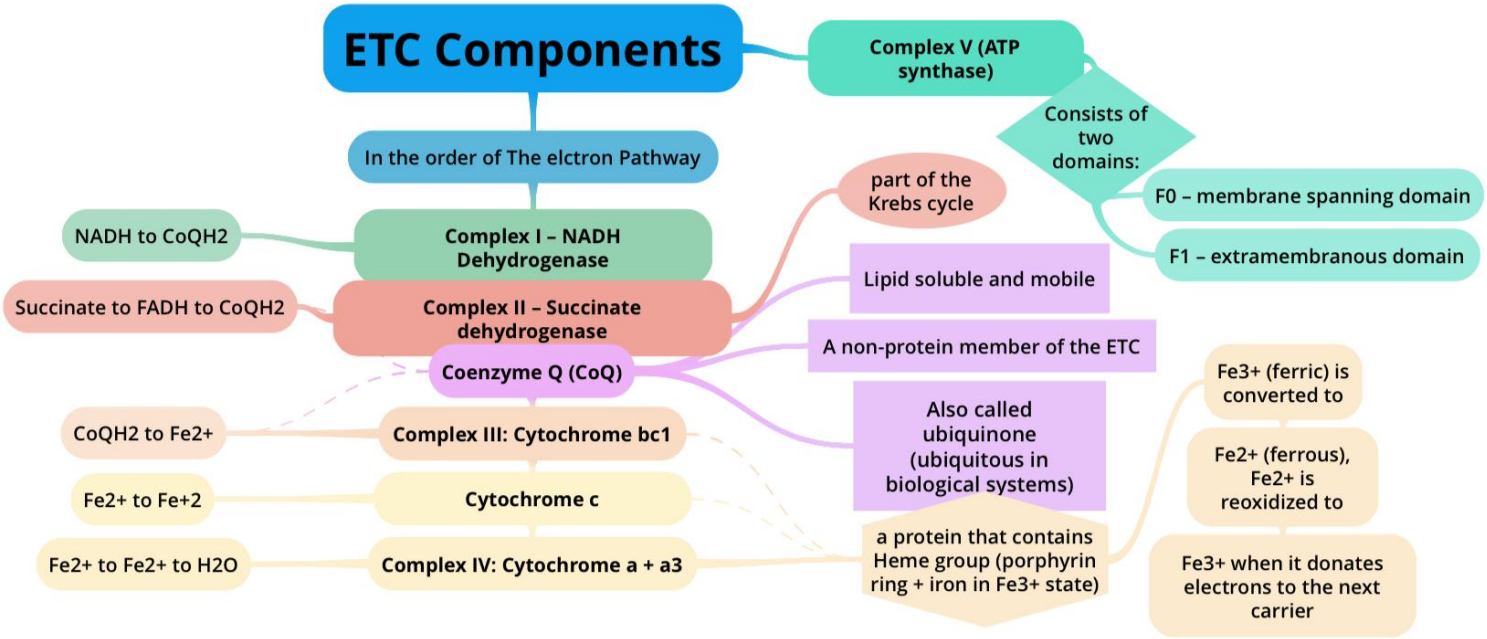
**Organization of the electron transport chain**

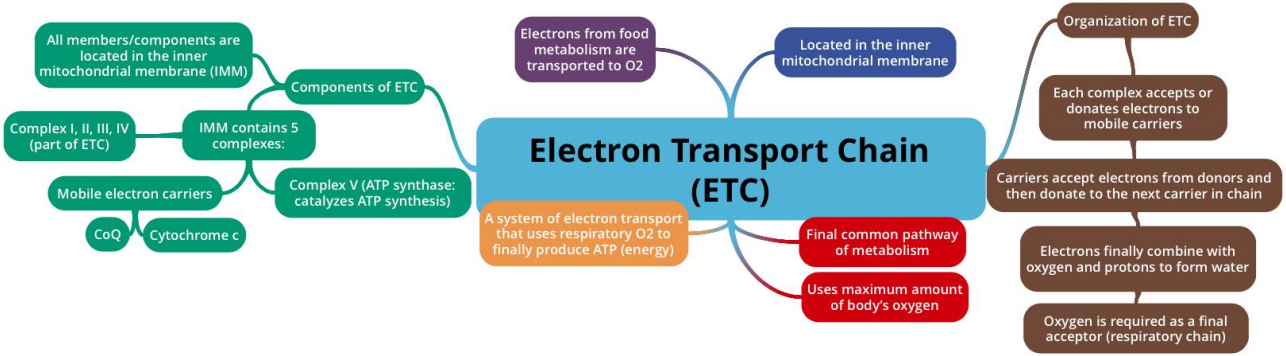
•Each complex accepts or donates electrons to mobile carriers
• Carriers accept electrons from donors and then donate to the next carrier in chain
• Electrons finally combine with oxygen and protons to form H2O.
• Oxygen is required as a final acceptor

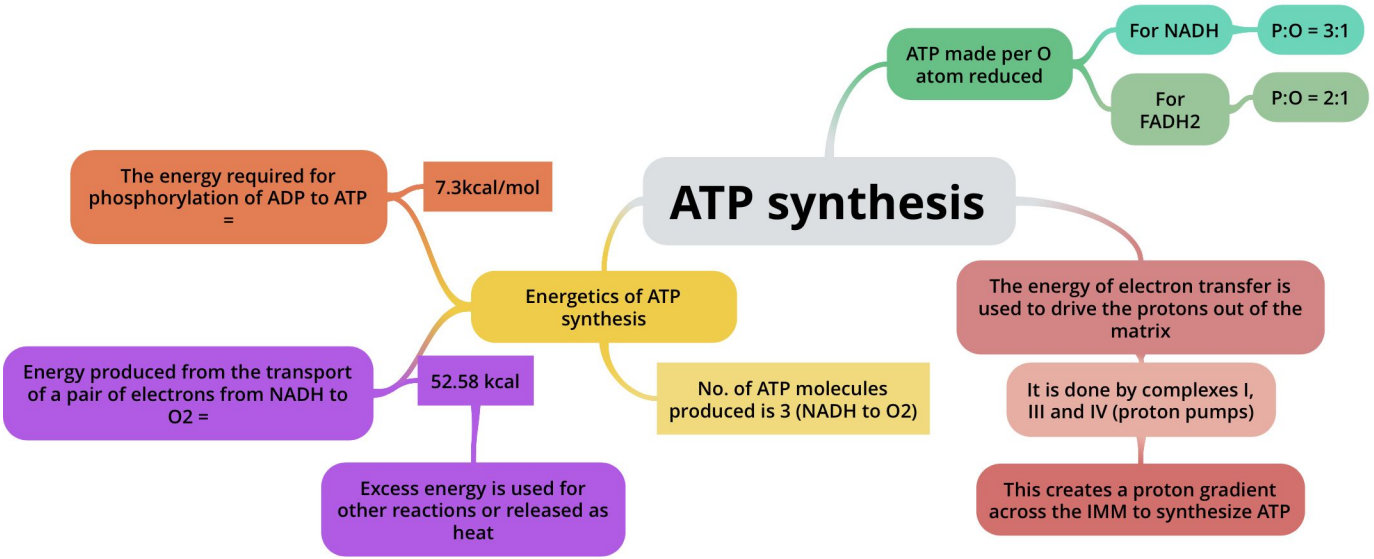
**Phosphorylation of ADP to ATP:**

1- Proton Pump (done by complexes I, III and IV)

2- ATP synthase (Complex V)


ETC Components
In the order of The elctron Pathway
Complex I – NADH Dehydrogenase
NADH to CoQH2
Complex II – Succinate dehydrogenase
Succinate to FADH to CoQH2
Coenzyme Q (CoQ)
Complex III: Cytochrome bc1
CoQH2 to Fe2+
Cytochrome c
Fe2+ to Fe+2
Complex IV: Cytochrome a + a3
Fe2+ to Fe2+ to H2O
Complex V (ATP synthase)
Consists of two domains:
F0 – membrane spanning domain
F1 – extramembranous domain
part of the Krebs cycle
Lipid soluble and mobile
A non-protein member of the ETC
Also called ubiquinone (ubiquitous in biological systems)
a protein that contains Heme group (porphyrin ring + iron in Fe3+ state)
Fe3+ (ferric) is converted to
Fe2+ (ferrous), Fe2+ is reoxidized to
Fe3+ when it donates electrons to the next carrier


Electron Transport Chain (ETC)
Components of ETC
All members/components are located in the inner mitochondrial membrane (IMM)
IMM contains 5 complexes:
Complex I, II, III, IV (part of ETC)
Complex V (ATP synthase: catalyzes ATP synthesis)
Mobile electron carriers
CoQ
Cytochrome c
Electrons from food metabolism are transported to O2
Located in the inner mitochondrial membrane
A system of electron transport that uses respiratory O2 to finally produce ATP (energy)
Final common pathway of metabolism
Uses maximum amount of body's oxygen
Organization of ETC
Each complex accepts or donates electrons to mobile carriers
Carriers accept electrons from donors and then donate to the next carrier in chain
Electrons finally combine with oxygen and protons to form water
Oxygen is required as a final acceptor (respiratory chain)


ATP synthesis
ATP made per O atom reduced
For NADH
P:O = 3:1
For FADH2
P:O = 2:1
The energy required for phosphorylation of ADP to ATP =
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Energetics of ATP synthesis
Energy produced from the transport of a pair of electrons from NADH to O2 =
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Excess energy is used for other reactions or released as heat
No. of ATP molecules produced is 3 (NADH to O2)
The energy of electron transfer is used to drive the protons out of the matrix
It is done by complexes I, III and IV (proton pumps)
This creates a proton gradient across the IMM to synthesize ATP

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.

Antimycin A

Amytal
Rotenone

CN– CO
Sodium azide

Site-specific inhibitors of ETC

# Inhibitors of ATP synthesis

Create proton leaks (allow protons to reenter the matrix without ATP synthesis)

Energy is released as heat (nonshivering thermogenesis)

Uncoupling proteins (UCPs):

Oligomycin

Binds to F0 domain of ATP synthase and closes the H+ channel

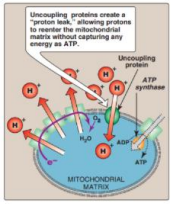


**Figure 6.14**
Transport of $H^+$ across the mitochondrial membrane by 2,4-dinitrophenol.

# MCQs:

**1-The main function of ETC is :**
A- Production of ATP  B- Production of O2  C- Production of CO2 .

**2-The oxidative phosphorylation found in :**
A- Inner surface of the cell  B- inner surface of the mitochondria  C- cytoplasm.

**3-IMM complex that is consider ATP synthase that catalyzes ATP synthesis ?**
A- complex V  B- complex II  C- Coq  D- cytochrome C

**4-What is required as a final acceptor (respiratory chain) ?**
A- Hydrogen  B- oxygen  C- enzyme

**5- Number of protein complexes which are part of ETC:**
A-2  B-4  C-5  D-3

**6-All of the following protein complexes are proton pumps, except:**
A- Complex I  B- Complex II  C- Complex III  D- Complex IV

Answers:
1-A
2-B
3-A
4-B
5-B
6-B

## Team leaders

- محمد حسن حكيم
- رهام الحلبي

## Boys team

- طارق العميم
- داوود اسماعيل
- صالح الوكيل
- سعيد آل سرار
- عبدالملك الشرهان
- محمد ابراهيم

## Girls team

- الهنوف الجلعود
- رهف الشنيبر
- شهد الجبرين
- لينا الرحمة
- منيرة المسعد
- ليلى الصّباغ
- العنود المنصور
- أرجوانة العقيل
- ريناد الغريبي
- رزان الزهراني
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