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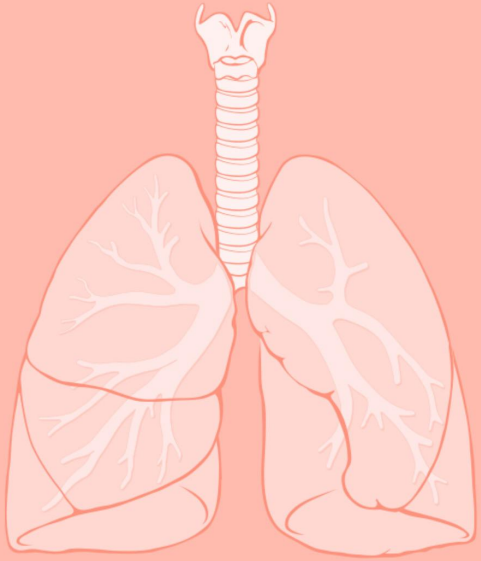
Respiratory chain



Color index :

Main text

IMPORTANT

Extra Info

Drs Notes

Respiratory Block - Biochemistry Team

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MED439 KING SAUD UNIVERSITY

A helpful video

Objectives:

- Understand how energy-rich molecules including glucose are metabolized by series of oxidation-reduction reactions ultimately yielding CO_2 and water.

- Explain the process of electron transport chain that releases free energy , which is used for ATP synthesis and heat production.

- Recognize the reaction taking place in mitochondria that are coupled to oxidative phosphorylation.

Introduction (Important explanation)

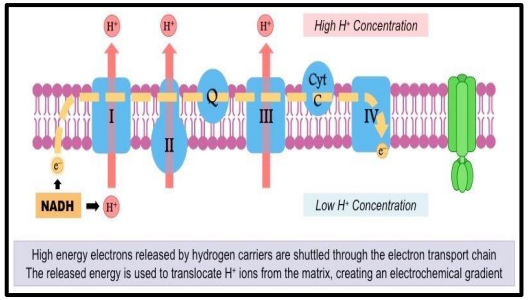
If you recall in foundation block, we learnt the procedures of krebs cycle

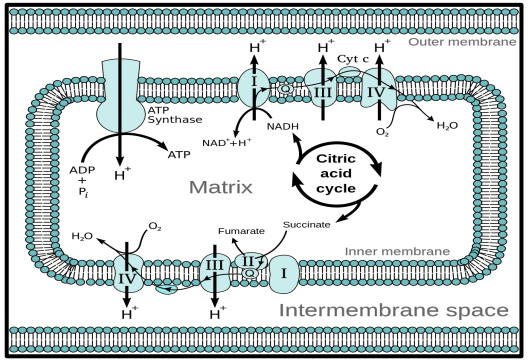
In each reaction there were byproducts coming out from the reactions such as NADH & $FADH_2$ right?

These high energy molecules are then drived to some complexes (proteins you could say)

Energy is transferred from one complex to another eventually reaching the final complex which is ATP Synthase

Complex five (final complex) is called ATP synthase because he's the big guy , he plays a major role in the synthesis of ATP





This creates a chemical gradient of protons right? [H^+] inside will be less than [H^+] outside, this has a purpose, let's find out why!

And when this - energy releasing - happens, each complex has a pump that will open and pump a proton from the inner membrane out to the inter membrane

They keep transferring electrons from one complex to another to get back to the low energy state

Complexes receive the electrons and become energy rich, right? But they tend to like the low energy environment

The mechanism is quite simple, krebs cycle occurs and then coenzymes will donate its electrons to the complexes

A helpful video

Electron Transport chain (ETC) :

Definition

system of electron transport that uses respiratory O_2 to finally produce ATP (energy).

Location

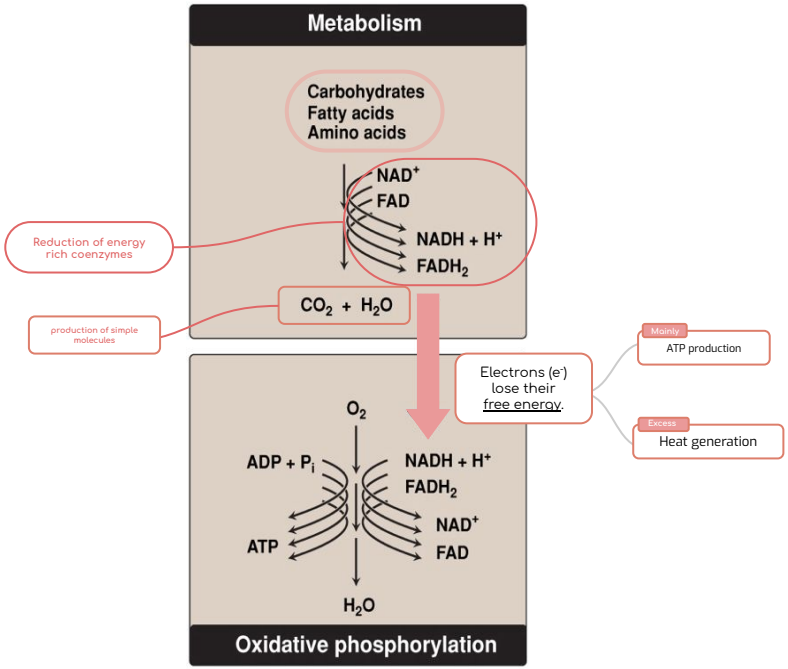
the inner mitochondrial membrane & it contains all the components of ETC

Characteristics

1- Final common pathway of metabolism
2- Uses the maximum amount of O_2

Mechanism

Electrons from food metabolism Transported to O_2



Structures of the mitochondria :

Outer membrane :

1-Contains special channels (formed by the protein porin).
2-Highly permeable

Inner membrane :

Impermeable to most small ions, small and large molecules. (Highly selective)

Intermediate space :

The space between the outer and the inner membrane.

Matrix :

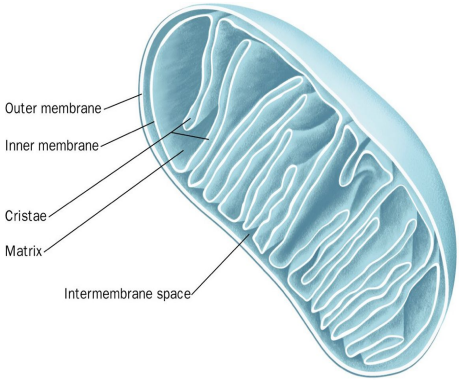
Gel like solution in the interior of the Mitochondria.
Contains: 1-TCA "krebs" cycle enzymes 2-Fatty acid oxidation enzymes 3-mtDNA & mtRNA 4-Mitochondrial ribosomes

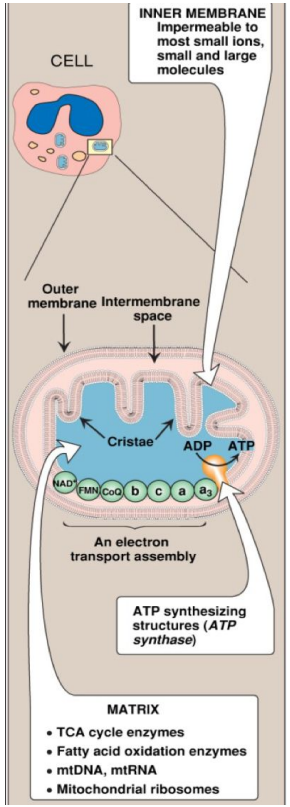
Cristae :

Folding of the inner membrane.

- Increase the surface area.

To increase production of ATP





Components of (ETC) :

Part of ETC

- **Complex I** (NADH Dehydrogenase) — collects the pair of electrons from NADH and passes them to CoQ
- **Complex II** (Succinate dehydrogenase) — Transfers electrons to CoQ & part of the TCA -krebs- cycle
- **Complex III** (Cytochrome bc_1) — Accepts electrons from CoQ and transfers them to Cytochrome C
- **Complex IV** Cytochrome a +a_3

Complex V

ATP synthase : catalyzes ATP synthesis

Mobile electron carriers

- Coenzyme Q (CoQ)
  - •Also called ubiquinone
  - •ubiquitous in biological systems
  - •the only non protein member of the ETC
  - •Lipid soluble and mobile
- Cytochrome C — Protein

Cytochromes in complex III & IV

Each cytochrome is a protein that contains part of the ETC.
Porphyrin ring + iron in Fe3+ state (heme group)

When it accepts electrons — Converted to Fe^{+3} / Fe^{+2} — Reoxidized to — When it donates electrons

Electron Transport Chain (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 H_2O
- Oxygen is required as a final acceptor (respiratory chain)

Carrier → Donor → Carrier → Donor → ATP Synthase

Summary of the process

Co-Enzyme Q receives an electron from complex I and complex II, then it gets reduced and become $CoQH_2$.

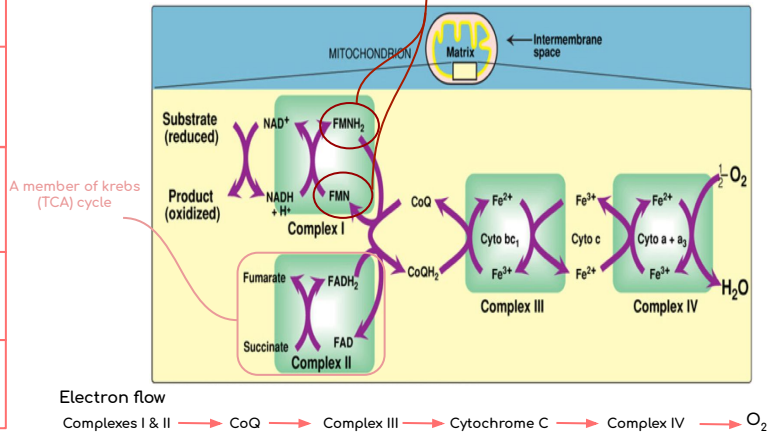
Then it gives the electron to cytochrome bc_1 " in complex III ", then $CoQH_2$ gets oxidized back to CoQ to do another round of taking the electron.

Complex III is a combination of two cytochromes cytochrome B and cytochrome C_1, which gives electrons to mobile carrier Cytochrome C.

Cytochrome C receives the electron and gives it to Cytochrome a + a_3 "in complex IV".

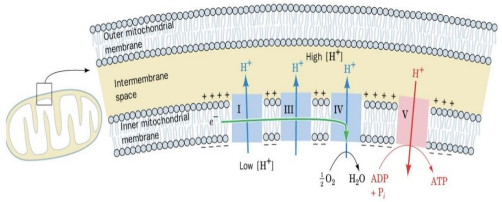
The final acceptor is the oxygen which gets combined with electrons and protons to form water.

You don't have to memorize it



ETC is coupled to proton transport for ATP synthesis :

- The energy of electron transfer is used to drive the protons out of the matrix into intermembrane space (proton pump)
- It is done by complexes I, III and IV (proton pumps)
- This creates a proton gradient across the IMM (Inner Mitochondrial Membrane) to synthesize ATP
- the energy (proton-motive force) generated by the gradient yields ATP synthesis



Electrochemical gradients

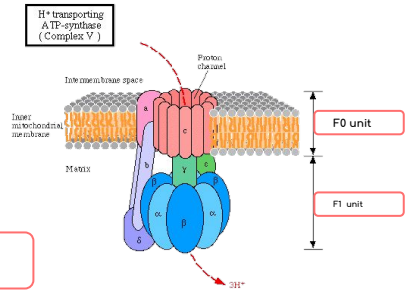
electrical gradient : (more positive charges in the intermembrane space than on the matrix)
pH (chemical) gradient : (the intermembrane space is at a lower pH than the matrix)

ATP synthase

- ATP Synthase (complex V) synthesizes ATP
  "using the energy of the proton gradient generated by the electron transport chain"

Consist of two domains :

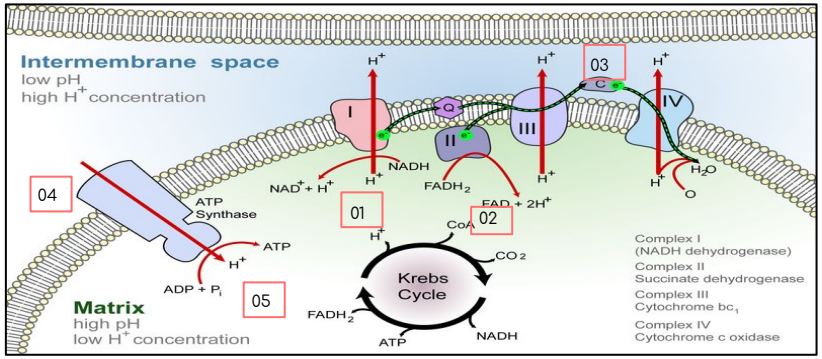
- F1 — **Extra** - membranous domain In the mitochondrial matrix
- F0 — **Membrane spanning** domain In the intermembrane space

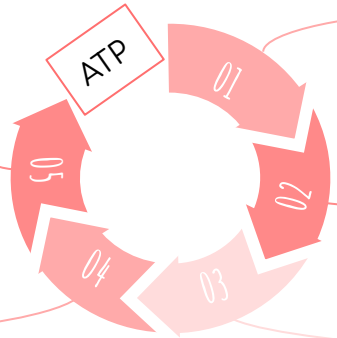


IMM has high selectivity so the only way protons can return is through ATP synthase

★ Explanation

Transport of protons :





At first, **complex I** (NADH dehydrogenase) oxidize and transfer two e^- to **CoQ** (Mobile electron carrier) providing energy needed for H+ pumping in the complex

Complex II (Succinate dehydrogenase) transfer e- to **CoQ** and pump H+ indirectly through **complex III & IV.**

Electrons transported from **Complex I & II** will move to **Complex III through CoQ, and Cytochrome C** will take these electrons and transfer them to **Complex IV** to provide energy for H+ pumping.

Pumped H+ in the intermembrane space move through **Complex V** and rotate F0 domain to cause conformational change in F1 domain.

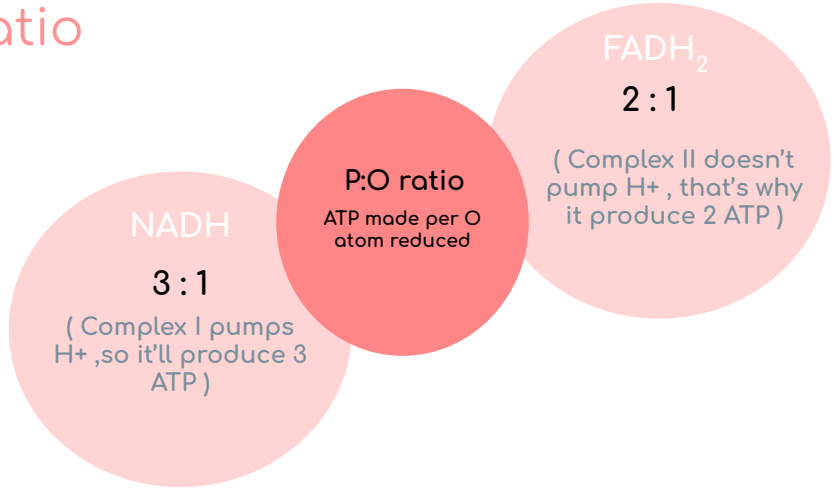
By attaching the proton to the beta subunit of the ATP synthase (which contains ADP + Pi) this conformational change will add Pi to ADP to form ATP. The formed ATP will move through **ATP/ADP transporter** to provide energy for body tissues

Energetics of ATP synthesis:

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

(52.58 - 21.9 = 30.68" excess energy" used in other reactions that need energy)

P:O ratio



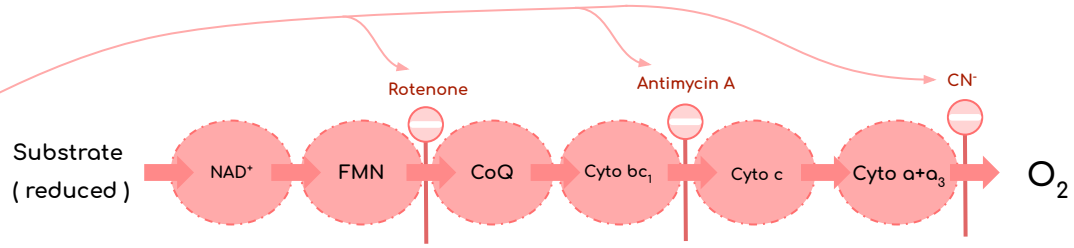
Why does $FADH_2$ produces less ATP than NADH?
-NADH transfers its electrons in complex I so it passes through 3 pumps (complexes I, III and IV)
-$FADH_2$ transfers its electrons in complex II so it passes only through 2 pumps (complexes III and IV)

#Med438

★ here means extra

Site-specific inhibitors of ETC

Blocking the electron transfer by any one of these inhibitors stops electron flow from substrate to oxygen because the reaction of the electron transport chain are tightly coupled like meshed gears



There are some drugs that inhibit ETC to reduce the metabolism in the body:

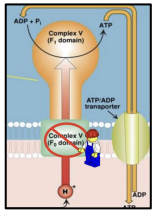
Rotenone → ★ inhibits electrons transported between FMN (complex I) and CoQ

Antimycin A → ★ inhibits electrons transported between cyto bc_1 (complex III) and cyto c

CN- (Cyanides) → ★ inhibit the cycle (oxidative phosphorylation) at the last step before the oxygen gets oxidized (complex IV)

When the inhibitors inhibit one of the complexes, the next complexes will be inhibited

Inhibitors of ATP synthesis

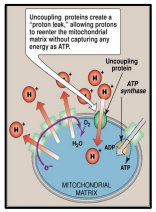


Inhibitors of ATP synthesis

Oligomycin

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

Uncoupling proteins (UCPs)



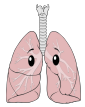
– Create proton leaks (allow protons to reenter the matrix without ATP synthesis)
– Energy is released as heat (nonshivering thermogenesis)

Take Home Messages

ETC is a common pathway of transferring energy-rich electrons from metabolism finally yielding CO_2 and water

The energy of the electrons transferred is used for ATP synthesis and heat production

Summary



Numbering based on ETC steps

Cellular respiration

- Glycolysis
- Krebs cycle
- Oxidative phosphorylation
  - respiratory chain (ETC)
    - Definition
      - The process which the NADH and FADH2 shuttle high-energy electrons extracted glycolysis and the krebs cycle into the electrons transport chain
    - Location
      - Inner membrane of the mitochondria
    - Component
      - First part
        - Proteins
          - 1- NADH --> complex I (NADH Dehydrogenase)
          - 1- FADH2 --> Complex II (Succinate dehydrogenase)
        - Mobile electron carriers
          - 2- Coenzyme Q = ubiquinone
      - Cytochromes (second part of ETC)
        - Protein
          - 3- Complex II (Cytochrome bc1)
        - Mobile electron carriers
          - 4- Cytochrome C
        - Protein
          - 5- Complex IV Cytochrome a +a3
    - Result
      - Electrons are finally passed to a terminal acceptor (O2) at the end of chain , forming water by oxygen
    - Inhibitors
      - Rotenone
      - Antimycin A
      - CN^- (Cyanides)
  - Chemiosmosis = phosphorylation
    - Definition
      - The process in which the ions = hydrogen H+ move by diffusion through ATP synthase from high concentration to low concentration
    - Location
      - Inner membrane of the mitochondria
    - Component
      - Protein
        - 6- ATP synthase = Complex V
    - Result
      - Produce ATP from ADP by ATP synthase
    - Inhibitors of ATP synthesis
      - Oligomycin
      - UCPs

Quiz

Q1 : Electron transport chain is located in:			
A) inner mitochondrial membrane	B) outer mitochondrial membrane	C) mitochondrial matrix	D) both A & C
Q2 : Which of the following is not a part of ETC:			
A) Complex I	B) Complex III	C) Complex IV	D) Complex V
Q3 : P:O ratio in NADH is:			
A) 1:3	B) 3:1	C) 2:1	D) 1:2
Q4 : Which of the following inhibitors bind to F0 domain:			
A) Rotenone	B) UCPs	C) Oligomycin	D) CN
Q5 : Complex III contain which of the following:			
A) Cytochrome C	B) Cytochrome $a+a_3$	C) Cytochrome bc_1	D) Cytochrome a_3
Q6 : Who's the all time best team leader?			
A) Shatha	B) A	C) Most likely A	D) A & B

SAQs :

Q1: What is the benefits of excessive energy?

Q2: Enumerate Complex V domains with their locations:

Q3: What type of energy is used to drive the proton out of the matrix:

Q4: Describe the mechanism of UCPs briefly:

★ MCQs Answer key:

١) A ٢) D ٣) B ٤) C ٥) C ٦) A

★ SAQs Answer key:

1) body reactions , as heat

2) F0 (membrane spanning domain)
F1 (extra-membranous domain)

3) Electron transfer energy

4) Slide 11

Girls team:

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Alia Zawawi
Norah Alshathry
Reem Alamri
Renad Alhomaidi
Norah Alasheikh
Fatimah Alhelal
Manal Altwaim

Boys team:

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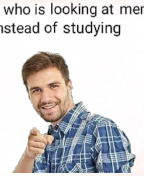
Hamad Almousa
Omar Alsuliman
Bassam Alasmari
Homoud Algadheb
Abdullah Alanzan
Abdullah Almazro
Ahmad Alkhayatt
Abdullaziz Alomar
Mishal Alhamed



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