Editing file

Electron Transport Chain (Respiratory Chain)

Respiratory Block

- Main text
- Important
- Girls Slides
- Boys Slides
- Doctor Notes
- Extra

objectives

- Understand how energy-rich molecules including glucose are metabolized by a series of oxidation-reduction reactions ultimately yielding CO2 and water

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

- Recognize the reactions of electron transport chain taking place in mitochondria that are coupled to oxidative phosphorylation

– Overview –

In general, the whole process of ETC is not fully understood however science develops day by day.

- Remember when we learnt in **Glycolysis** and **Krebs Cycle** we will end with 10 NADH and 2 $FADH_2$.
- Now we will study how these molecules transfer their electrons through ETC to benefit from their energy.
- ETC is a series of Complexes transfer electrons through the **inner mitochondrial membrane.**
- **O_2 is the final destination of ETC**, it will accept the electrones and will be reduced to form H_2O.
- Through ETC, Hydrogen ions are pumped which will make the ATP

Electron transport chain (ETC)

what is ETC?

- A system of electron transport that uses respiratory O_2 to finally produce ATP (energy)
- it is the final common pathway of metabolism

where?

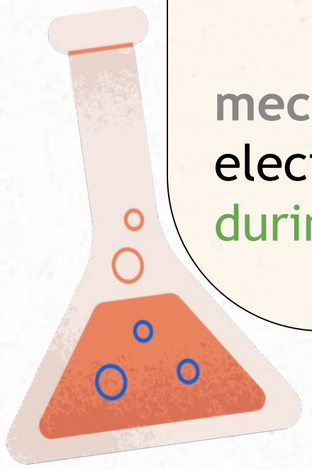
located in the inner mitochondrial membrane

characteristics:

- uses maximum amount of body's oxygen

mechanism?

electron from food metabolism are transported to O_2 (which will be reduced to H_2O and during this process you make your ATP)

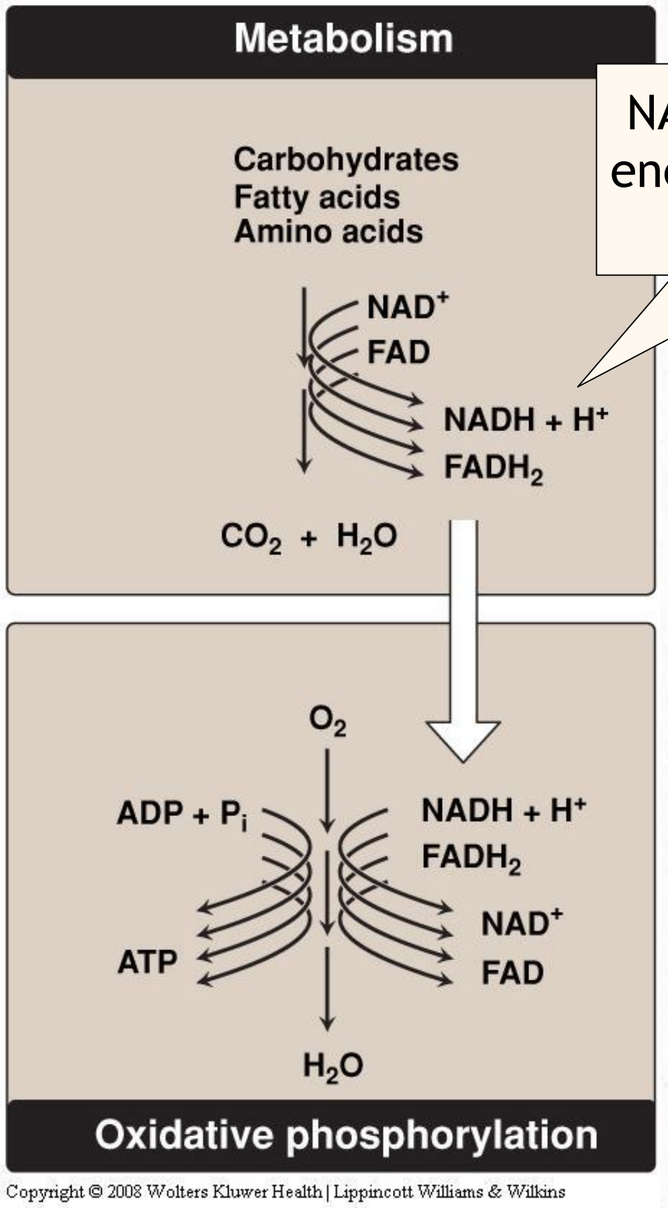


Metabolic breakdown of energy-yielding molecules

Dr:"must know difference"

Oxidation	Reduction
Gain of oxygen	Loss of oxygen
Loss of hydrogen	Gain of hydrogen
Loss of electrons	Gain of electrons

Electrons (e^-) lose their free energy



NADH & FADH2 are energy-rich reduced coenzymes

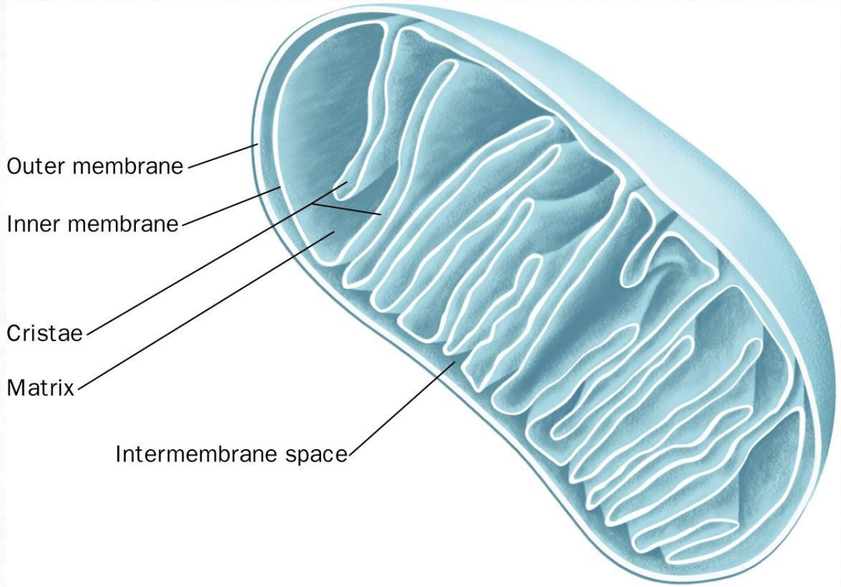
Excess energy generates heat

Boys Dr didn't focus too much

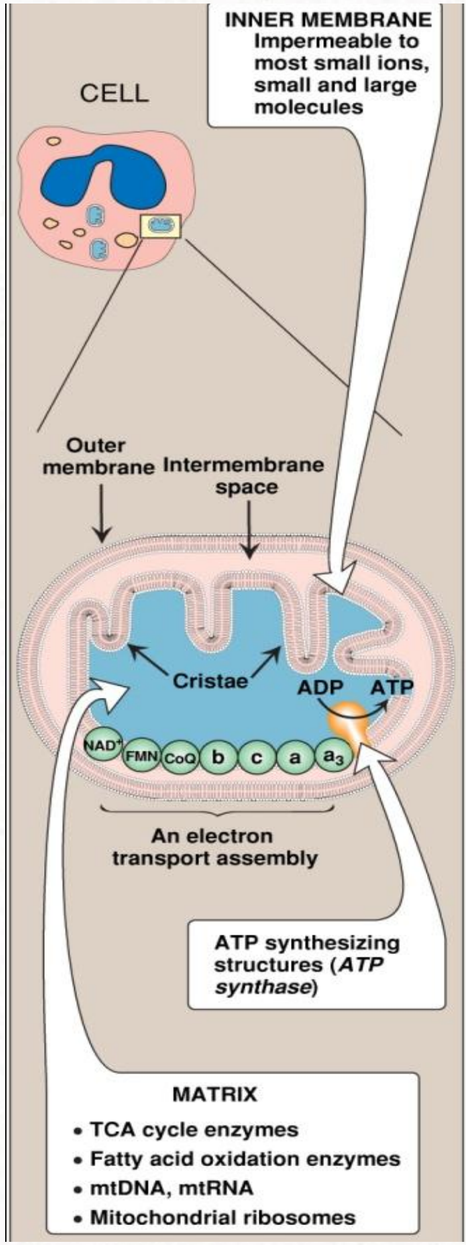
Mitochondria

singular form of mitochondria is mitochondrion

- **Outer membrane:**
  Contains special channels making it highly permeable to most small ions
- **Inner membrane**
  all ETC components present here (except cytochrome C)
  it is very selective, even small ions can not pass
- **Cristae**
  highly folded structures.
  they are responsible for increasing area of the surface
- **matrix**
  gel-like substance that contain enzymes, DNA and other
- **Intermembrane space**
  the region between the outer and the inner mitochondrial membranes



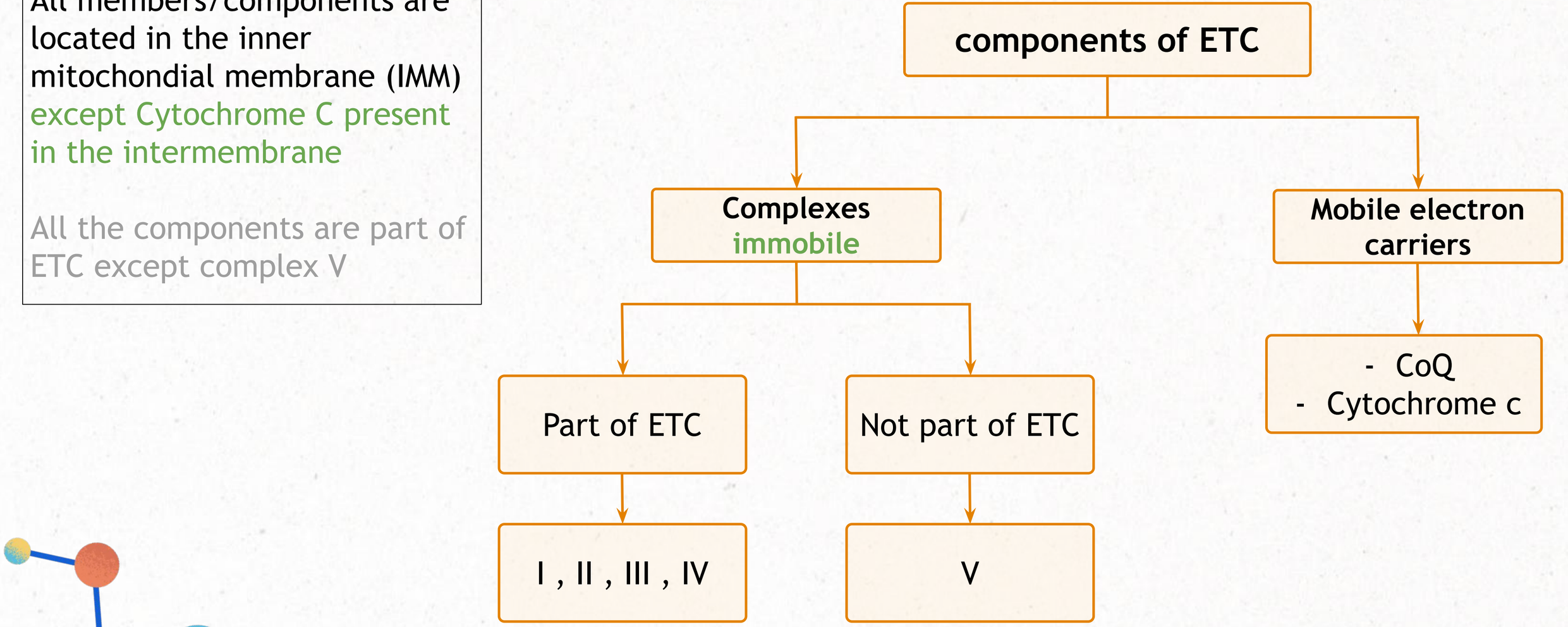
An electron micrograph of an animal mitochondrion



Components of ETC

All members/components are located in the inner mitochondial membrane (IMM) except Cytochrome C present in the intermembrane

All the components are part of ETC except complex V



cont...

Complex	Name	Function
I	NADH Dehydrogenase	Collects the pair of electrons from NADH and passes them to CoQ; acts as a proton pump
II	Succinate Dehydrogenase	Part of the TCA/Krebs cycle (succinate ➔ fumarate + $FADH_2$) transfers electrons to CoQ
III	Cytochrome bc1	transfer electrons; acts as a proton pump Electrons flow from: CoQ ➔ Complex III ➔ Cyt. c ➔ Complex IV
IV	Cytochrome a+a3	
V	ATP synthase	Synthesizes ATP; consists of two domains: • **F0**- membrane spanning domain • **F1**- extramembranous domain

complex V is not part of ETC but it is coupled to it.

Electrons Carriers:

★ **Coenzyme Q (CoQ):**
it is also called ubiquinone (ubiquitous in biological systems)
A non-protein member of the ETC 'the only non-protein'
Lipid soluble and mobile

★ **Cytochromes:**
Each cytochrome is a protein that contains **Heme group** (porphyrin ring + iron in Fe^{3+} state)

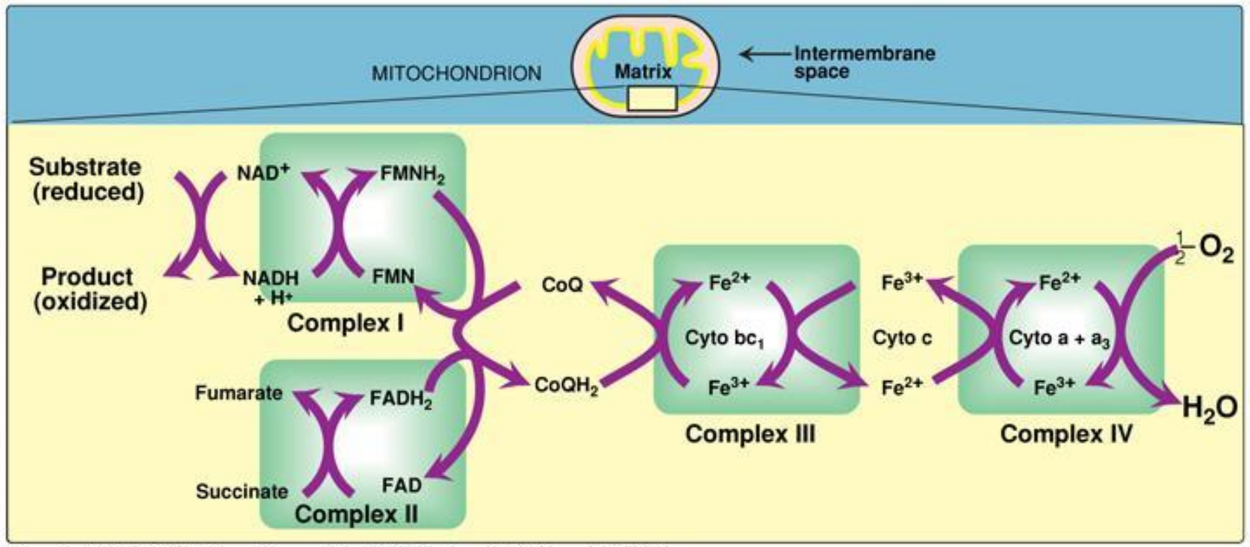
When cytochromes accept electron:
- Fe^{3+} (ferric) is converted to Fe^{2+} (ferrous)
- Fe^{2+} is reoxidized to Fe^{3+} when it donates electrons to the next carrier

ETC cytochromes:
- cytochrome bc1 (complex III)
- cytochrome C
- cytochrome a+a3 (complex IV)

Just understand the main general concept

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 $e^- + O_2 + H^+ \rightarrow H_2O$
- **Oxygen** is required as a final acceptor (respiratory chain)



Electron Transport Chain

glycolysis & krebs cycle

NADH ➡ NAD+

e-

Complex I

FMN➡FMNH2

Takes e- from NADH & gives it to CoQ

Complex II

Succinate➡Fumarate
FAD➡FADH2

Takes e- from FADH2 & gives it to CoQ

e-

Coenzyme Q

CoQ ⟳ CoQH2

Takes e- from complex I & complex II to give it to Complex III

e-

Complex III

Fe^{3+} cyto bc Fe^{2+}

ferric(Fe^{3+}) on the Cytochrome bc1 reduced by CoQ and converted it to ferrus (Fe^{2+})

e-

Cyto C

Fe^{3+} ⟳ Fe^{2+}

Takes e- from complex III to give it to Complex IV

e-

Complex IV

Fe^{3+} cyto a+a Fe^{2+}

–Cytochrome a+a3 takes e- (from cyto.c) ➡iron becomes Fe^{2+}

–Cytochrome a+a3 passes e- to oxygen ➡iron becomes Fe^{3+} again

½ O2

H2O

ATP

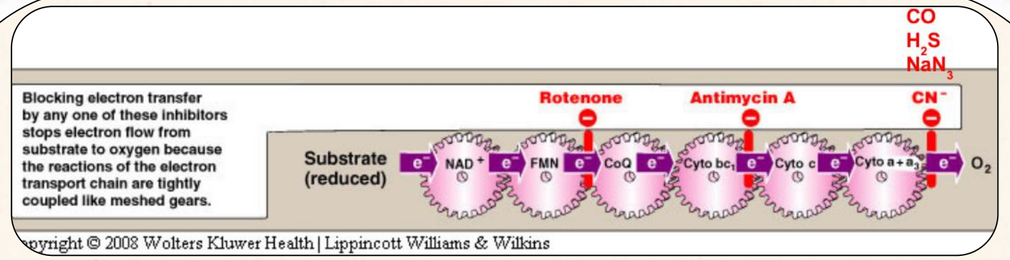
Result of glycolysis & krebs cycle:

- 10 NADH ➡ goes to complex I
- 2 FADH2➡goes to complex II

CoQ doesn't have to take an e- from both complex I and an e- from complex II in order to transport it to complex III

- Are complexes 1-5 stable or mobile? stable
- NADH is NOT part of complex I
- FADH2 is a component of complex II
- when CoQ is reduced it will gain H+ and e- CoQ➡**CoQH2**

site specific inhibitors of ETC



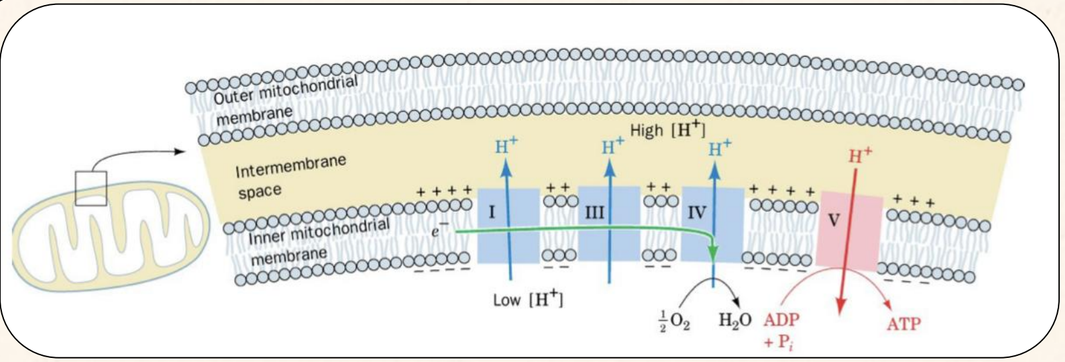
dr's note: it is chemical substances used sometimes as Anti-insecticides (مضادات حشرية) blocks one of these circles which leads to reduce or stop the production of ATP then death of the cell.

-Rotenone: prevent FMN from transferring electron to CoQ.
this will lead to ➔ 1- ATP synthesis decreased.
2- oxygen consumption decreased.

*هنا ما يوقف انتاج ATP فقط يقل؛ لأن ETC ممكن تبدأ من complex 1 or 2

-Antimycin-A: prevent cytochrome bc1 from transferring electron to cytochrome c.

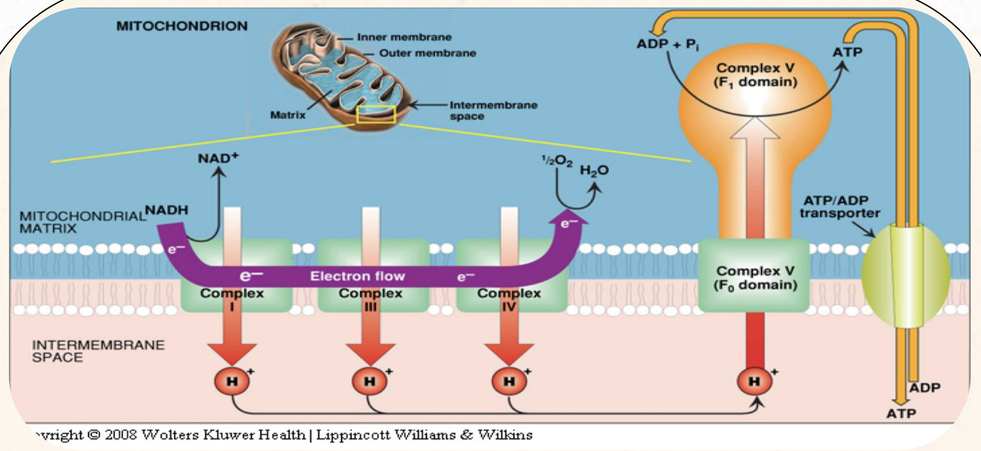
-CN (Cyanide), CO, H_2S, NaN_3: prevent cytochrome $a+a_3$ from transferring electron to oxygen.



ETC is coupled to proton transport for ATP synthesis

- 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 (inner mitochondrial membrane) to synthesize ATP.

transport of protons



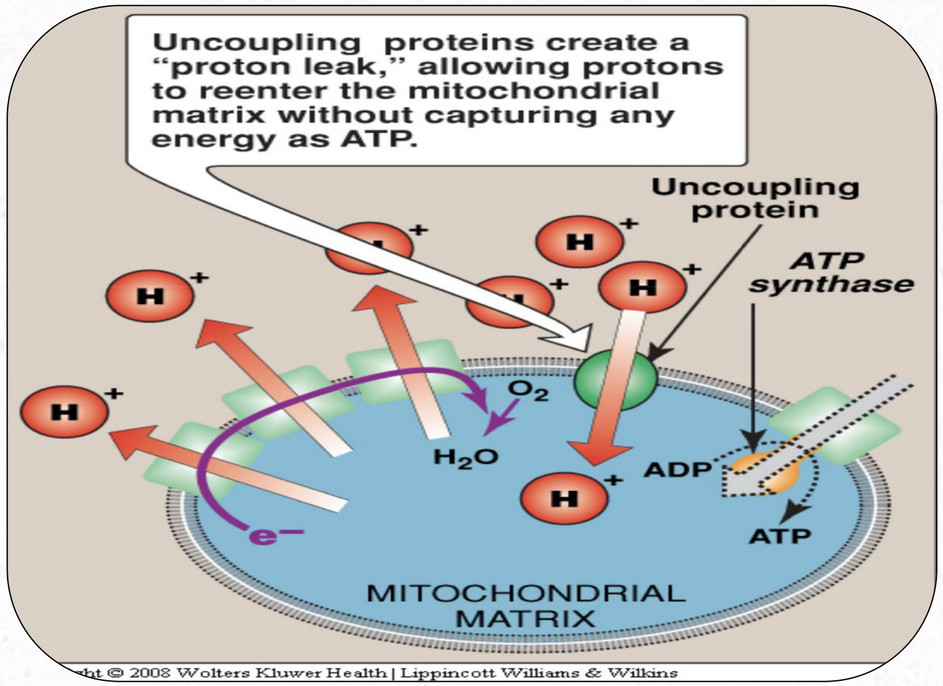
- because of proton pump will increase the concentration of H^+ at intermembrane space this will activates complex 5.
- when **complex 5** activated it converts ADP+P → ATP, and pump H^+ back to mitochondrial matrix.
- H^+ will bind to Complex 5 at F0 then transferred into F1 and make a conformational changes that lead to the synthesis of ATP

Energetics of ATP synthesis

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

ATP made per O atom reduced		
for NADH	3ATP	one O
for $FADH_2$	2ATP	one O

inhibitor of ATP synthesis



Mechanism of both is important***

- 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 CO2 and water.

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

References: Lippincott's Illustrated Reviews, Biochemistry, 6th Edition, Denise R. Ferrier, Lippincott Williams & Wilkins, USA, pp. 73-79

MCQ

Q1) What products of glucose oxidation are essential for oxidative phosphorylation?			
A- Acetyl CoA	B- NADH and $FADH_2$	C- Pyruvate	D- NADPH and ATP
Q2) Which of the following happen during the Electron Transport Chain?			
A- H^+'s travel down the ETC, pumping high energy electrons into the intermembrane space.	B- H^+'s diffuse through ATP Synthase,turning it so it can make ATP.	C- High energy electrons travel down the ETC, pumping H^+'s into the intermembrane space.	D- none of the above
Q3) Which complex of the electron transport chain in cellular respiration does not directly impact the intermembrane space's pH?			
A- Complex III	B- Complex II	C- Complex IV	D- Complex I
Q4) If unknown drug destroys the H^+ gradient that forms in the electron transport chain. What is the most likely consequence?			
A- No effect will occur	B- ATP production will increase	C- Oxygen consumption will increase	D-The cells will be forced to perform fermentation
Q5) What is the final electron acceptor in the electron transport system, and what is formed?			
A-oxygen; H_2O	B- ADP; ATP	C- NAD; NADH	D- NAD; FADH2

Answers:
1- B
2- C
3- B
4- D
5- A

SAQ

Q1) Where does ETC located?

Q2) which members of ETC is (Lipid soluble + non-protein) molecule?

Q3) What are the complexes responsible for driving the protons out of the matrix?

Answers

Q1) In the inner mitochondrial membrane

Q2) CoQ

Q3) complexes I, III and IV (proton pumps)

Biochemistry Team

Leaders

Lama Alahmari

Faisal Bakri

Members

Ghaida Alotaibi

Reema Aldhabaan

Norah Albahily

Khalid Alghamdi

Osama Alhenaki

Faisal Alghamdi

Nasser Alabdulsalam