Biochemistry Team 435

جامعة الملك سعود
King Saud University 1957

ELECTRON TRANSPORT CHAIN (RESPIRATORY CHAIN)

Color index:

- Important
- Extra explanation

"LET YOUR SMILE CHANGE THE WORLD BUT NEVER LET THE WORLD CHANGE YOUR SMILE."

435 Biochemistry Team

Phosphorylation

This slide is Extra ..

Phosphorylation

Substrate level

2 ATP

You form high energy bonds by
ADP ➤ ATP

Oxidative level

22 ATP

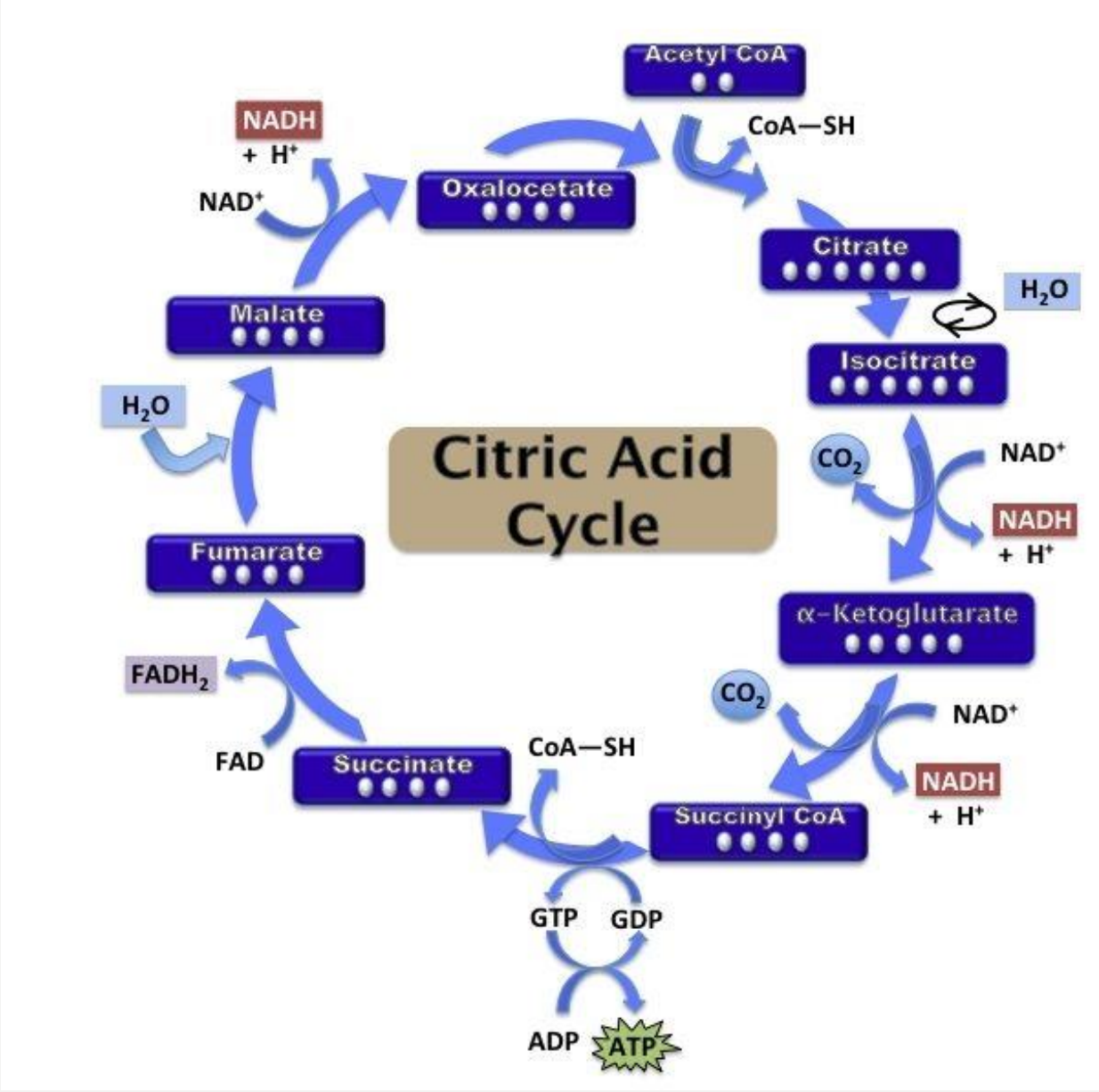
You form high energy bonds by
ADP ➤ ATP
+
You transfer electrons in ETC

Note:

#In oxidative phosphorylation we add phosphate group and transfer electrons(from reduced coenzymes to oxygen) in ETC.

#net ATP produced by Krebs cycle = 24 ATP

This slide is Extra ..



-End Product of Krebs cycle:

Oxaloacetate

-At the end of Krebs cycle:

2 ATP

6 NADH

2 FADH2

***NADH=3ATP**

***FADH2=2ATP**

Net = 24 ATP

OBJECTIVES:

- ✓ Understand how energy-rich molecules including glucose are metabolized by a 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 reactions of electron transport chain taking place in mitochondria that are coupled to oxidative phosphorylation.

Electron Transport Chain (ETC)

- **What is ETC ?**

-A system of electron transport that uses respiratory O2 to finally produce ATP (energy).

- **Purpose:** production of ATP (energy).

- **Where does it located ?**

- It is Located in the inner mitochondrial membrane.

#Important: It is **the Final** common pathway of metabolism.

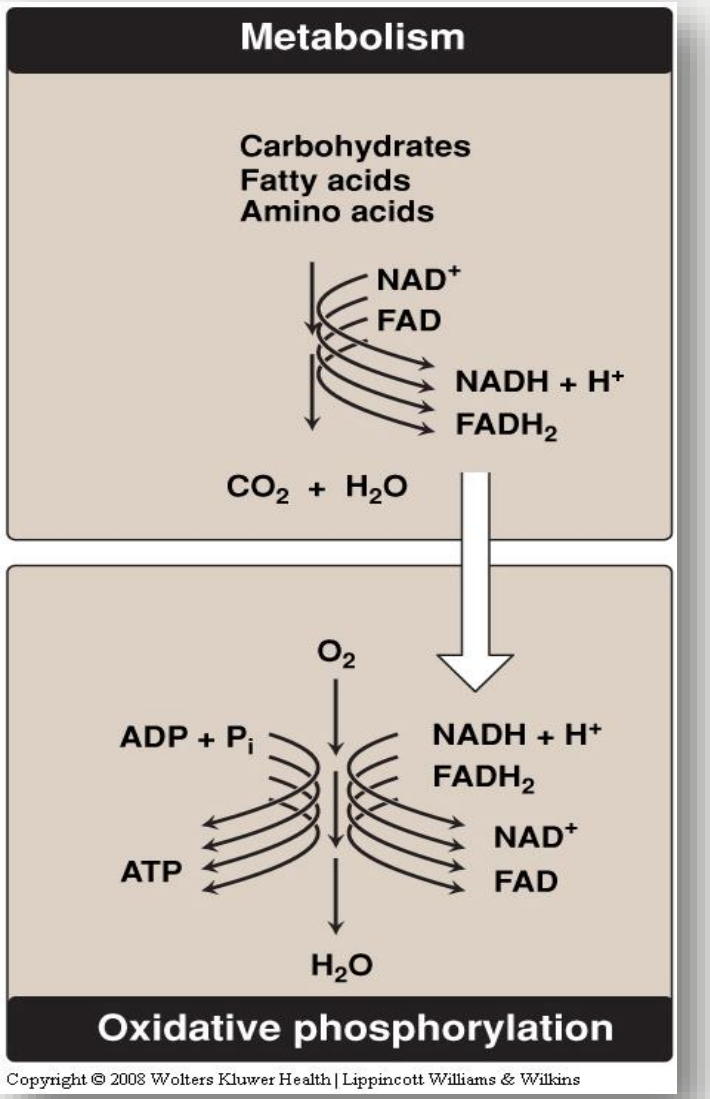
- **Some characteristics:**

- Electrons from food metabolism are transported to O2 (The terminal *final* acceptor of electrons: O2).
- it Uses the maximum amount of body's oxygen.

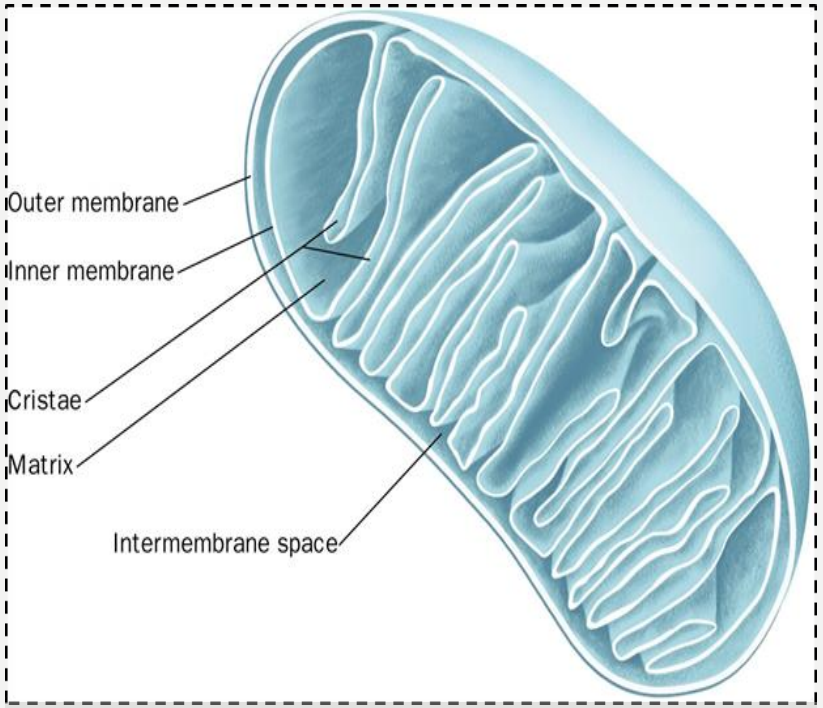
Metabolic breakdown of energy – yielding molecules

Extra Explanation:

Carbohydrates are metabolized by oxidation reactions yielding co2+water. This metabolic reaction donates electrons to NAD + FAD to become NADH +FADH " **energy – rich reduced form** ". Then, These coenzymes donate (give) a pair of electrons to specialized sets in ETC. as electrons passed down the ETC ,They loss free energy – used to move protons **across inner mitochondrial membrane** then production of ATP from ADP and it is **called** oxidative phosphorylation.



MITOCHONDRIA



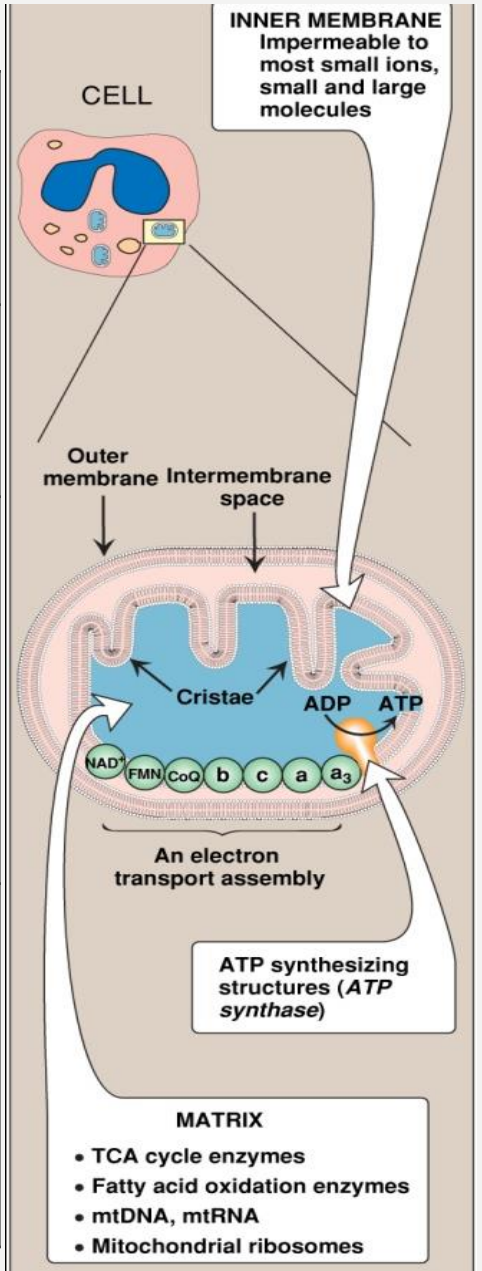
Cutaway diagram of a mitochondrion

An electron micrograph of an animal mitochondrion

Mitochondria structures

Mitochondria

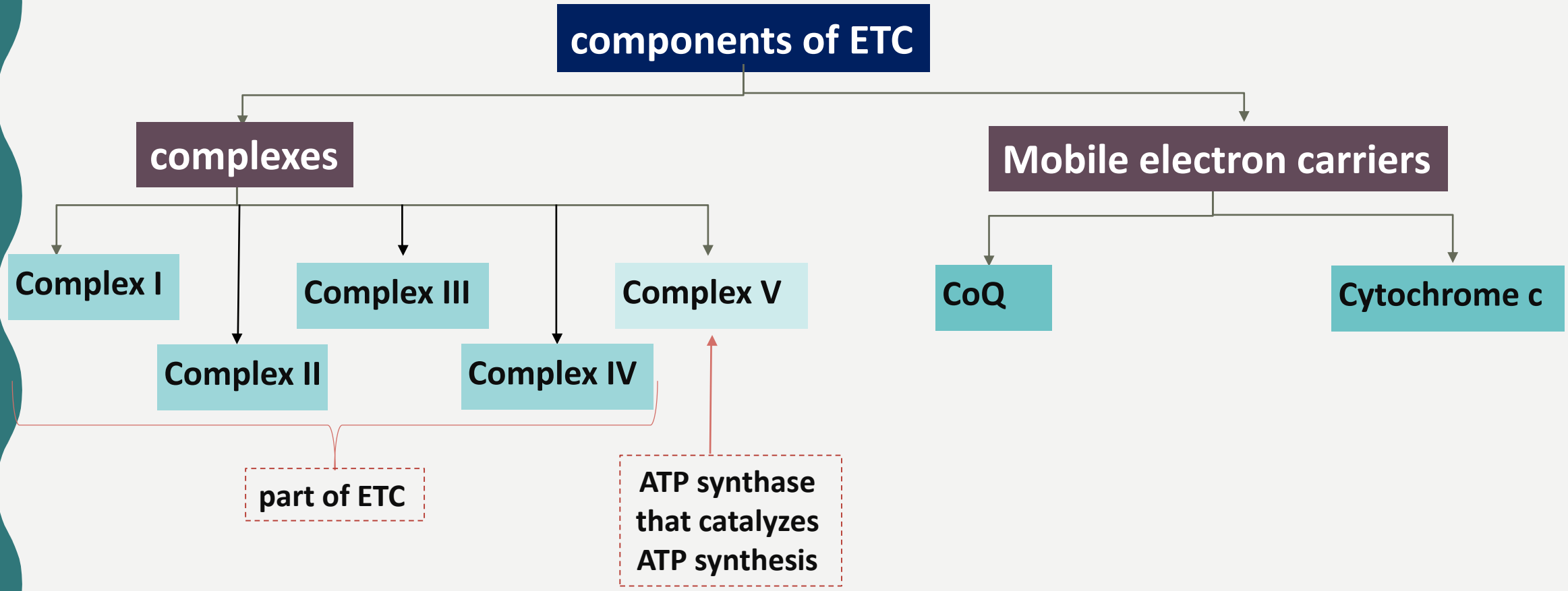
structure	Characteristics:
Outer membrane:	Contains special channels **(porin proteins)** making it permeable to most ions & small molecules
Inter-membrane space	Space between outer membrane and inner membrane
Inner membrane (site of ETC):	- Specialized structure, **rich in proteins**, impermeable to most small ions & molecules. **- It is highly convoluted, the convolutions are called cristae serves to greatly increase the surface area of the inner membrane.**
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.



Component of ETC

- **Where does the components of ETC are located?**

All members/components are located in the **inner mitochondrial membrane** (IMM) (an exception is cytochrome C which is located in **the inter-membrane space**).



ORGANIZATION OF ETC

Each complex:

Accepts or donates electrons to mobile carriers.

Carriers:

- Accept electrons from donors.

-Then donate to the next carrier in chain.

Remember:

- Oxidation is losing H (electrons).
- Reduction is giving H (electrons).

Electrons finally combine with oxygen and protons to form **water**.

"Electrons + oxygen + protons = water"

Oxygen is required as a final acceptor (respiratory chain).

Complex I and complex I I :

- **Complex I - NADH Dehydrogenase:**

-This complex: collects the pair of electrons from NADH and passes them to CoQ.

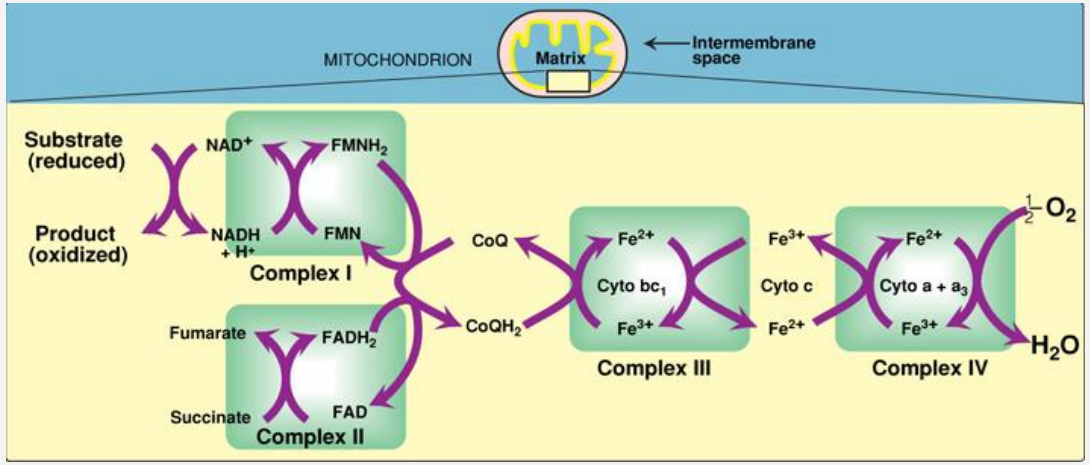
-It is an enzyme that transfers 2 electrons from NADH to it's coenzyme (which called FMN) and reduce it to FMNH2 , then it transfers the electrons to Coenzyme Q (electron carrier) which will get converted into CoQH2.

- **Complex I I -Succinate dehydrogenase:**

-It is also a part of the *TCA cycle.

-**Transfers electrons to CoQ.**

-It is an enzyme that oxidizes the succinate to form the fumarate,the 2 electrons formed move from(the coenzyme and FADH2) to the iron-sulker protein and Coenzyme Q.



*TCA: Tricarboxylic acid cycle (krebs cycle)

COENZYME Q (COQ)

Also called ubiquinone (because it is ubiquitous in biological system)

ubiquitous=most common

A non-protein member of the ETC (electron transport chain)

Lipid soluble and mobile (moving)

"CoQ is a mobile electron carrier and can accept hydrogen atoms from NADH dehydrogenase (Complex I), from succinate dehydrogenase (Complex II), and from other mitochondrial dehydrogenases, transfers electrons to Complex III (cytochrome bc_1), then, links the flavoprotein dehydrogenases to the cytochrome. "

Cytochromes + Complex III and IV

- **What are cytochromes ?**

any of several carrier molecules in the mitochondria of plant and animal cells
cytochromes participate in the stepwise transfer of electrons in oxidation reactions .

Cytochromes = protein + Heme group

- **When cytochromes accept electron :**

-Fe^{3+} is converted to Fe^{2+} . (by a reduction reaction)
-When Fe^{2+} donates an electron to the next carrier
Fe^{2+} reoxidized to Fe^{3+} .

Remember .. !

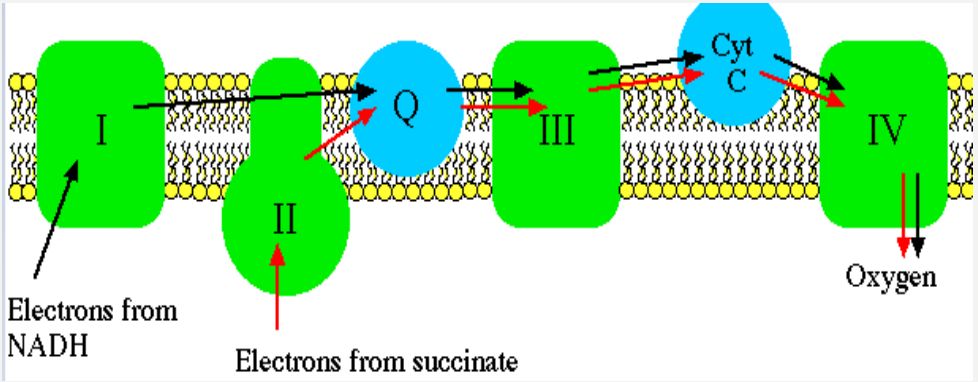
In Cytochromes:

Heme group = porphyrin ring + iron in Fe^{3+} (Ferric)

In HB:

Heme group = porphyrin ring + iron in Fe^{2+} (Ferrous)

- **Complex III :** cytochrome bc1
- **Complex IV :** cytochrome a + a_3 (it is also known cytochrome oxidase)



- **Electron flow from :**

Coenzyme Q → complex III → cytochromes C → complex IV

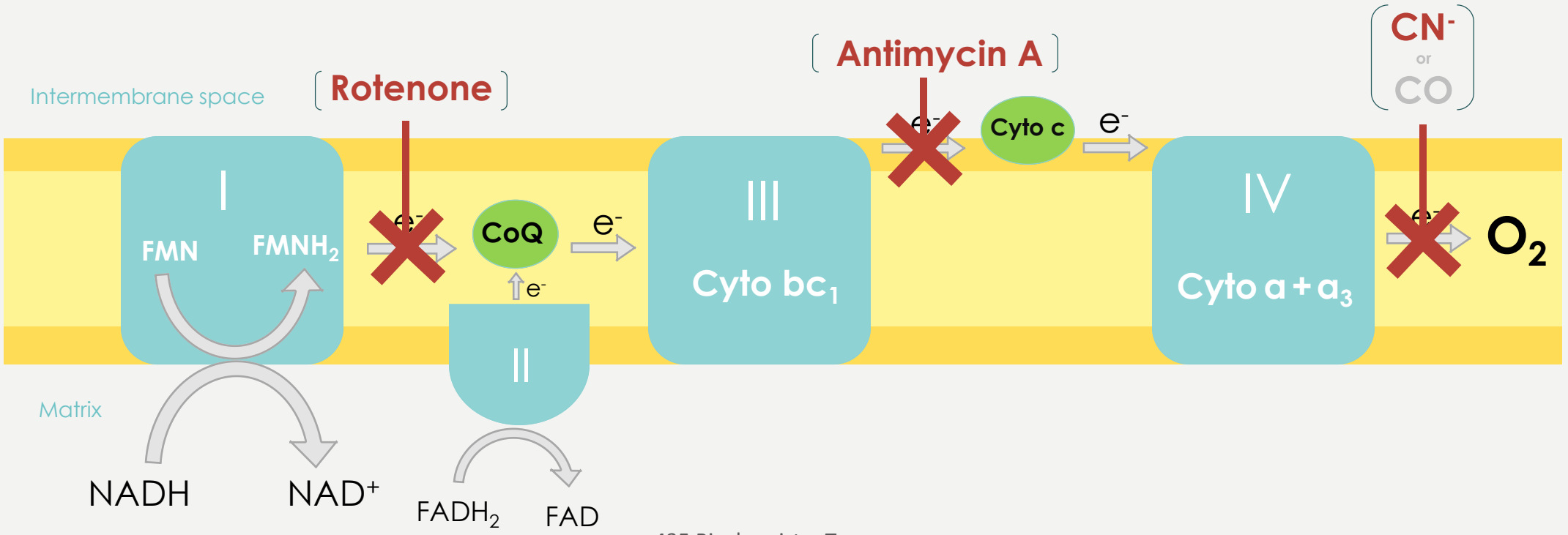
Site specific inhibitors of ETC

- These are compounds **prevent the passage of electrons** by binding to a component of the chain, blocking the oxidation \ reduction reaction = inhibition of **ATP** synthesis.

therefore

All electron carriers before the block = **Fully reduced**

All electron carriers after the block = **Oxidized**



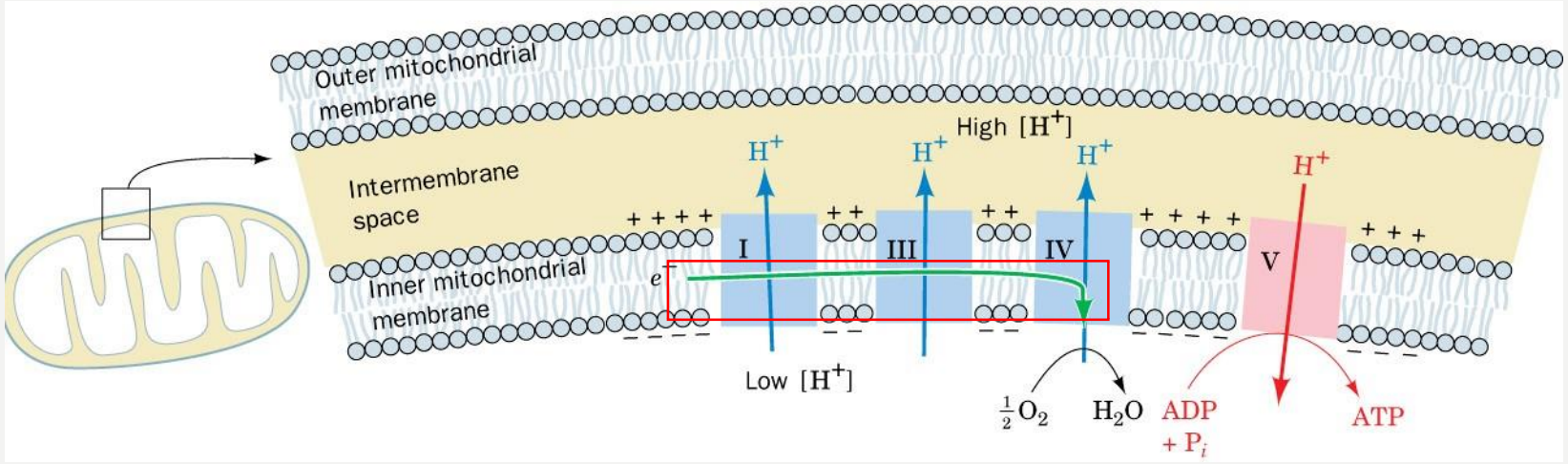
Site specific inhibitors of ETC

Rotenone	block the ETC between NADH dehydrogenase (**Complex I**) and **CoQ**.
Antimycin A	block the ETC between **Cyto bc_1** and **Cyto c**
CN^- "Cyanide" Or **CO**	block the ETC between **Cyto $a+a_3$** and **O_2**

- Remember that Hb has higher affinity for CO than O_2, therefore it causes hypoxia when it inhaled.
- **It also inhibits ETC in the Cyto $a+a_3$.**

ETC is coupled to proton transport for ATP synthesis

- The energy of electron transfer is used to drive the protons out of the matrix ***the flow of H^+ from matrix to intermembrane space*** → PH outside is **lower** due to **increased** H^+.
- **It is done by** complexes I, III and IV (act as proton pumps)
- This creates a **proton gradient** across the IMM (**inner mitochondrial membrane**) to synthesize ATP.



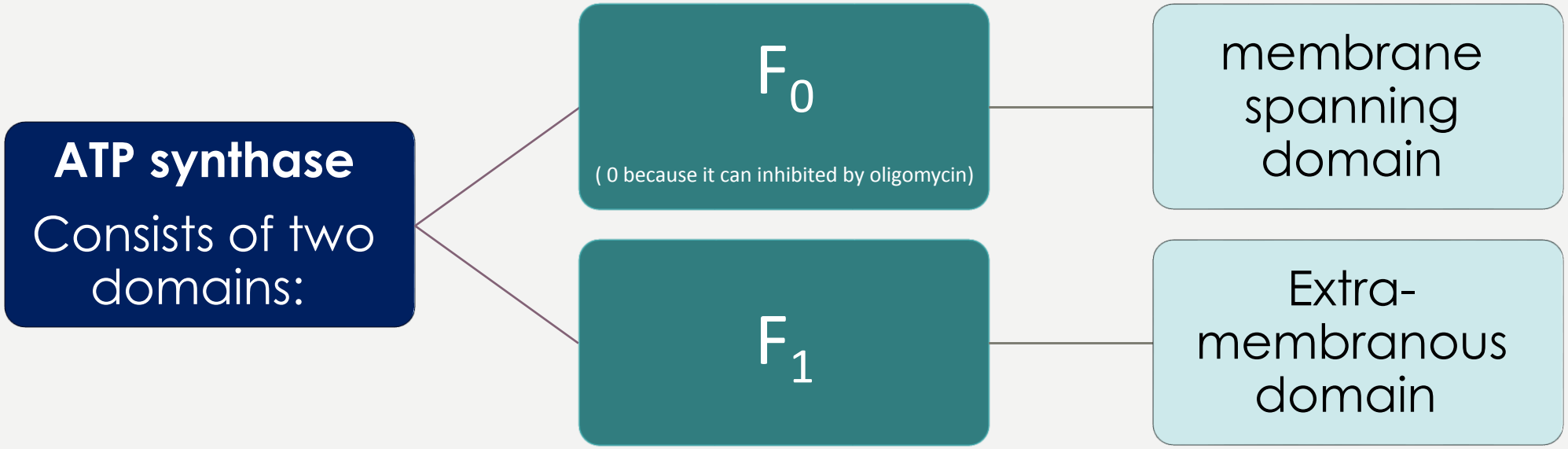
Notes:

- Coupling of electron transport (green arrow)and ATP synthesis
- complex II has no function in pumping H^+ *

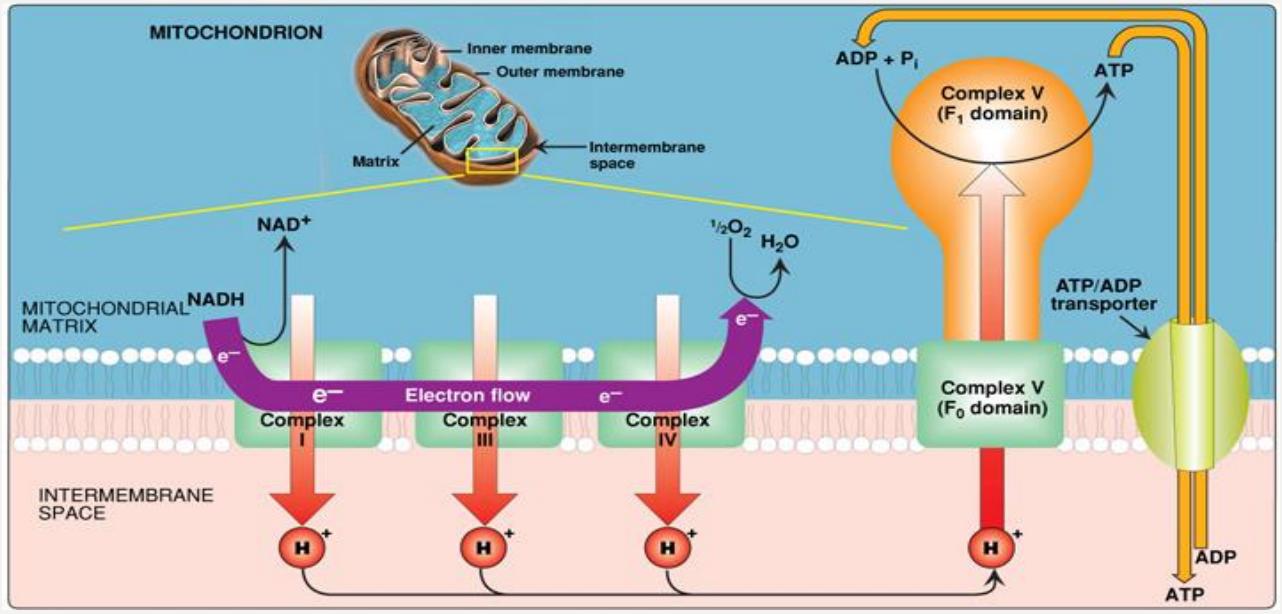
Electron Transport Chain

ATP synthase

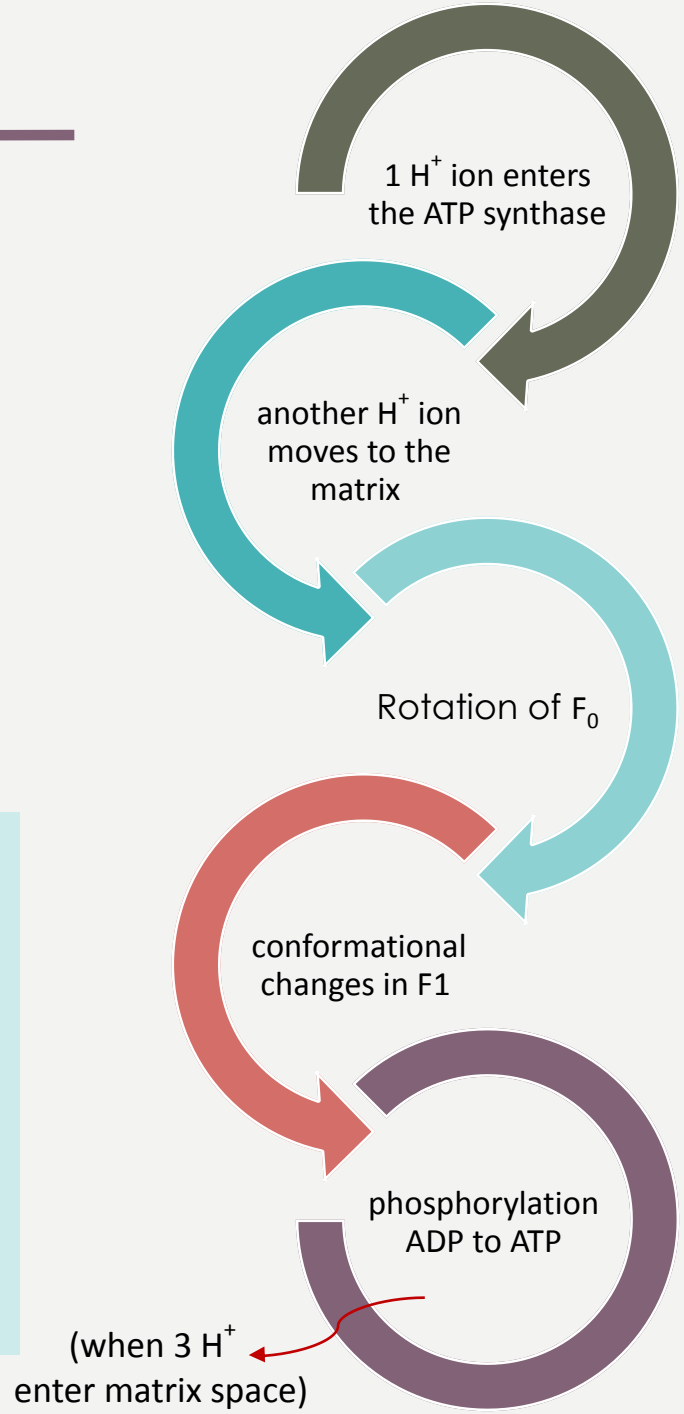
ATP synthase (Complex V) synthesizes ATP using the energy of the proton gradient generated by the electron transport chain.



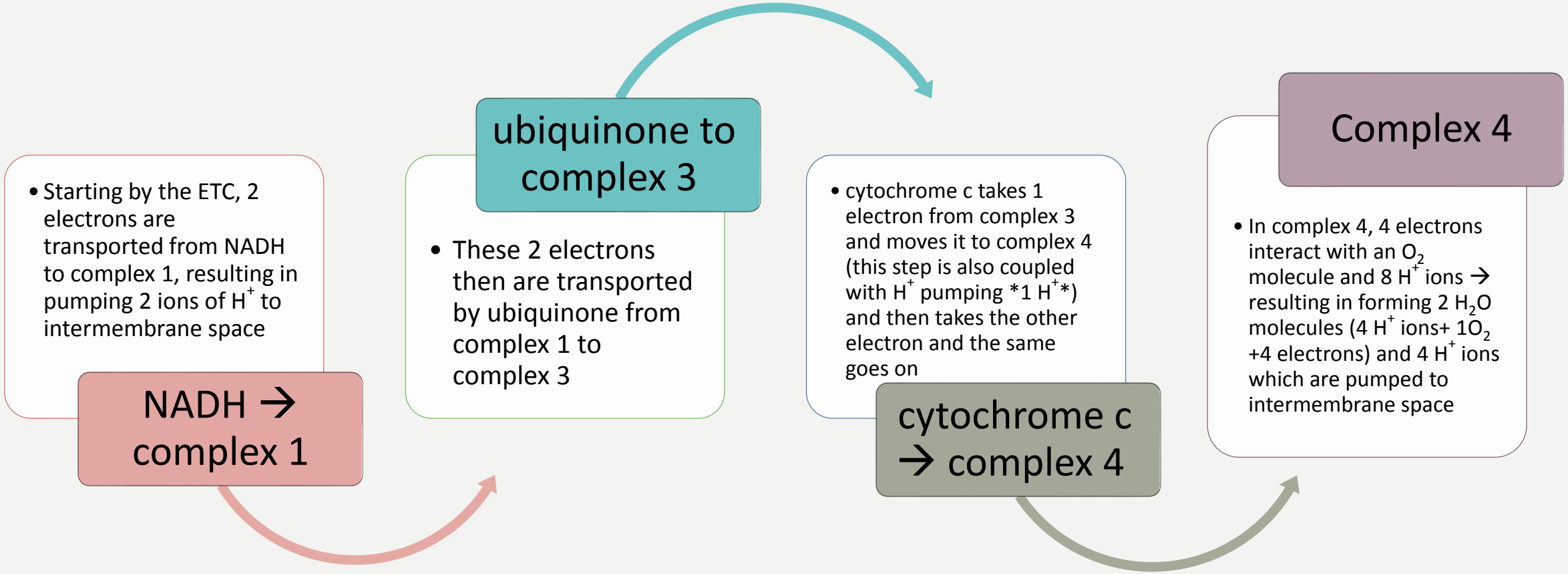
Transport of protons



- When 1 H^+ ion enters the ATP synthase → another H^+ ion leaves the ATP synthase moving to the **matrix** → This results in rotation of upper part of ATP synthase (F_0),which **causes** → conformational changes in the extra-membranous F1 domain that allow it to bind ADP + Pi, (phosphorylate ADP to ATP), and release ATP.
- When 3 H^+ ions enter **matrix space**, the energy result **enables** the ATP synthase to synthesize 1 ATP from ADP+P_i.
- (When both sides ***matrix space+ intermembrane space*** contain the **same** amount of H^+ ions there will be no gradient = **no energy for ATP synthesizing**).



HOW DOES THE MITOCHONDRIA MAINTAIN THE CONCENTRATION GRADIENT?



Notes:

- Pumping of H+ ions creates an electrical gradient (with more positive charges on the outside of the membrane than on the inside) and a pH gradient (the outside of the membrane is at a lower pH than the inside).
- The concentration gradient is maintained in the mitochondria by ETC

Proton Gradient

*This video was played by Dr.Sumbul

Energetics of ATP synthesis

-Energy **required** for phosphorylation of ADP to ATP → = **7.3kcal/mol**

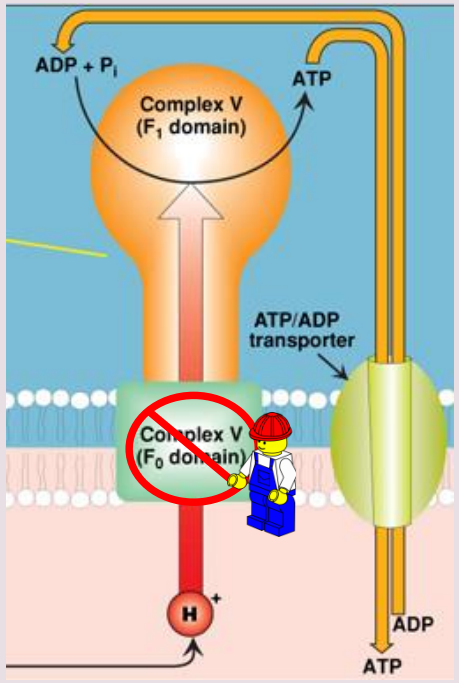
-Energy **produced** from the transport of a pair of electrons from NADH to O2 → = 52.58 kcal

*Excess energy is used for other reactions or released as **heat.**

INHIBITORS OF ATP SYNTHESIS

Oligomycin

- **Binds to F_o domain of ATP synthase and closes the H+ channel .**



Oligomycin:

It's a drug that binds to the F_o and closes the proton channel and preventing reentry of the proton so it prevents phosphorylation of ADP to ATP.

لتسهيل الحفظ:

oligomycin is like olegomycine which **Lego** is

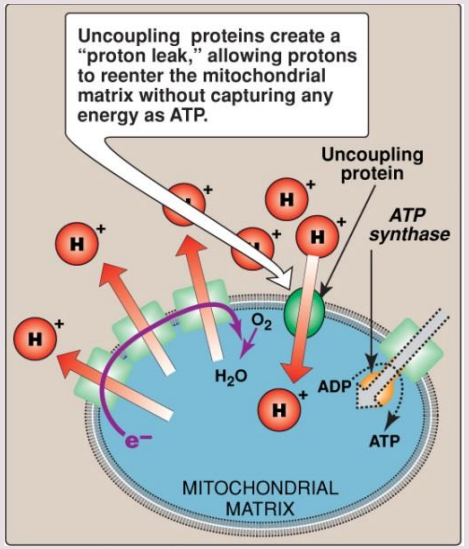
UCPs:

It occurs in the IMM of mammals, including humans.

- هذي البروتينات تسوي قنوات تسمح للبروتينات تدخل مره ثانيه للماتركس من دون ما تنتجATP ،
- تجعلنا نخسر تركيز البروتونات وعليه لن يكون هنالك تصنيع للاي تي بي!!!

Uncoupling proteins (UCPs)

- **Create proton leaks (allow protons to reenter the matrix without ATP synthesis).**
- **Energy is released as heat (non-shivering thermogenesis).**



Summary

Electron transport chain	
What is it ?	Final common pathway of metabolism It is a system of electron transport that uses respiratory O2 to finally produce ATP
Occurs in	the inner mitochondrial membrane

	Metabolic breakdown of energy-yielding molecules		
Process	Reactant	Product	The result
Metabolism	Carbohydrates (or) Fatty acids (or) Amino acids	$CO_2 + H_2O$	NAD^+ and FAD are reduced to store energy: • $NAD^+ \rightarrow NADH + H^+$ • $FAD \rightarrow FADH_2$
Oxidative phosphorylation	O_2	H_2O	$NADH + H^+$ and $FADH_2$ are oxidized releasing electrons : • $NADH + H^+ \rightarrow NAD^+$ • $FADH_2 \rightarrow FAD$

Mitochondrion	
Inner membrane	Impermeable to most of small ions, small and large molecule
Cristae	It increases the surface area
Matrix	Contains TCA cycle enzymes, fatty acids oxidation enzymes, mtDNA, mtRNA, mitochondrial ribosomes

Cytochromes (a protein that contains heme group [porphyrin ring + iron in Fe^{3+} state])	
When it accepts electron	Fe3+ is converted to Fe2+
when it donates electrons to the next carrier	Fe2+ is reoxidized to Fe3+

Summary

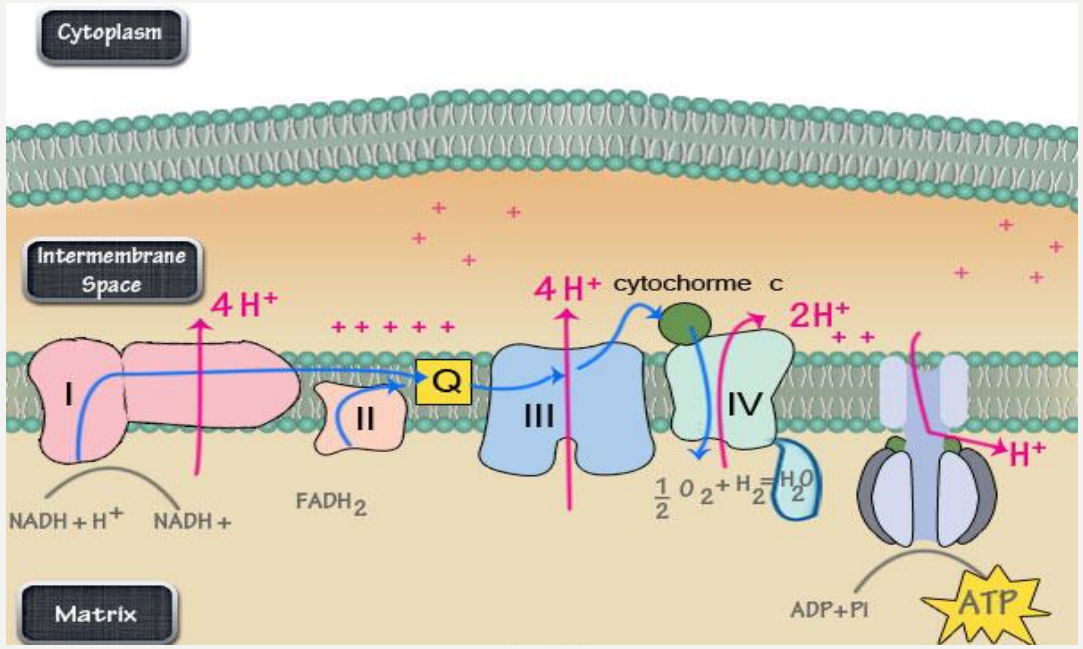
Components of ETC [all are located in the inner mitochondrial membrane (IMM)]		
5 complexes	Complex I (NADH Dehydrogenase)	This complex collects the pair of electrons from NADH and passes them to CoQ
	Complex II (succinate Dehydrogenase)	• It is also a part of the TCA cycle • Transfers electrons to CoQ
	Complex III	Cytochrome bc1
	Complex IV	Cytochrome a + a_3
	Complex V (ATP synthase)	It catalyzes ATP synthesis. It onsists of two domains: ✧ F0 – membrane spanning domain ✧ F1 – extramembranous domain
Mobile electron carriers	CoQ "ubiquinone"	non-protein member of the ETC, lipid soluble and mobile
	Cytochrome C	-

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 H_2O.
• Oxygen is required as a final acceptor

P:O ratio (ATP made per O atom reduced)			
For NADH	P:O = 3:1	For $FADH_2$	P:O = 2:1

Biochemistry Team 435

Summary



hydrogen electron

- as electrons pass from complex to complex they power the movement of hydrogen atoms into the intermembrane space (done by complexes I, III and IV [proton pumps])
- The number of hydrogen atoms (also called proton gradient) will build up and flow back to the matrix through ATP synthase (complex V) powering the production of ATP

Energetics of ATP synthesis	
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 (NADH to O_2)	3
* Excess energy is used for other reactions or released as heat	

Site specific inhibitors of ETC	
Rotenone	FMN → coQ
Antimycin A	$Cyto_{bc1}$ → $Cyto_c$
CN^-	$Cyto_{a+a3}$ → O_2

Inhibitors of ATP synthesis	
Oligomycin	Binds to F0 domain of ATP synthase and closes the H+ channel
Uncoupling proteins (UCPs)	• Create proton leaks • Energy is released as heat (nonshivering thermogenesis)

SAQ

-What is the function of cristea ?

-Give 2 features of coenzyme Q ?

-Which are the 5 complex in IMM and give one feature ?

Answers

-What is the function of cristea ?

Increase the surface area .

-Give 2 features of coenzyme Q ?

Non-protein member of ETC.

Lipid soluble , mobile.

-Which are the 5 complex in IMM and give one feature ?

- Complex I (NADH) dehydrogenase >> collect the pairs of electron from NAADH ans passes them to CoQ .
- Complex II (succinate dehydrogenase) >> part of the TCA cycle
- complex III (cytochrome bc1) >> part of ETC .
- Complex IV (cytochrome a + a3) >> part of ETC.
- Complex V (ATP synthase) >> synthesizes ATP.

MCQS:

1-The main function of ETC is :

A-Production of ATP .

B-Production of O2.

C-Production of CO2 .

2-The oxidative phospholyration found in :

A-Inner surface of the cell.

B-inner surface of the mitochonderia .

C-cytoplasm.

3-which of the following is a feature of outer membrane:

A-Contains cristae.

B-Highly permeable to ions & small molecules.

C-Site of ETC.

D-Specialized structure .

4-IMM complex that is consider ATP synthase that catalyzes ATP synthesis ?

A-complex V

B- complex II

C- Coq

D- cytochrome C

5-What is required as a final acceptor (respiratory chain) ?

A-Hydrogen

B- oxygen

C- enzyme

6- Which one of these complexes convert succinate to fumarate?

A- complex I

B-complex I I

C- complex I I I

7- which of these substances is ubiquitous in the biological system?

A- NADH dehydrogenase

B-succuinate dehydrogenase

C- Coenzyme Q

1-A
2- B
3-B
4-A
5-B
6-B
7-C

MCQS

8- The concentration gradient is maintained in the mitochondria by:

A- ETC

B- ATP synthase

C- Complex 2

D- inner mitochondrial membrane

9- ATP synthase uses the energy of :

A- protons (hydrogen)

B- electrons

C- proton gradient generated by the ETC

D- ETC

10- In complex 4, when 4 electrons interact with 1 O2 the number of H+ ions that were pumped is:

A-8

B-1

C-4

D-2

11 – the P:O ratio for FADH2 is :

A-3:1

B-1:3

C-2:1

D-1:2

12 – Number of protein complexes which are part of ETC:

A-2

B-4

C-5

D-3

13-All of the following protein complexes are proton pumps, except:

A- complex I

B- Complex II

C- Complex III

D-Complex IV

8-A
9-C
10-C
11-C
12-B
13-B

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