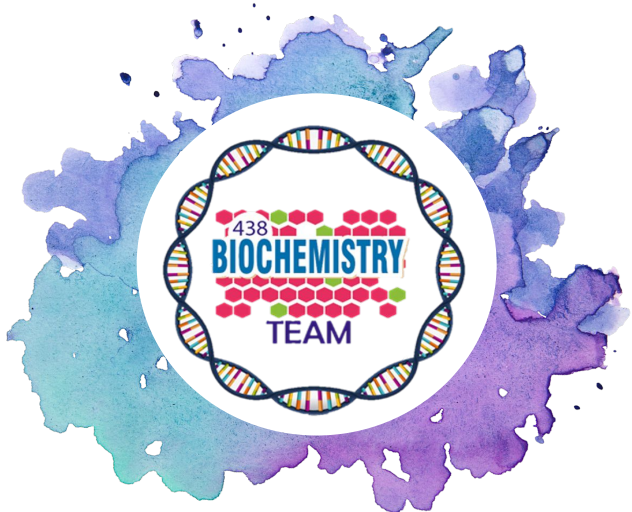
editing file

Respiratory Block

Respiratory chain

Color Index:

- Original content
- Important
- Extra info, Dr's notes
- Only in girls' slides
- Only in boys' slides



Objectives:

Slide No. 3

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

Slide No. 5

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

Slide No. 7

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

★ **Objective:** Understand how energy-rich molecules are metabolized by series of oxidation-reduction reactions ultimately yielding CO2 and water.

Electron Transport chain (ETC)

Definition

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

Location

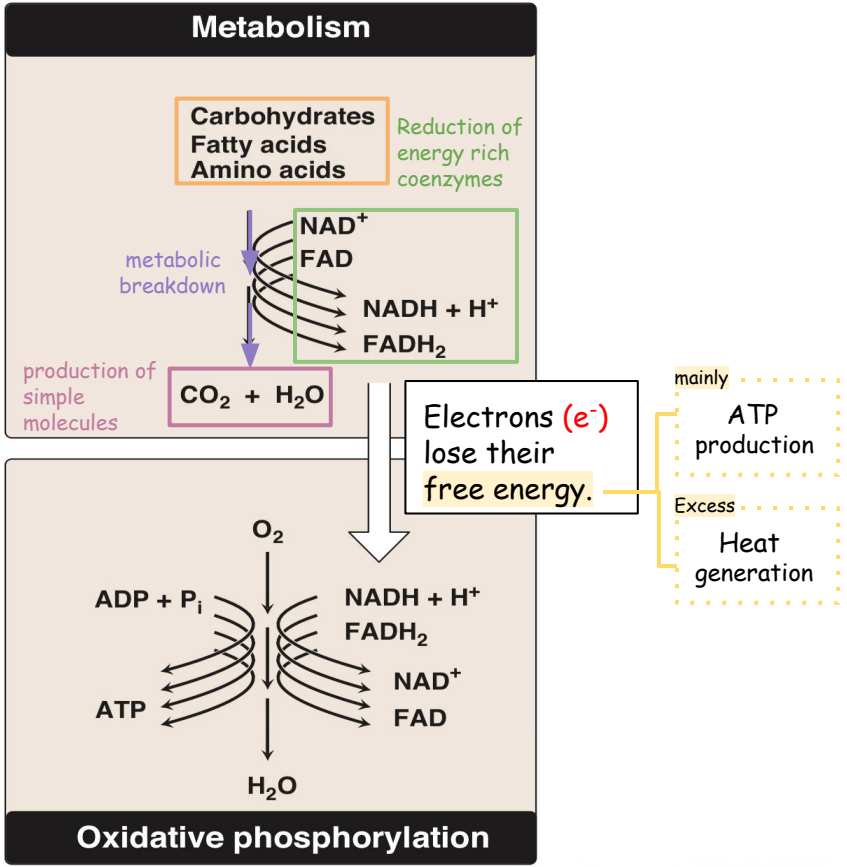
The inner mitochondrial membrane (IMM).

Characteristics

- Final common pathway of metabolism.
- Uses the maximum amount of O_2.

Mechanism

Electrons from food metabolism Transported to O_2.



Structure of the mitochondria

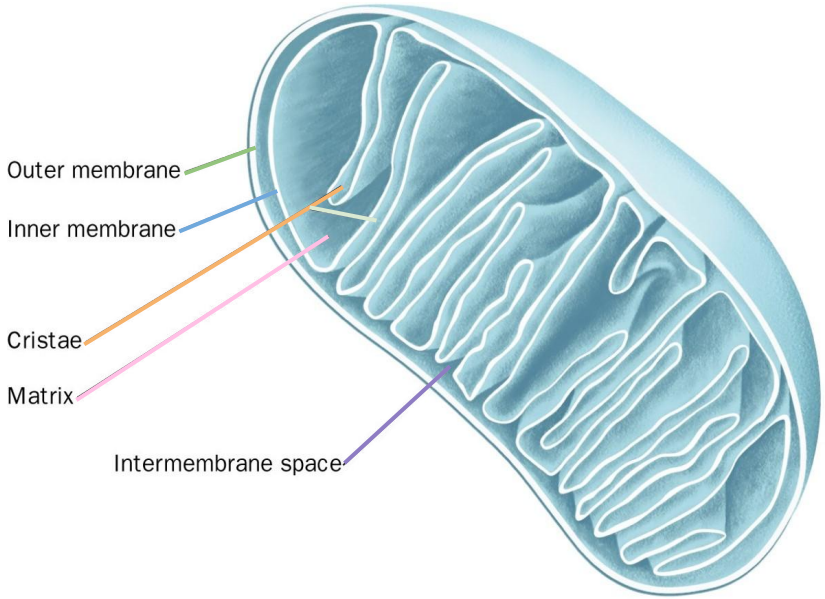
Outer membrane:
- Contains special channels (formed by the protein porin).
- Highly permeable

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

Intermembrane space:
The space between the outer and the inner membrane.

Matrix:
Gel like solution in the interior of the Mitochondria.
- **Contains:**
  - TCA cycle enzymes
  - Fatty acid oxidation enzymes
  - mtDNA & mtRNA
  - Mitochondrial ribosomes.

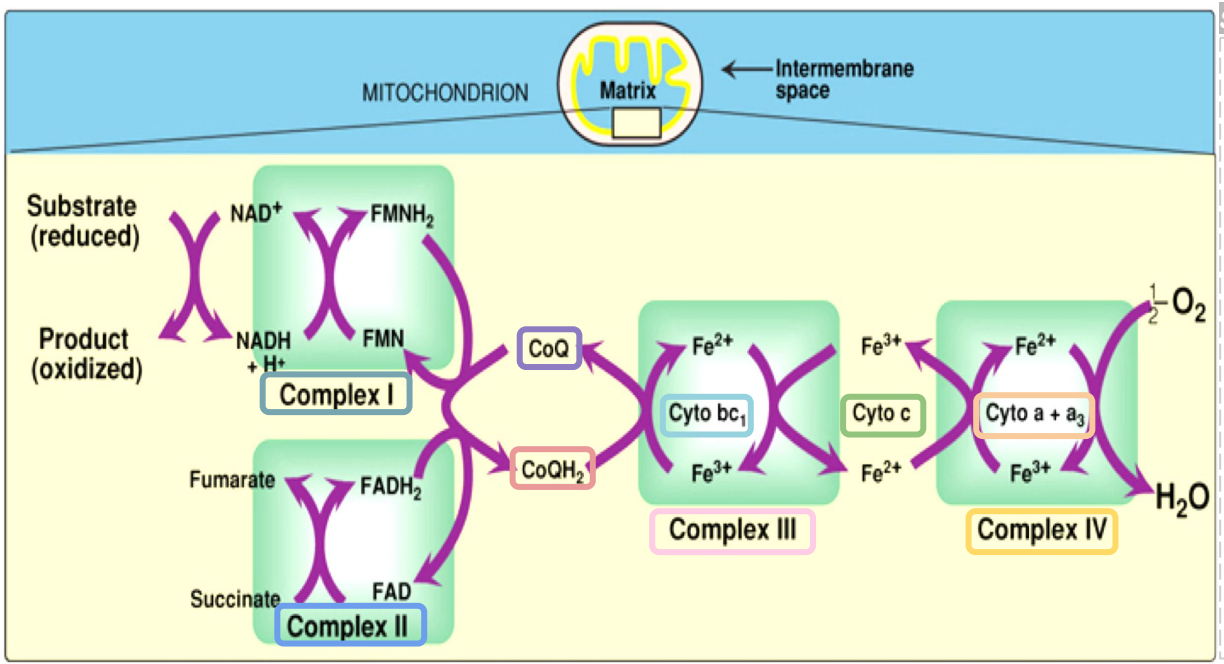
cristae:
Folding of the inner membrane.
- Increase the surface area.



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

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.



Summary of the process:

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

2. Then it gives the electron to cytochrome bc1 "in complex III", then $CoQH_2$ 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 C_1, which gives electrons to mobile carrier Cytochrome C.

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

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

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

★ Notice that **no ATP** has been generated yet from this process (ETC), the ATP generating step is discussed later in this lecture.

Proton pumps

Mobile electron carriers

Components of Electron transport Chain

Complex I (NADH Dehydrogenase)	Complex II (Succinate dehydrogenase)	Co-Enzyme Q	Complex III	Complex IV		Complex V (ATP synthase)
collects the pair of electrons from NADH and passes them to CoQ	Transfers electrons to CoQ From $FADH_2$	Also called ubiquinone (ubiquitous in biological systems) "present in all biological systems"	Cytochrome bc_1	Cytochrome $a+a_3$ also called cytochrome c oxidase	Cytochrome C	Catalyzes ATP synthesis "Not a part of ETC"
	part of the TCA cycle	The only non-protein member of the ETC	Cytochromes			
		Lipid soluble and mobile	Each cytochrome is a protein that contains Porphyrin ring + iron in Fe^{3+} state = Heme group When it donates electrons — Reoxidize to $Fe3^+$ / $Fe2^+$ — Converted to — When it accepts electrons			

Electrons flow: complexes I&II → CoQ → Complex III → Cytochrome C → Complex IV

★ **Objective:** Recognize the reaction taking place in mitochondria that are coupled to oxidative phosphorylation.

ETC is coupled to proton transport for ATP synthesis

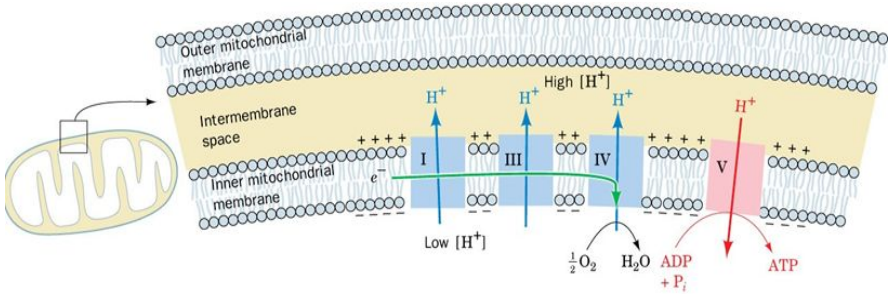
The energy of electron transfer is used to drive the protons out of the matrix **(proton pump)** → Creates a proton gradient across the *IMM → The energy (proton-motive force) generated by the gradient drive ATP synthesis

- 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)



Coupling of electron transport and ATP synthesis

*IMM: Inner Mitochondrial Membrane

ATP synthase

ATP Synthase (complex V) synthesizes ATP

"using the energy of the proton gradient generated by the electron transport chain"

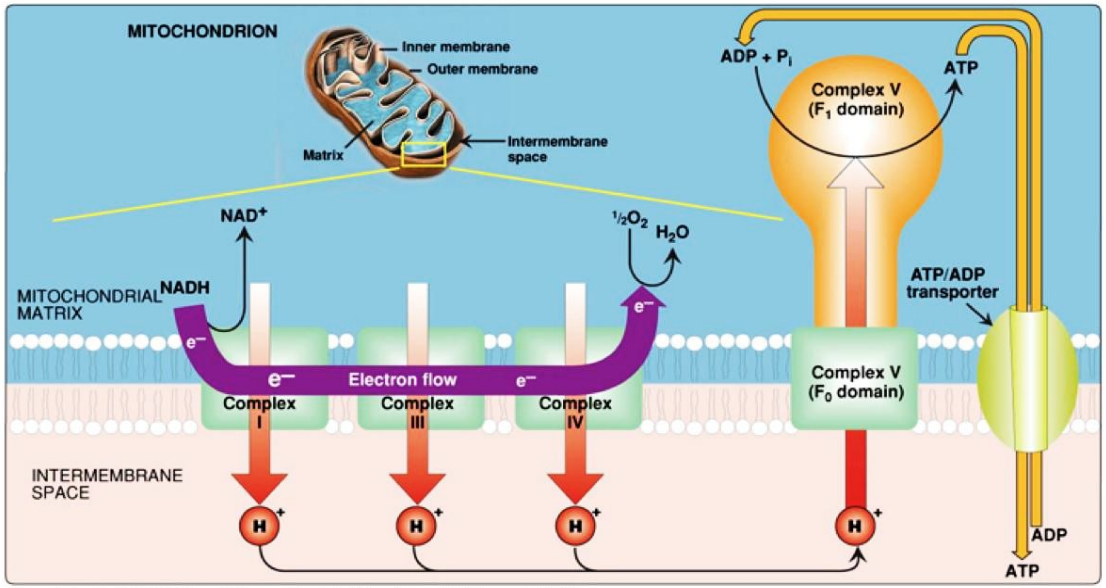
★ Consist of two domains:

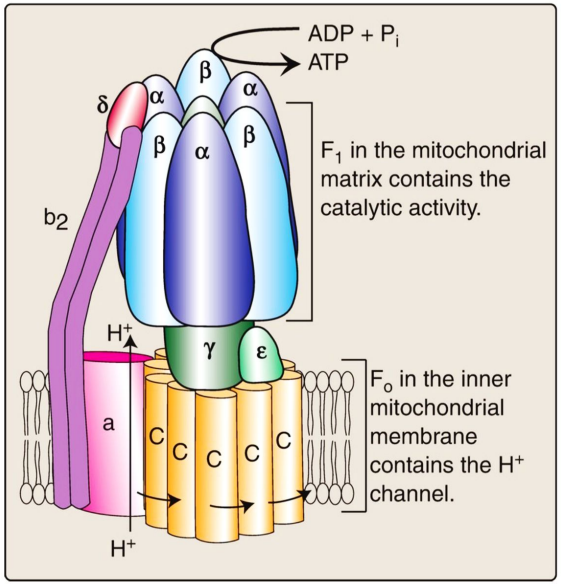
- **F_1**
  - Extra- membranous domain (In the mitochondrial matrix)
- **F_0** (O because it can inhibited by oligomycin)
  - Membrane spanning domain (In the intermembrane space)

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

Transport of protons

➔ Recall chemiosmotic from Zoology 109





H⁺ ion re-enter the matrix by passing through a H⁺ channel in the F_0 domain

Rotation of the c ring of F_0

Conformational changes in the three β subunits of F_1

★ Binding of ADP + P_i

★ Phosphorylation of ADP to ATP and release ATP

★ In F_1 domain

Energetics of ATP synthesis

- Energy **produced** from the transport of a pair of electrons from **NADH** to O_2 = **52.58 kcal**
- Energy **required** for phosphorylation of ADP ⟶ ATP = **7.3kcal/mol** (energy of the Phosphate bond)
- NO. Of ATP molecules produced is **3** (**NADH** ⟶ O_2) 3 x 7.3 = 21.9 kcal

52.58 - 21.9 = 30.78

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

NADH
3:1
3 ATP are made per oxygen atom reduced.

P:O ratio
ATP made per O atom reduced

$FADH_2$
2:1
2 ATP are made per oxygen atom reduced .

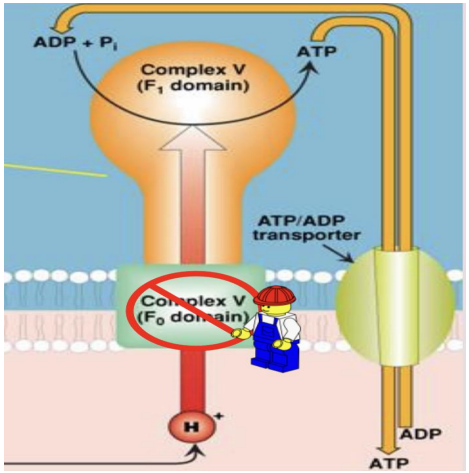
➔ **Extra: Why does $FADH_2$ produces less ATP than NADH?**

- 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)

Inhibitors of ATP synthesis

Oligomycin

- Binds to F_0 domain of ATP synthase and closes the H+ channel



From 435♡

لتسهيل الحفظ: oligomycin is like olegomycine which Lego is

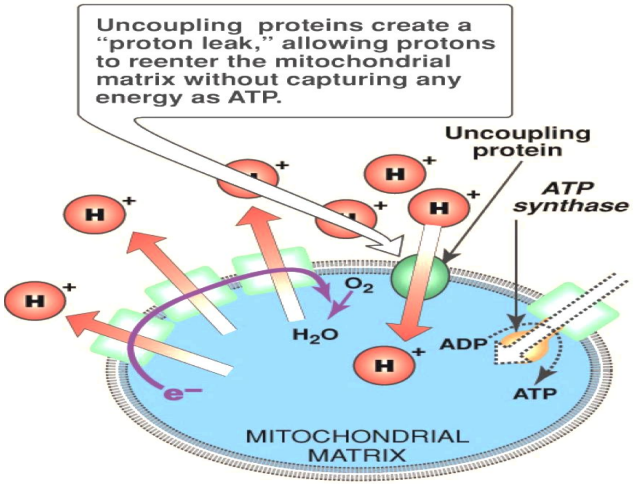
From lippincott

Responsible for heat production in the mitochondria-rich **brown adipocytes** of mammals.

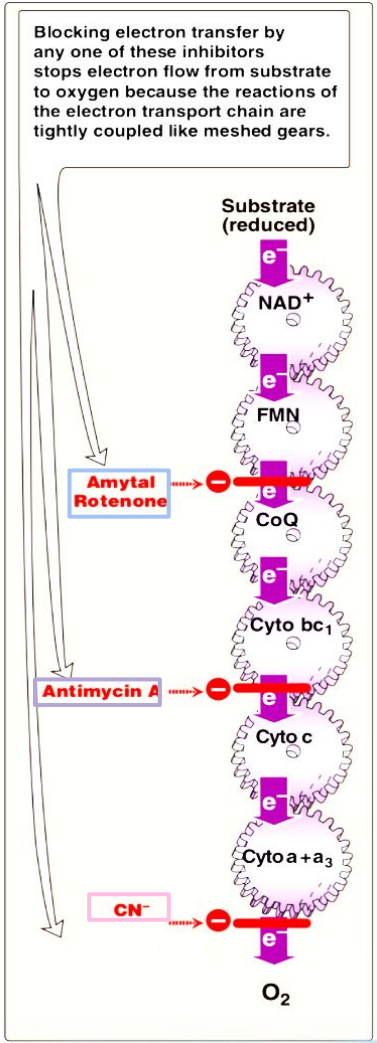
In brown fat, unlike the more abundant white fat, ~90% of its respiratory energy is used for thermogenesis **in infants** in response to cold.

Thus, brown fat is involved in energy expenditure, whereas white fat is involved in energy storage.

Uncoupling proteins (UCPs)



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



Site-specific inhibitors of ETC

These respiratory inhibitors prevent the passage of electrons by binding to a component of the chain, blocking the oxidation-reduction reaction.

➔ Therefore, all electron carriers before the block are fully reduced, whereas those located after the block are oxidized.

Note: Inhibition of electron transport inhibits ATP synthesis because these processes are tightly coupled.

➔ So, there's **No** production of ATP and energy dissipated as heat. known as **non-shivering thermogenesis**.

- Rotenone:
  inhibits between FMN (complex I) and CoQ
- Antimycin A:
  poison which inhibits between cyto bc_1 (complex III) and cyto c
- CN:
  when there is cyanide (CN^-) or CO or sodium azide poisoning they will inhibit the Cycle (oxidative phosphorylation) at the last step before the oxygen gets oxidized (complex IV)

In males' slides only

Take home message

- 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

Passing through Fo channel in the ATP synthase complex (Complex V)
resulting in → Conformational changes in the F_1 domain of ATP synthase that allow the synthesis of ATP from ADP + P_i

by

Protons to reenter the mitochondrial matrix

allowing

The inner mitochondrial membrane

across

An electrical and a pH gradient

creating

The matrix to the intermembrane space

from

Pumping of protons (H^+)

coupled with

Electron flow

leads to

Electron transport chain

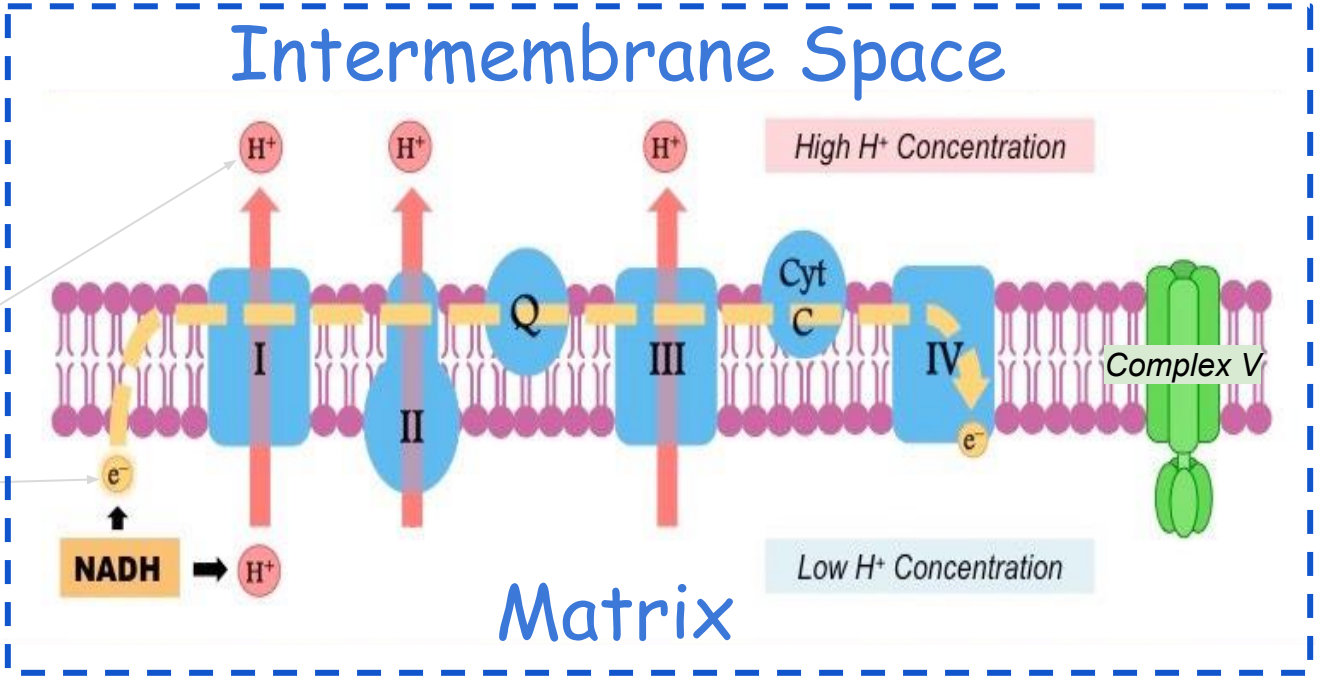
donate electrons to

NADH and $FADH_2$

produce

Oxidative processes

→ such as the TCA cycle



Quiz

MCQs

Q1: 2,4-Dinitrophenol (DNP), an uncoupler of oxidative phosphorylation, was used as a weight-loss agent in the 1930s. Reports of fatal overdoses led to its discontinuation in 1939. Which of the following would most likely be true concerning individuals taking 2,4-DNP ?

a. ATP levels in the mitochondria are greater than normal.
b. Body temperature is elevated as a result of hypermetabolism.
c. The proton gradient across the inner mitochondrial membrane is greater than normal.
d. The rate of electron transport is abnormally low.

Q2: Which of the following has the strongest tendency to gain electrons?

a) Coenzyme Q **b)** Cytochrome c **c)** NAD^+ **d)** Oxygen

Q3: Which one of the following is not a site-specific inhibitor of ETC:

a) Rotenone **b)** Antimycin A **c)** CN^- **d)** Ca

Q4: Which one of the following is a non-protein member of ETC:

a) CoEnzyme Q **b)** CytoChrome BC_1 **c)** CytoChrome C **d)** CytoChrome $a+a_3$

Q5: Number of protein complexes which are part of ETC:

a) 2 **b)** 4 **c)** 3 **d)** 5

Q6: The amount of energy **required** for phosphorylation of ADP to ATP is:

a) 52.58 Kcal/mol **b)** 7.3 Kcal/mol **c)** 8.6 Kcal/mol **d)** 3.7 Kcal/mol

SAQs

Q1: What is the function of complex I (NADH Dehydrogenase)?

Q2: What are the components of cytochromes?

Q3: CO binds to and inhibits Complex IV of the electron transport chain. What effect, if any, should this respiratory inhibitor have on phosphorylation of ADP to ATP?

Q4: Mention two inhibitors of ATP synthesis.

★ **MCQs Answer key:**

1) B 2) D 3) D 4) A 5) B 6) B

★ **SAQs Answer key:**

1) Collects pair of electrons from NADH and pass it to CoQ .
2) A protein that contains Heme group porphyrin ring + iron in Fe 3^+ state)
3) Results in an inability to maintain the proton (H^+) gradient. Therefore, phosphorylation of ADP to ATP is inhibited, as are ancillary reactions such as calcium uptake by mitochondria, because they also require the H^+ gradient.
4) Oligomycin , Uncoupling proteins (UCPs)

This lecture was done by

Girls team :

- Ajeed Al-rashoud
- Alwateen Albalawi
- Elaf Almusahel
- Lina Alosaimi
- Nouf Alhumaidhi
- Noura Almazrou
- Noura Alturki
- Nouran Arnous
- Reem Alqarni
- Shahd Alsalamh
- Taif Alotaibi

Boys team :

- Abdullah Altuwaijri
- Alkaseem binobaid
- Fares Aldokhayel
- Naif Alsolais
- Saad Dammas

كل العقبات التي كُنت تجزم على أنكَ لن تتجاوزها هي اليوم خلفك فأحلم واسعى لتحقيق حلمك.

438 BIOCHEMISTRY TEAM

Team leaders:

Deema Almaziad

Mohannad Alqarni