CYTOLOGY

Premed 2018 - JU

◉ Sheet ○ Slides

Number

11

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Phagocytosis

- Is the process the cell eats **something from outside** such as bacteria (this process contains the formation of pseudopodia)

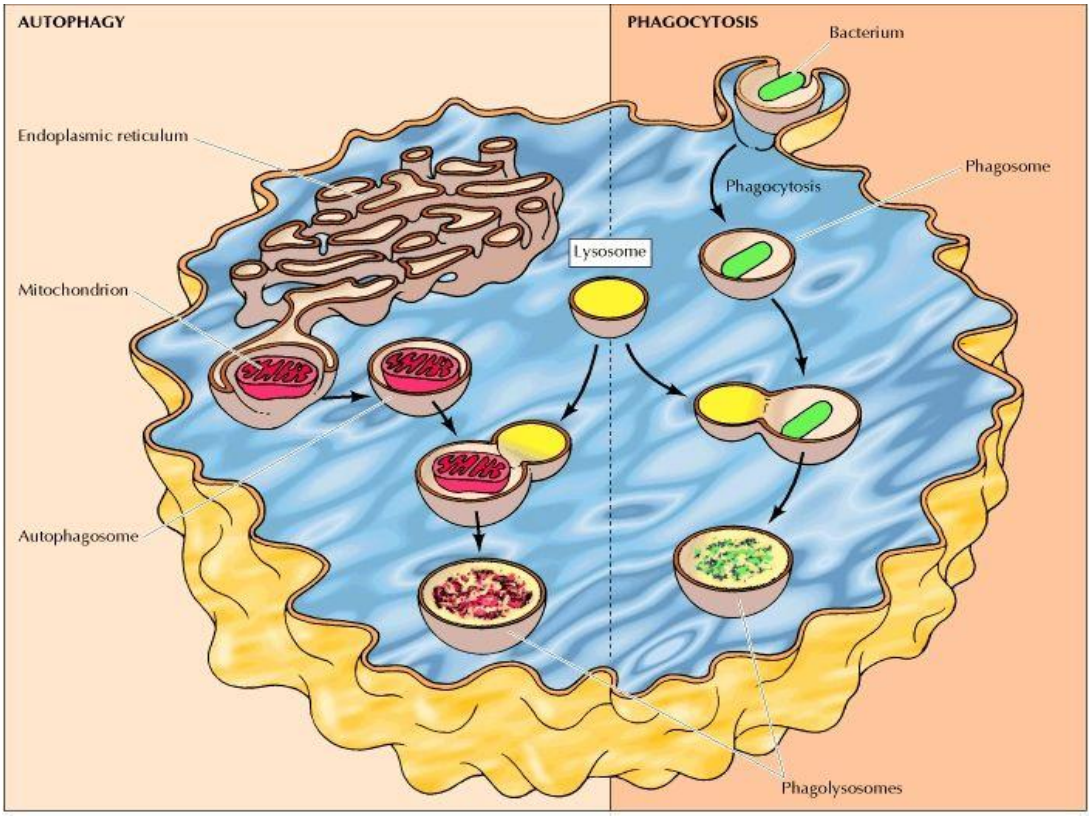
- The particles are transferred to the lysosome by a phagosome (which is a vacuole in the cytoplasm of a cell, containing a phagocytosed particle which enclosed within a part of the plasma membrane) to be hydrolyzed there.

Autophagy

- The same as the phagocytosis but here the cell eats **its own components**.

- This happens when the cell doesn't need some of its components.

- The cell encloses the unnecessary part in a cytosolic membrane which makes something called an autophagosome that transfers the unnecessary part to the lysosome and fuse with it to hydrolyze its contents.



- Look at the picture above. The autophagy is done on the mitochondrion to reduce the energy usage in the cell (although mitochondria is the energy factory in the cell, but it also need a lot of energy to do its work).

-Why do the cells do this process?

For example:

* If there's a problem in an organelle, the cell doesn't need it.

* To rescue the cell from death when there's a lot of organelles and a small amount of energy.

If this failed, the cell is going to activate the process of programmed cell death which called apoptosis.

Note: **apoptosis** (program cell death) is a normal death of the cell as a part of the organism's development or growth (e.g. embryo's growth) while **necrosis** **(associated with diseases)** is the death due to a disease.

وعاجز الرأي مضياع لفرصته *** حتى إذا فات أمر عاتب القدرا

Mitochondria

- Function: generation of metabolic energy in eukaryotic cells – Generation of ATP from the breakdown of carbohydrates and fatty acids.

-Energy factory.

- Most mitochondrial proteins are translated on free cytosolic ribosomes and imported into the organelle.

-Membrane enclosed (double membrane).

Mitochondrial structure:

1- Outer membrane.

2-Inner membrane.

3- Matrix.

4- Intermembrane space.

-The outer membrane is highly permeable to small molecules while the inner is not, why?

→ Because of its porins.

-There's an intermembranous space (similar in composition to the cytosol) between them (inner and outer membranes) where some processes take place but the majority happen in the inner membrane and in the matrix.

- Intermembrane space = intracristal space + peripheral space

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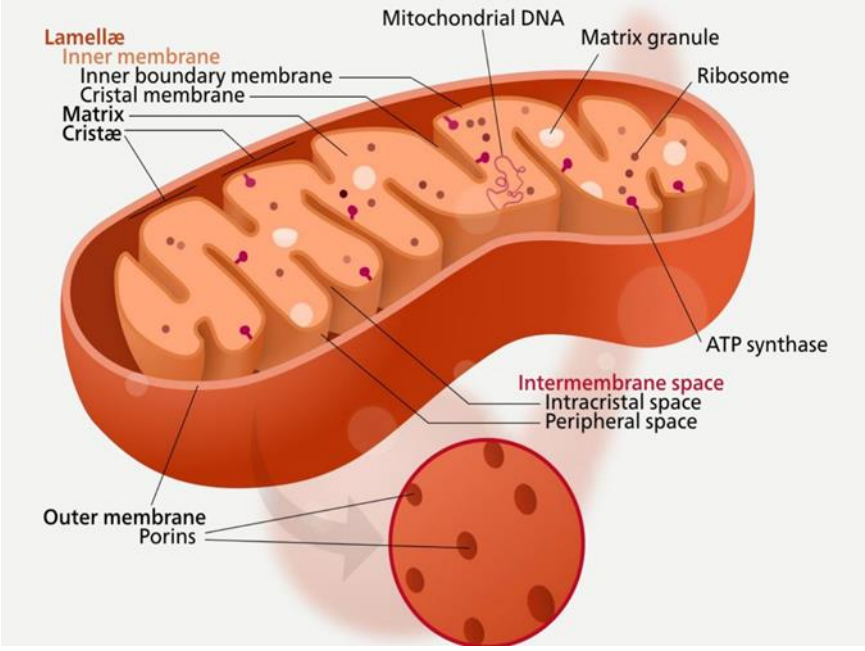
-The inner membrane is characterized by extensions into the matrix which called **cristae (its importance is to increase surface area)**.



-There's a lot of proteins in the inner membrane which constitute more than 70% of the membranous structure.

- Inner membrane has an important role in oxidative phosphorylation, ATP generation and transport of metabolites (pyruvate and fatty acids).

- Inner membrane is also Impermeable to most ions and small molecules, thus maintains H+ gradient that drives oxidative phosphorylation.

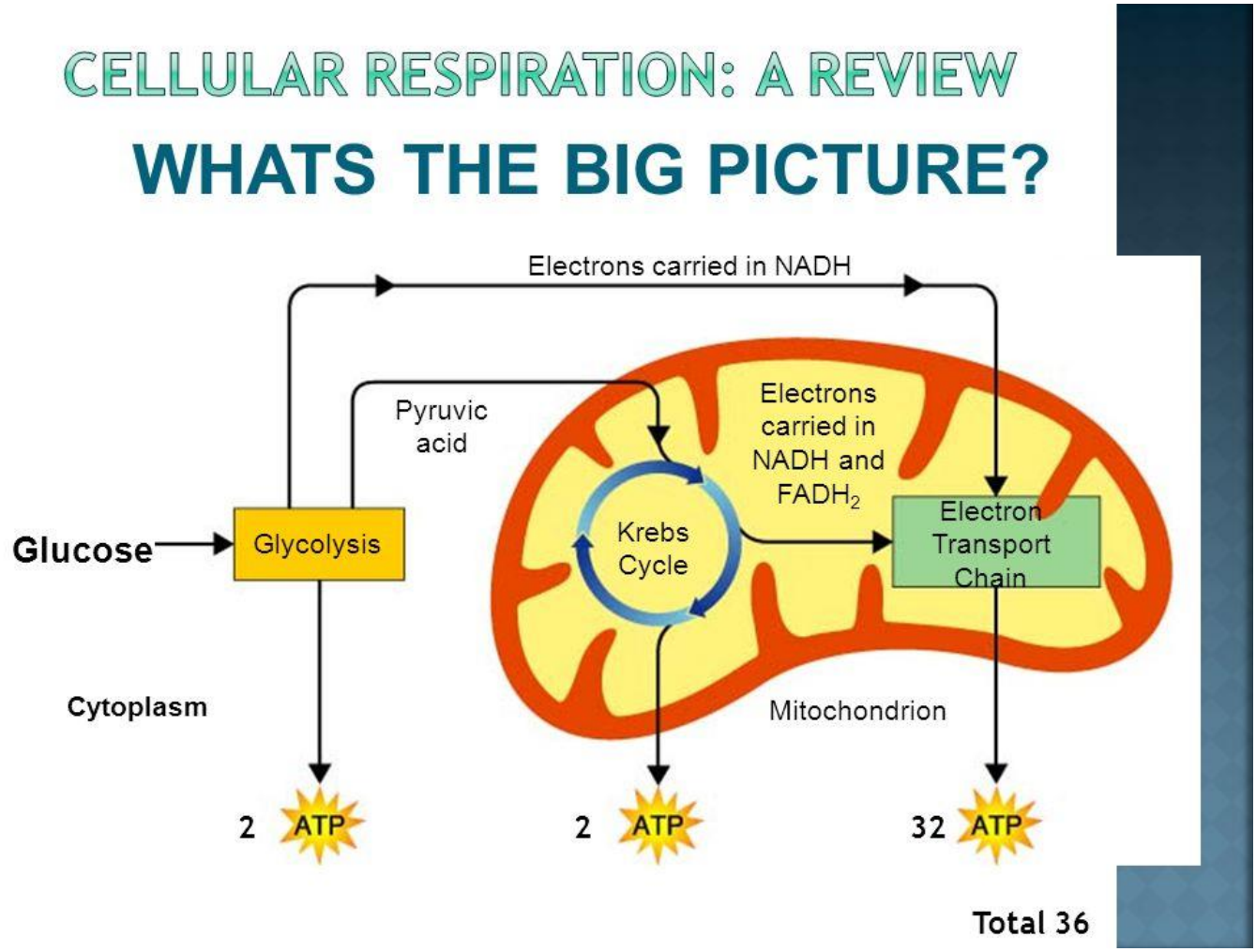
-What distinguish the mitochondria is the presence of the DNA.

- Mitochondrial DNA encodes tRNAs, rRNAs, some mitochondrial proteins, and some mitochondrial enzymes.

-The mitochondrial DNA is a cyclic DNA like in bacteria.

-Some of its proteins and enzymes are encoded in this DNA.

-It generates energy from sugars and fatty acids by the process of cellular respiration.



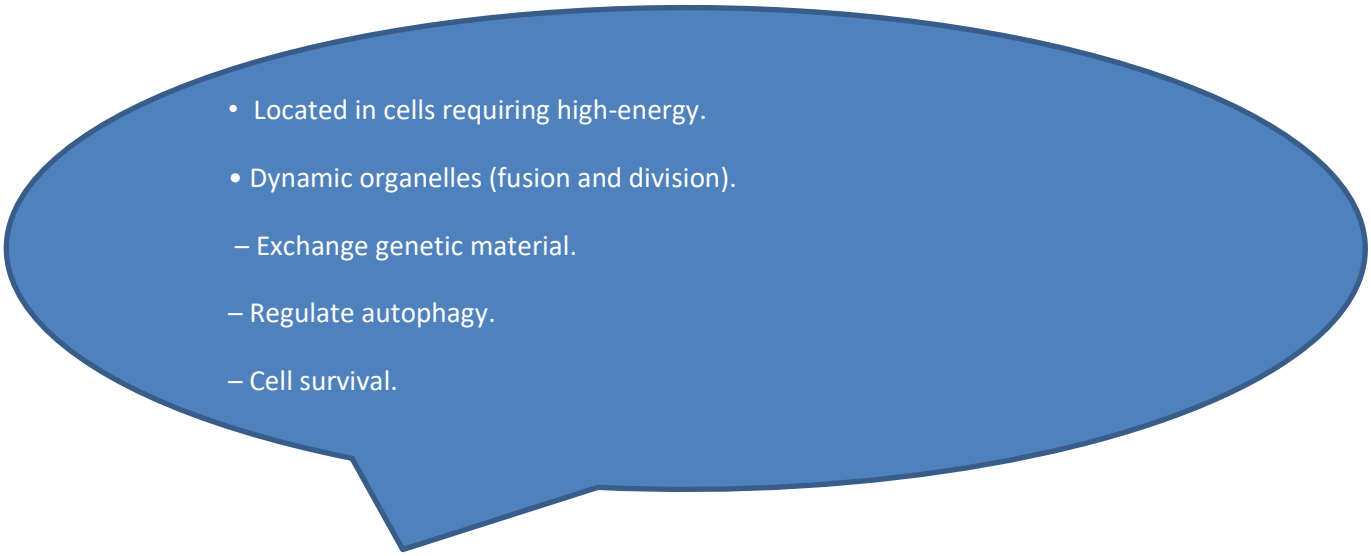
-What is included about the cellular respiration is as follows:

1)Krebs cycle is where the largest number of NADH & FADH2 is produced (by the oxidation of the pyruvate).

2)In the glycolysis, two pyruvate molecules are derived from the glucose molecule.

3)The ATPs are generated from the electron carriers (NADH & FADH2) in the electron transport chain.

Mitochondrial fusion Vs fission



-In the autophagy, we get rid of some mitochondria, but when the cell is normal again the number of mitochondria is increased again by mitochondrial **fission** (division) **& fusion** (both processes happen in an equilibrium under different conditions).

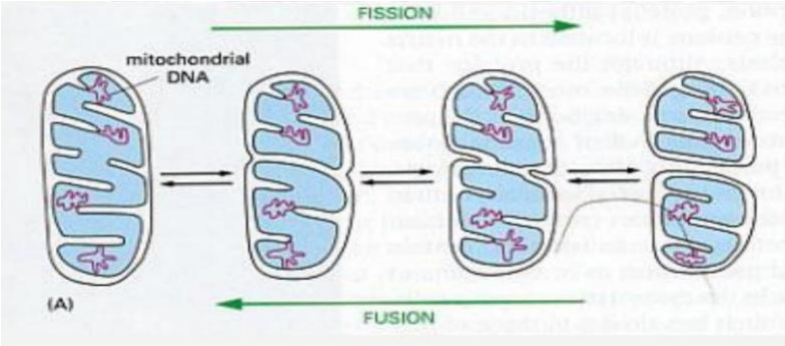
When does fusion happen and when does fission happen?

1)**Fusion**: (Centralization)

A) *The oxidative capacity* of the mitochondria is increased.

- two mitochondria = One large mitochondrion.

fusion ⟶ Larger surface area ⟶ larger number of proteins ⟶ more efficient removal of the oxidative stress because of the increasing in the number of the efficient reactions.



B) Repair of the abnormal mitochondrion (not always) by fusing it with a normal one.

c) Limitation of mtDNA mutations during aging.

Mitochondrial mutation during aging

-The mitochondrial DNA may get exposed to some factors which change the structure to generate mutations (not inherited mutations).

-When a mitochondrion with a mutation in its DNA fuse with a normal one, the normal one will affect the abnormal so ***the number of mutations that are transmitted to the next generation is decreased***.

2)**Fission**: (Decentralization)

A) increasing in *resistance to oxidative stress*.

- After fusion, I have a larger number of mitochondria and they are able to deal better with the oxidative stress.

B) segregation of damaged mitochondria.

- The damaged part will go to autophagy (mitophagy) and the normal part will continue its work as a normal mitochondrion.

Autophagy: eating of internal structures that including mitochondria.

Mitophagy: type of autophagy specifically for mitochondria.

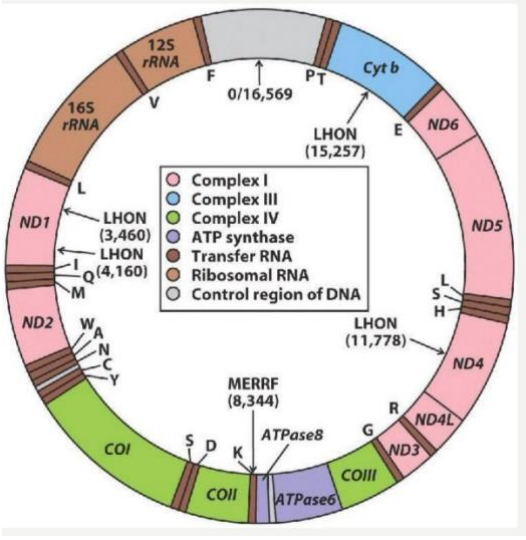
The genetic system of mitochondria

- In the mitochondrial DNA (which is circular DNA) there's 16000 base pairs whereas in the nuclear DNA there's about 3 billion pairs.

- Multiple copies per organelle.

-What about genes?

*The mitochondrial DNA encodes for only 13 protein (involved in electron transport chain and oxidative phosphorylation), 2 rRNAs (16S + 12S) , and 22 tRNAs (20 code for amino acids and the other two tRNAs code for stop codons).



-There's a theory claims that the mitochondrial DNA comes from a bacterium through a process called **endosymbiosis**.

Mitochondrial genetic code and mutations

- Different genetic code by tRNA.
- Only 22 tRNA.
- Germ-line mutations in mito-DNA.
- Mutations in mito-tRNA genes result in:
Metabolic syndrome (diabetes and obesity).

- Mutations in mitochondrial genes of electron transport chain result in Leber's hereditary optic neuropathy. (Doctor doesn't mention this in the lecture)

-When fertilization happens between an ovum and a sperm, the sperm only inters its nucleus into the ovum so we just get the two nuclei and the cytosol of the ovum so all of your mitochondria come from your mom.
We conclude that any mitochondrial inherited disease comes from the ovum.

-From the table below (the difference in codes between nuclear & mitochondrial DNA) :

Notice that AGG codes nuclear DNA for Arg whereas it's a stop codon in mitochondria so they differ in their codes.

Universal = Nuclear.

Table 12.1 Differences between the Universal and Mitochondrial Genetic Codes

Codon	Universal code	Human mitochondrial code
UGA	Stop	Trp
AGA	Arg	Stop
AGG	Arg	Stop
AUA	Ile	Met

-The proteins synthesized in mitochondrial DNA are mostly involved in the metabolism.

That's why when we get mutations on these proteins, this resulting in genetic mitochondrial diseases, they are going to affect the electron transport chain and it might cause obesity (for example).

Thank you all, I love you all, have a good time.

إن أردتَ الشفاءَ فاقْصِدْ طَبيباً
حَاذِقاً ذا لطافةٍ وذكاءِ

واحترسْ أن يكونَ فَظّاً غَليظاً
إنَّ لُطْفَ الطبيبِ نِصْفُ الدَّواءِ