10

Cytology

Doctor 2019 | Medicine | JU

◉ Sheet ○ Slides

Done By

AHMAD AYMAN

Contributed in the Scientific Correction

IBRAHIM MAJED

Contributed in the Grammatical Correction

IBRAHIM MAJED

Doctor

DR. AMER AND DR. ZIAD

WHY WE NEED TO BREATHE ?!!

To extract Oxygen of course. 😂

The early Earth was populated by anaerobes, which captured and utilized energy by oxygen-independent metabolism like glycolysis and fermentation.

Oxygen accumulated in the primitive atmosphere after cyanobacteria appeared, which carried out a new type of photosynthetic process in which water molecules were split apart and molecular oxygen was released.

Aerobes evolved to use oxygen to extract more energy from organic molecules, and they eventually gave rise to all of the oxygen-dependent prokaryotes and eukaryotes living today.

In eukaryotes, the utilization of oxygen as a means of energy extraction takes place in a specialized organelle, the mitochondrion.

Much of human anatomy and physiology is devoted to ensuring an adequate Oxygen supply. (This statement means that a lot of our organs and systems are designed to provide enough Oxygen to all of our cells.)

Oxygen is used by our cells to power cellular metabolism by providing energy through the pathway of respiration. (This means that oxygen is required to extract energy from food.)

Without the ability to use oxygen, organisms could only extract a limited amount of energy from their foodstuff. In contrast, organisms that incorporated O_2 into their metabolism could extract much higher percentage of their foodstuff energy content.

MITOCHONDRIA IN CELLS

Depending on cell type, mitochondria can have a very different overall structure. They can appear as individual bean-shaped organelles, or as a highly branched, interconnected tubular network.

Size and number of mitochondria reflects the energy requirements of cells (If you look inside muscle fibers ,cardiac or skeletal, you'll find that mitochondria present in large numbers, arranged in rows between the *myofibrils* where we have actin and myosin filaments. Also, if a cell is active in motility or secretion you'll find a large amount of mitochondria)

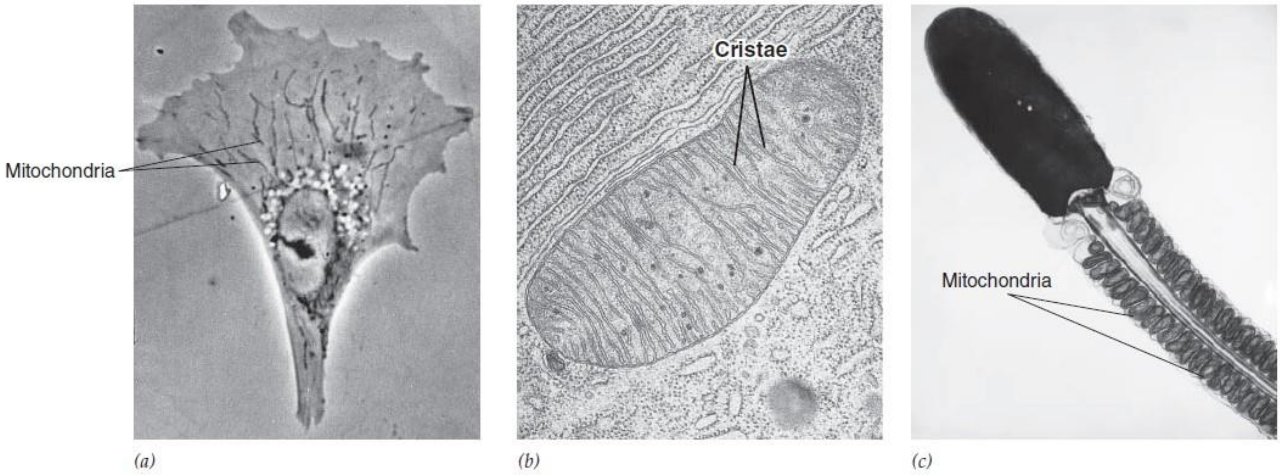


Figure (a) shows a living fibroblast (a cell type in connective tissues).

Figure (c) shows localization of mitochondria in the midpiece surrounding the proximal portion of the flagellum of a sperm (The movement of a sperm are powered by ATP produced in these mitochondria .)

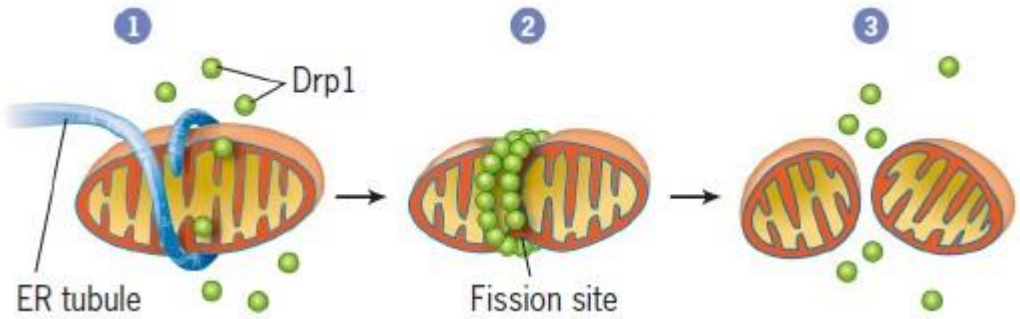
DYNAMISM OF MITOCHONDRIA

Mitochondria can fuse with one another or split in two (fission).

The balance between fusion and fission is likely a major determinant of mitochondrial number, length , and degree of contraction.

Mitochondrial fission is apparently induced by contact with thin tubules from the ER which can encircle the mitochondrion like a noose.

These *ER tubules* appear to initiate constriction, which is then completed through the action of soluble proteins that are recruited to the outer surface of the mitochondrion from the cytosol .



OTHER FUNCTION CARRIED OUT BY MITOCHONDRIA

The main function of them is cellular respiration, to accomplish this function, mitochondria are often associated with fatty-acid-containing oil droplets from which they derive raw materials to be oxidized .

Mitochondria occupy 15 to 20 percent of the volume of an average mammalian liver cell and contain more than a thousand different proteins.

While energy metabolism has been the focus of interest in the study of mitochondria, these organelles are also involved in other activities :

1-Mitochondria are the sites of synthesis of numerous substances, including certain amino acids and the heme groups (in cytochromes) .

2- Mitochondria also play a vital role in the uptake and release of calcium ions, which are essential triggers for cellular activities (A function shared with smooth ER).

3- Cell death, which plays an enormous role in the life of all multicellular animals, is also regulated by events that occur within mitochondria.

MITOCHONDRIAL STRUCTURE

The outer boundary of a mitochondrion contains two membranes: the outer mitochondrial membrane and the inner mitochondrial membrane.

The outer mitochondrial membrane serves as its outer boundary (encloses the whole mitochondrion) and the inner mitochondrial membrane is divided into two major domains that carry out distinct functions and have different protein residents (The inner boundary membrane and the cristae) .

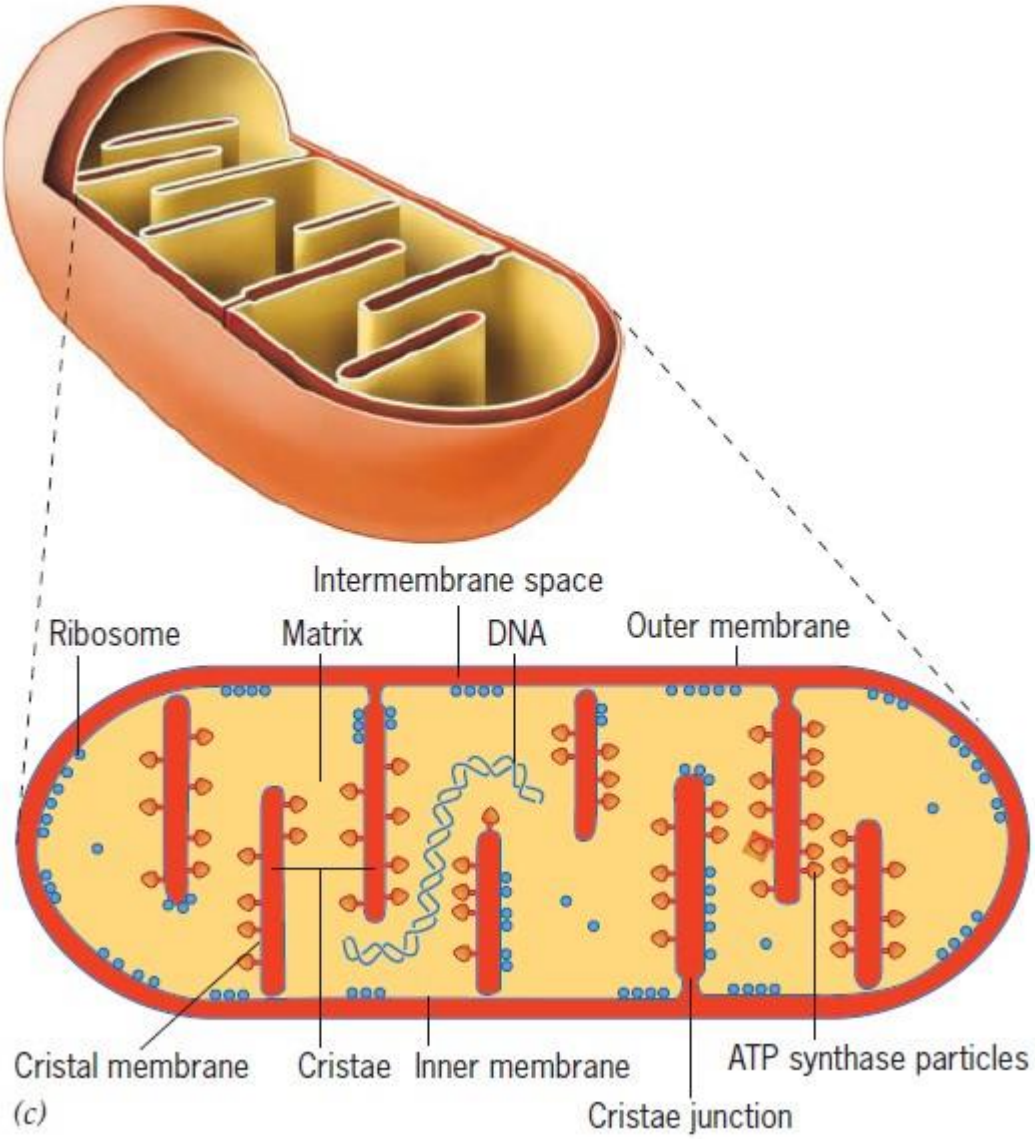
The inner boundary membrane domain is rich in the proteins responsible for the import of mitochondrial proteins and forms with the outer membrane a double-membrane envelope.

The other domain lies in the interior of the organelle as a series of invaginated membranous sheets, called ***cristae***.

The cristae contain a large amount of membrane surface which houses the machinery needed for aerobic respiration and ATP formation.

The inner boundary membrane and internal cristal membranes are joined to one another by narrow tubular connections, or cristae junctions.

The membranes of the mitochondrion divide the organelle into two aqueous compartments, one within the interior of the mitochondrion, called the matrix, and a second between the outer and inner membrane, called the intermembrane space.



The compartments of the mitochondrion and its membranes .

The membranes of the mitochondrion divide the organelle into two aqueous compartments : one within the interior of the organelle , called the ***matrix*** and one between the inner and outer membranes called the intermembrane space. (look at the figure up)

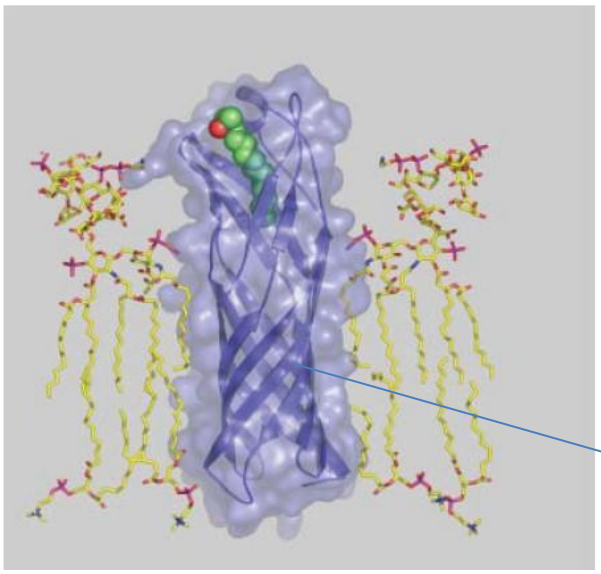
The outer membrane is about 50% protein and contains a large pore-forming protein called porin as well as a curious mixture of enzymes involved in such diverse activities as:

1- Oxidation of epinephrine (adrenaline)
2- The degradation of tryptophan (an amino acid)
3- Elongation of fatty acids

The inner membrane is more than 75% protein, it contains cardiolipin but not cholesterol, both are true of bacterial membranes.

The outer membrane contains a large pore-forming protein called porin (which are integral proteins that have a relatively large integral channel surrounded by a β strands).

The inner membrane is impermeable to even small molecules, virtually all molecules and ions require special membrane transporters to gain entrance to the matrix (which is important for generating an H^+ gradient)



The β strands

The porin (which makes the outer membrane more permeable)

The mitochondrial matrix

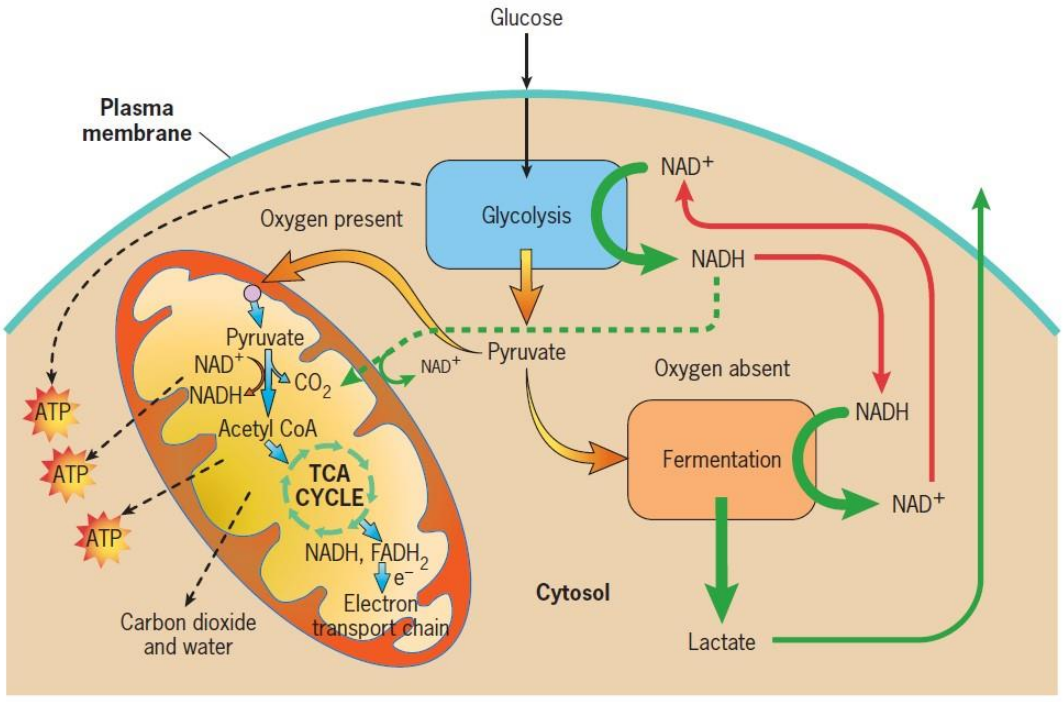
The mitochondrial matrix contains ribosomes (of considerable smaller size than those found in cytosol) and several molecules of circular DNA to manufacture their own RNAS and proteins.

The DNA encodes a small number of mitochondrial polypeptides (13 in humans) that are tightly integrated into the inner mitochondrial membrane along with polypeptides encoded by genes residing within the nucleus.

Mitochondrial DNA (mtDNA) is a relic thought to be the legacy from a single aerobic bacterium that took up residence in the cytoplasm of a primitive cell that ultimately became an ancestor of all eukaryotic cells.

For a number of reasons, mtDNA is well suited for use in the study of human migration and evolution.

The mitochondrial matrix is the site of *TCA CYCLE* .



PEROXISOMES

Peroxisomes are membrane- bound vesicles that contain oxidative enzymes.

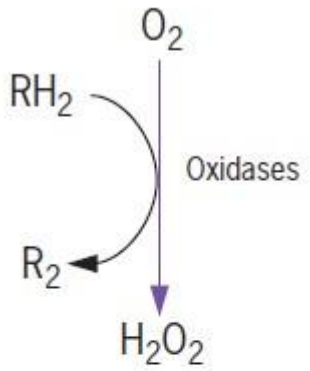
These organelles were named peroxisomes because they are the site of synthesis and degradation of hydrogen peroxide (H_2O_2), a highly reactive and toxic oxidation agent , which is produced by a number of peroxisomal enzymes

They oxidize very-long-chain fatty acids, and synthesize plasmalogens (a class of phospholipids).

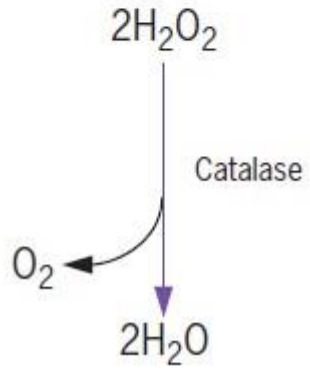
They form by splitting from pre- existing organelles, import preformed proteins, and engage in oxidative metabolism.

Hydrogen peroxide, is formed in peroxisomes and is broken down by the enzyme catalase. (Into O_2 and H_2O)

It's important to notice that removing hydrogen from compound involves oxidation and vice versa.



Peroxisomes contain enzymes that carry out the two-step reduction of molecular oxygen to water . In the first step , on oxidase removes electron from a variety of substrates (RH_2) such as uric acid or amino acids . In the second step the enzyme catalase converts the hydrogen peroxide formed in the first step to water.

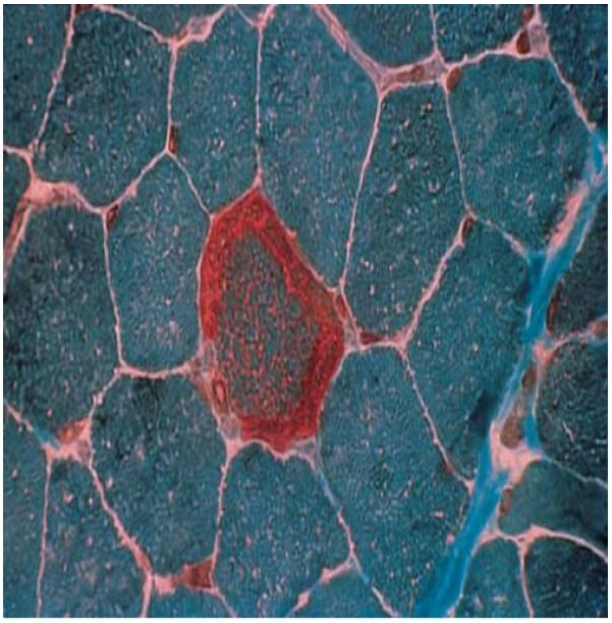


DISEASES THAT RESULT FROM ABNORMAL MITOCHONDRIAL OR PEROXISOMAL FUNCTION

A variety of disorders result from abnormalities in mitochondria structure and function; *most are characterized by degeneration of muscle or brain tissue, both use large amounts of ATP.*

Conditions range from diseases that lead to death during infancy; to disorders that produce seizures, blindness, deafness, and/or stroke-like episodes; to mild conditions like intolerance to exercise or non-motile sperm.

The majority of mutations linked to mitochondrial diseases are traced to mutations in mtDNA and are inherited maternally (Means from the mother only , that because we inherited our mtDNA from our moms only, the mitochondria present in a cell of a human embryo are derived exclusively from mitochondria that were present in the egg at the time of conception without any contributions from the sperm)



degenerating muscle shows red-staining blotches due to abnormal proliferation of mitochondria

mtDNA Mutations

Accumulations of mutations in mtDNA is considered a major cause of aging.

Mice homozygous [1] for a mutant gene (called Polg) that encodes the enzyme that replicates mtDNA accumulate more mutations than normal littermates.

1 : (homozygous means : having two identical copies of the same gene متماثل الطراز)
(الجيني like what we studied in tawjihi)

These "mutator" mice appear normal for the first 6 to 9 months of age, but then rapidly develop signs of premature aging, such as hearing loss, graying hair, and osteoporosis; their lifespan is reduced in half.

Additional findings suggest that mutations in mtDNA may cause premature aging but are not sufficient for the normal aging process.

A premature-aging phenotype caused by increased mutations in mtDNA

Zellweger syndrome

(ZS) is a rare inherited disease characterized by a variety of neurologic, visual, and liver abnormalities leading to death during early infancy.

Patients with Zellweger syndrome lack peroxisomal enzymes due to defects in translocation of proteins from the cytoplasm into the peroxisome.

ZS can arise from mutations in at least 12 different genes, all encoding proteins involved in the uptake of peroxisomal enzymes from the cytosol.

X-ALD

Adrenoleukodydstrophy (X-ALD) is caused by lack of a peroxisomal enzyme, leading to fatty acid accumulation in the brain and destruction of the myelin sheath of nerve cells. In Lorenzo's Oil, the parents of a boy stricken with X-ALD discover that a diet rich in certain fatty acids is able to retard the progress of the disease.

REVISION

The organelle that is involved in fission of mitochondria is :

A) Peroxisome
B) Rough Endoplasmic Reticulum
C) Microfilaments
D) Vesicles

The Enzymes that remove two hydrogen atoms from organic substrates are called :

A) Hydrases
B) Catalases
C) Oxidases
D) None

The Disease that results from lack of a peroxisomal enzyme :

A) X-ALD
B) Deafness
C) Zellweger
D) A+C

Elongation of fatty acids takes place in :

A) Mitochondrial matrix
B) Cristae
C) Intermembrane space
D) Outer membrane

The organelle that is involved is oxidative metabolism :

A) Mitochondrion
B) Peroxisome
C) Nucleus
D) A +B

THANK YOU !