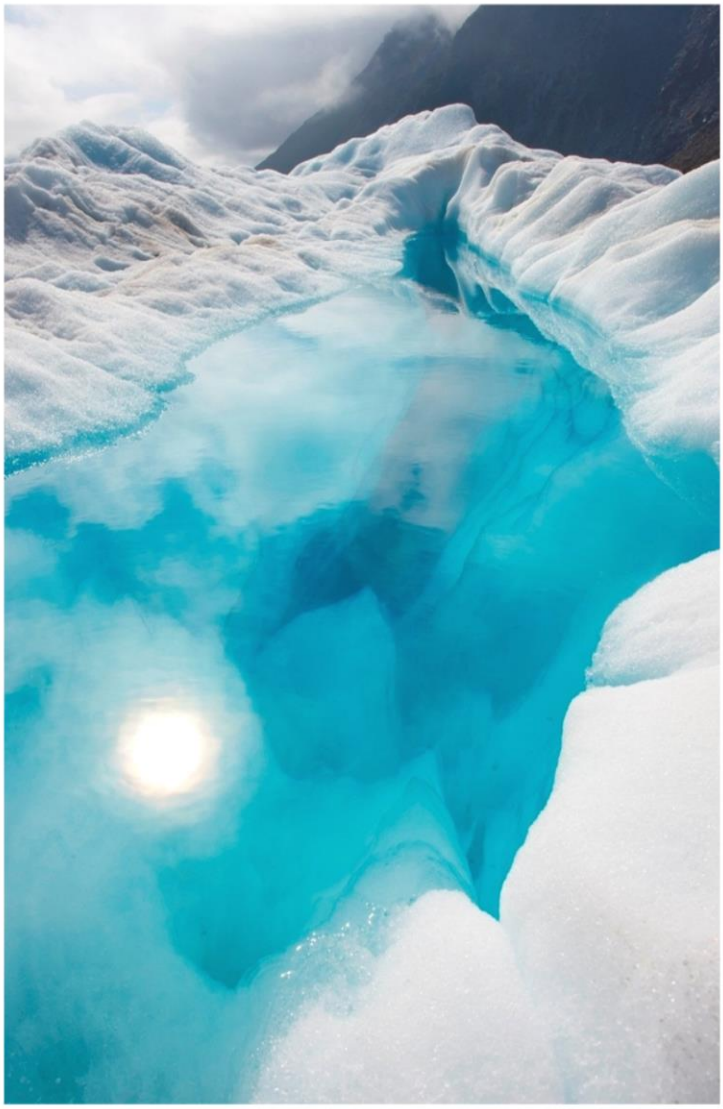


Mitochondrion and aerobic respiration

CHAPTER (9)

Done by: Abdelhadi Okasha
5th Sheet

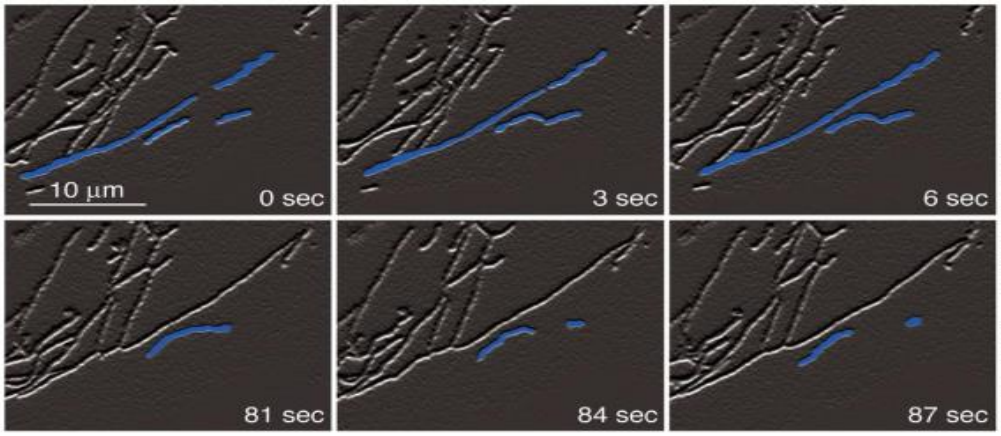
9.0 | Why We Need to Breathe (Not important)

-To provide cells with oxygen: blood runs red with hemoglobin carrying it.
- Much of human anatomy and physiology is devoted (مصمم) to ensuring an adequate (كافي) oxygen supply.
- Oxygen is used to power cellular metabolism by providing energy through the biochemical pathway of respiration, much of which takes place within mitochondria (in eukaryotic cells).

9.1 | Mitochondrial Structure and Function

- Anaerobes (لا تستخدم الأكسجين في انتاج الطاقة -أقل انتاجًا طاقة-)
- Aerobes (تستخدم الأكسجين في انتاج الطاقة -أكثر انتاجًا طاقة-)
- The early Earth was populated by anaerobes, which captured and utilized energy by oxygen-independent metabolism like glycolysis and fermentation, but before 2.4 and 2.7 billion years, cyanobacteria appeared and carried out a new type of photosynthetic process in which water molecules were split apart and molecular oxygen was released.
- Aerobes appeared after that and used oxygen to extract more energy from organic molecules.
- In eukaryotes, the utilization of oxygen as a means of energy extraction takes place in a specialized organelle, the mitochondrion.

- Mitochondria are large enough to be seen in the light microscope, so they were discovered in early stages
-mitochondria have a very different overall structure→depending on the cell type
-Typical mitochondria are bean-shaped organelles, and may be round or threadlike, it may appear branched, interconnected tubular network.
-fibroblast has an elongated mitochondria
- Size and number of mitochondria reflect and depends on the energy requirements of the cell.
- Mitochondria are dynamic organelles capable of dramatic changes in shape.
- Mitochondria can fuse with one another (fusion), or split in two (fission).
- The balance between fusion and fission is likely a major determinant of mitochondrial number, length, and degree of interconnection.



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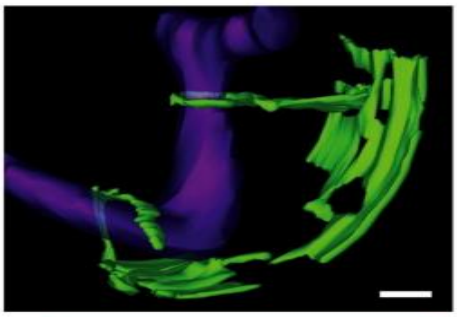
Dynamic nature of mitochondria revealed in mouse fibroblasts with a fluorescent tagged mitochondrial protein.

-Mitochondrial fission is apparently induced by:

1. contact with thin tubules from the ER, which can encircle the mitochondrion like a noose and initiate constriction

2) soluble proteins (Drp1 in mammals) form helices the outer surface of the mitochondrion from the cytosol.

3) GTP binding and hydrolysis causes a conformational change in the Drp1 helices that fully constricts the mitochondrion, splitting it into two smaller organelles



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3D model of contacts between ER and mitochondria

Model for mitochondrial fission: ER tubules and Drp1 mediate mitochondrial constriction.

- Mitochondria occupy 15 to 20 percent of the volume of an average mammalian liver cell, and contain more than a thousand different proteins.
- (Main function of mitochondria:) generate ATP, (How?) mitochondria are often associated with fatty acid containing oil droplets from which they derive raw materials to be oxidized.
- A number of inherited neurologic diseases are caused by mutations in genes that encode components of the mitochondrial fusion machinery

other functions of mitochondria:

1)synthesis of numerous substances, like certain amino acids and the heme groups.

2)uptake and release of Ca ions, (Function) essential triggers for cellular activities

3) Cell death (regulated by events that occur within mitochondria)

Mitochondrial Membranes

- The mitochondria contains two membranes:

1.outer membrane: serves as its outer boundary

2.inner membrane: subdivided into two major domains that have different protein residents and carry out distinct functions.

-these two domains are:

a) inner boundary membrane: rich in the proteins responsible for the import of mitochondrial proteins.

b) cristae: lies in the interior of the organelle as a series of invaginated membranous sheets, They contain a large amount of membrane surface, which houses the machinery needed for aerobic respiration and ATP formation.

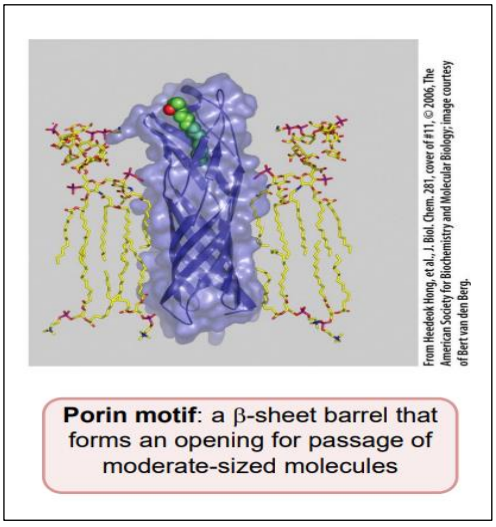
- cristae junctions: narrow tubular connections that joins the inner boundary membrane and internal cristal membranes.

- an inner membrane associated protein complex called MitOS, (also known as MICOS or MINOS) is located at the cristae junctions and is required for normal organization of cristae.

- The mitochondria is divided into two aqueous compartments:

1) intermembrane space: between the outer and inner membrane

2) matrix: it's within the interior of the mitochondrion, it has a gel-like consistency owing to the presence of a high concentration (up to 500 mg/ml) of water-soluble proteins, that are used for cell suicide



- Outer and inner membrane properties:

1) Outer membrane:

a- it is composed of %50 lipid by weight and %50 proteins

b- it also contains a mixture of enzymes for many activities such as oxidation of epinephrine, the degradation of tryptophan, and the elongation of fatty acids.

c- Contain porins, porin is : (protein) a b-sheet barrel that forms an opening for passage of moderate-sized molecules

2) Inner membrane:

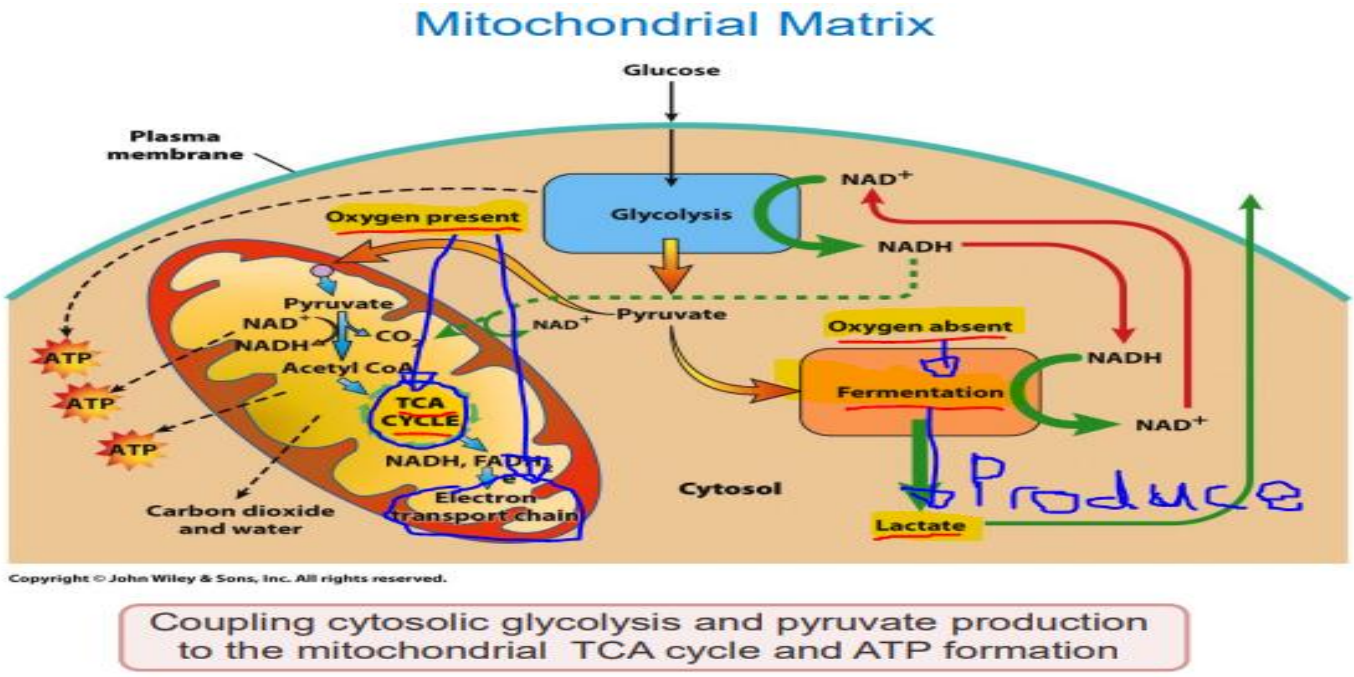
a- more than 75% protein, on the other hand: lipids are about 25%

b- The inner membrane is impermeable to even small molecules, virtually all molecules and ions require special membrane transporters to gain entrance to the matrix.

c- The inner membrane contains cardiolipin but not cholesterol, both are true of bacterial membranes.

Mitochondrial Matrix

- The mitochondrial matrix contains ribosomes (smaller of the cytosol's) 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 (مدمجة) with polypeptides encoded by genes in the nucleus, this happens inside the inner mitochondrial membrane.
- Human mitochondrial DNA also encodes 2 ribosomal RNAs and 22 tRNAs that are used in protein synthesis within the organelle.
- 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. (*)



Coupling cytosolic glycolysis and pyruvate production to the mitochondrial TCA cycle and ATP formation

- After glycolysis, if the cell is

a) aerobic: TCA cycle and electron transport chain will happen in mitochondria to produce energy

b) anaerobic: Fermentation will occur to produce lactate so we can make more glycolysis in cytosol

9.9 | Peroxisomes

- Definition: membranebound vesicles that contain oxidative enzymes.
- Function:

1) They oxidize very-long-chain fatty acids (24 to 26 carbons)
2) and synthesize plasmalogens (an unusual class of phospholipids that are very abundant in the myelin sheaths that insulate axons in the brain, so loss of them will cause neurons dysfunction)

- Peroxisomes and mitochondria are similar in many things, such as form by splitting from preexisting organelles, import preformed proteins, and engage in oxidative metabolism.
- How do they form?

They form by splitting from preexisting organelles

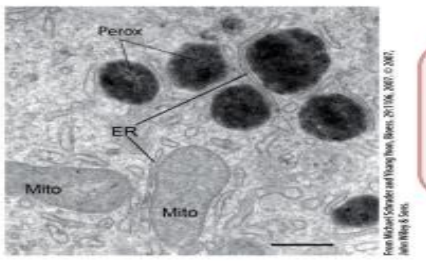
- Why peroxisomes were named like that?

because they are the site of synthesis and degradation (by catalase) of hydrogen peroxide (H_2O_2) , a highly reactive and toxic oxidizing agent.

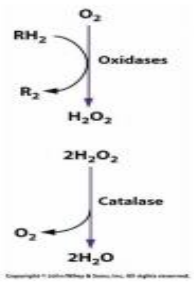
- Peroxisomes are also present in plants; plant seedlings contain a specialized type of peroxisome, called a glyoxysome.
- Plant seedlings rely on stored fatty acids to provide the energy and material to form a new plant.
- One of the primary metabolic activities in these germinating seedlings is the conversion of stored fatty acids to carbohydrate.

Fatty acids → Acytel CoA → Citrate → glucose
Oxaloacetate → Citrate

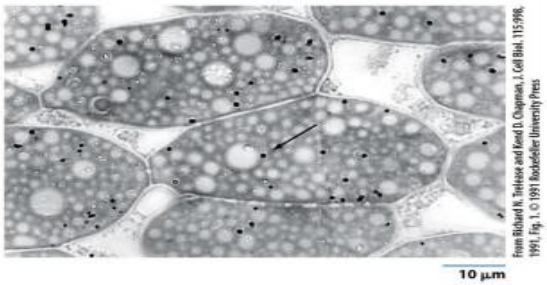
(series of enzymes of the glyoxylate cycle localized in the glyoxysome)



Electron micrograph of a rat liver cell section stained for catalase



Peroxisomes contain enzymes to carry out the two-step reduction of molecular oxygen to water



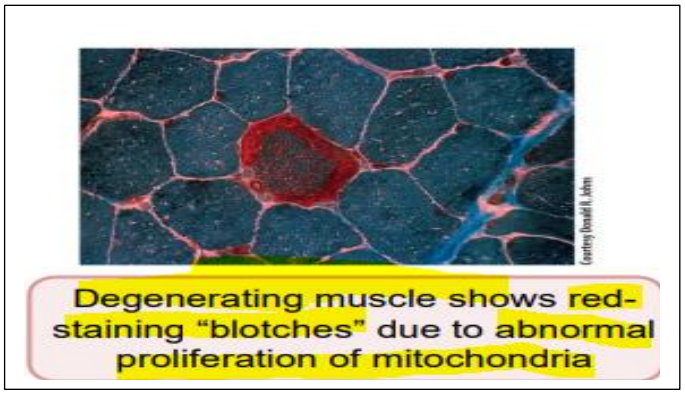
Glyoxysome localization within plant seedlings. Light micrograph of a section through cotyledons from imbibed cotton seeds. Glyoxysomes (arrow) have been made visible by a stain for catalase.

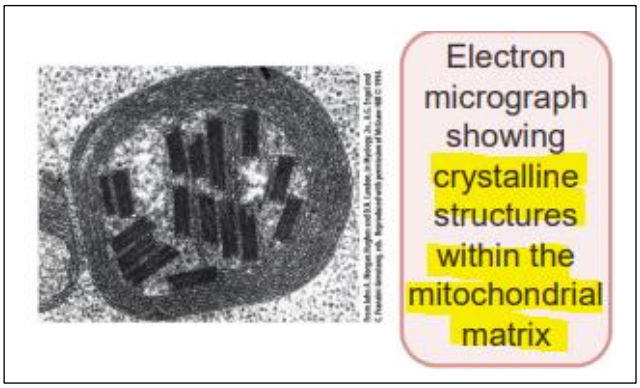
| The Human Perspective

- variety of disorders result from abnormalities in mitochondria structure and function; most are characterized by degeneration of muscle or brain tissue, (why?) both use large amounts of ATP.
- What are probable Conditions?

1) death during infancy.
2)disorders that produce seizures, blindness, deafness, and/or stroke-like episodes.
3) 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





- We'll take 3 diseases caused by genetic disorders in mitochondria/peroxisomes:

1) A premature-aging phenotype (in mice)

- Cause: Accumulations of mutations in mtDNA, because of mutation in nuclear gene called Polg, as polg is responsible of encoding the enzyme that replicates mtDNA (DNA Polymerase)

Note: mutation occur when mutant genes are homozygous

- Clinical symptoms: 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.

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

Cause: 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.

3) 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.