Medical Biology

Lec 4
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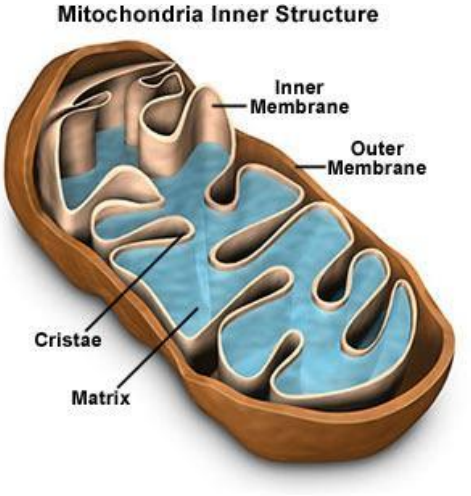
Mitochondria (powerhouse):

Are spherical or filamentous organelles 0.5- 1 µm wide and the length about 10 µm. their distribution in cell varies, they tend to accumulate in parts of the cytoplasm where metabolic activity is more intense, such as the apical ends of ciliated cells. These organelles transform the chemical energy of the metabolites present in cytoplasm into energy that is easily accessible to the cell.



About 50% of this energy is stored as high- energy phosphate bonds in ATP molecules. ATPase releases energy when required by the cell to perform the type of work, whether it be osmotic, mechanical, electrical, or chemical.

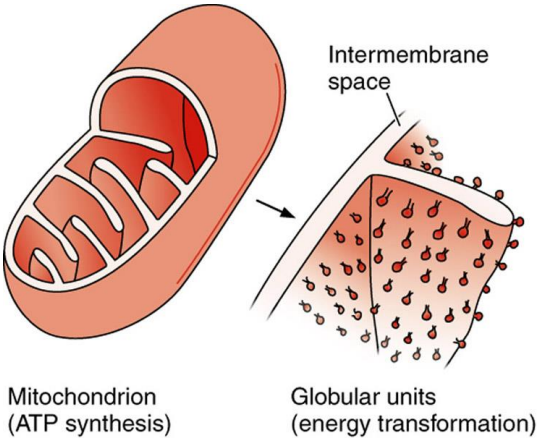
Mitochondria usually have a characteristic structure under the electron microscope, composed of an outer and an inner mitochondrial membrane. The inner membrane projects folds, called **cristae**.

Between the inner and outer mitochondrial membrane, the space is called **intermembrane space**. The compartment located between cristae called **intercristae, or matrix space**, is enclosed by the inner membrane.

The cristae:

- Increase the internal surface area of mitochondria.
- Contain enzymes and other components of oxidative phosphorylation and electron transport system.

The ADP to ATP phosphorylating system is located in globular structures connected to the inner membrane by cylindrical stalks.



The no. of mitochondria is related to the metabolic activity of the cells in which they reside.

Mitochondria are composed mainly of **protein, lipids, DNA and RNA.**

1. The DNA isolated from the mitochondrial matrix is double stranded and has a circular structure, very similar to that of bacterial chromosomes. These strands are synthesized within the mitochondria, their duplication is independent of nuclear DNA replication.
2. Mitochondria contain the 3 types of RNA: rRNA, mRNA and transfer RNA.
3. Mitochondrial ribosomes are smaller than cytosolic ribosomes. Protein synthesis occurs in mitochondria, but because of the reduced amount of mitochondrial DNA, only small proportion of the mitochondrial proteins is produced locally.

Metabolites are degraded within mitochondria by the catalytic activity of the enzymes of the citric acid cycle, and the energy liberated in this process is partially captured through oxidative phosphorylation. The result of these reactions is the production of Co_2, water, and heat, as well as the accumulation of energy in the high- energy compound ATP.

Mitochondrial permeability:

The outer membrane is freely permeable. The inner membrane is rather impermeable to ions and metabolites; therefore, it must use carrier for passage of these materials.

Mitochondrial functions:

1. convert organic materials into cellular energy in the form of ATP.
2. apoptosis (programmed cell death).
3. cellular proliferation.
4. some mitochondrial functions are performed only in specific types of cells, e.g. mitochondria in liver cells contain enzymes that allow them to detoxify ammonia, a waste product of protein metabolism.

Recent Mitochondria Research:

1. Scientists have been using DNA in mitochondria to track genetic diseases. Scientists have found that in mammals, mitochondrial DNA (mtDNA) is 99.99% inherited from the mother. This research has also show that through mitochondrial mutations, many diseases can occur, some of these diseases are:
Alzheimer's, Parkinson's, and complete or partial blindness. However, newly found mitochondrial medicine leads to understanding the role of mitochondrial DNA mutations in these genetic diseases.
2. Mitochondrial research has also taken samples of different genetic types from people of different races to compare them and try to construct a family tree that shows when each group probably began evolving away from one another.
3. Scientists are using mitochondrial DNA analysis in forensic science. Scientists can use this DNA to find a criminal by matching the DNA at the scene of the crime with DNA from the suspect.

Replication of Mitochondria:

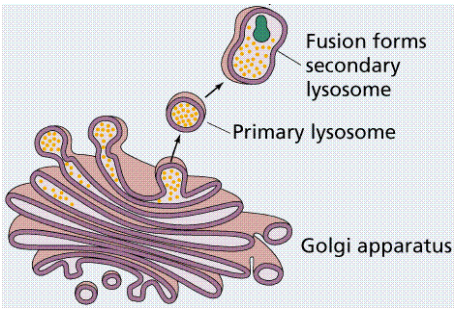
Mitochondria replicate similarly to bacterial cells, when they get large, they undergo fission. This involves furrowing of the inner and then the outer membrane as if someone was pinching the mitochondrion. The two daughter cells of the mitochondria must first replicate the DNA.

Clinical notes:

A maternally inherited mutation in the mitochondrial genome (This called mitochondrial disorders). Skeletal muscle fiber is very sensitive to mitochondrial defects, these diseases usually begin with drooping of the upper eye lid and progress to difficulties in swallowing and limb weakness. They are caused by DNA mutation or defects that can occur in the mitochondria or the cell nucleus.

Lysosomes

Lysosomes are membrane- bounded vesicles, produced by Golgi apparatus in animal cells and plant cells, lysosomes contain about 50 different degradative enzymes that can hydrolyze proteins, nucleic acids, carbohydrates, lipids, the most common enzymes are:
Lipase, carbohydrases, proteases, nucleases, phosphatases. These enzymes are active at an acid pH (5) which is the pH of the interior of lysosomes.



Functions of lysosomes:

They are the **digestive system** of the cell:

1. serving to degrade material taken up from outside the cell (endocytosis).
2. digest obsolete (الهرمـة) components of the cell itself called (autodigestion), e.g. the fingers of human embryo are at first webbed, but they are freed from one another because of lysosomal action.

Types of lysosomes:

1. **primary lysosomes:** they are lysosomes which have **not** entered digestive stage, they are small, and called storage granules.

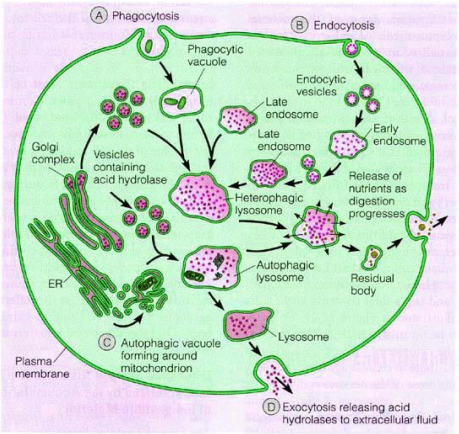
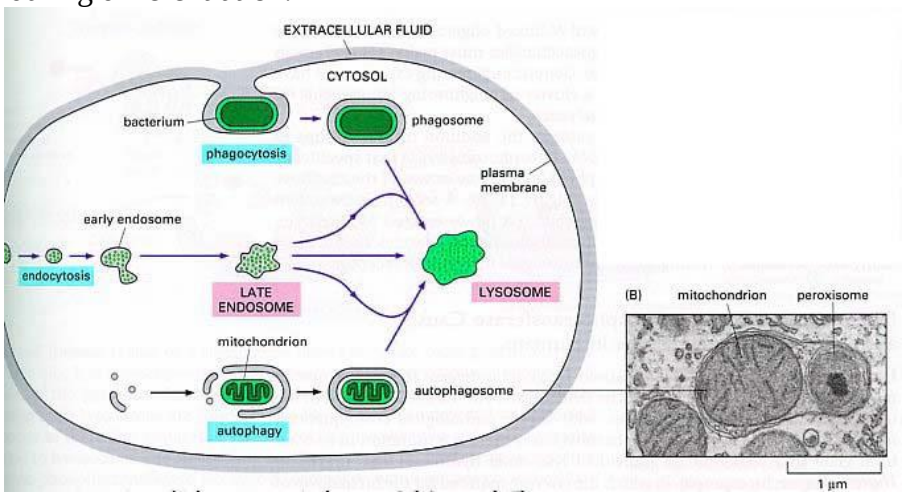


Figure 12-21 The Formation of Lysosomes and Their Roles in Cellular Digestive Processes. Illustrated in this composite cell are the major processes in which lysosomes are involved. The pathways depicted are Ⓐ phagocytosis, Ⓑ receptor-mediated endocytosis, Ⓒ autophagy, and Ⓓ extracellular digestion.

2. **secondary lysosomes:**
    a. **Heterophagosomes:** in phagocytosis, specialized cells, such as macrophages, take up and degrade large particles, including bacteria, cell debris, and aged cells that need to be eliminated from the body. Such large particles are taken up in phagocytic vacuoles (phagosomes) which then fuse with lysosomes, resulting in digestion of their contents. The lysosomes formed in this way (phagolysosomes) can be quite large and heterogeneous.
    b. **Autophagosomes:** lysosomes are also responsible for autophagy; the gradual turnover of the cells owns components. The first step of autophagy appears to be the enclosure of an organelle (e.g. mitochondria) in the membrane derived from the endoplasmic reticulum. The resulting vesicle (an autophagosomes) then fuses with a lysosome and its contents are digested. In addition, autophagy plays an important role in development by participating in the remodeling of tissue during differentiation.
    c. **Residual bodies:** are formed if the digestion is incomplete in some cells, such as ameba and other protozoa. In the other cells they may remain for a long time and may be important in the aging process. e.g. the pigment inclusions found in nerve cells and cardiac muscle cells.

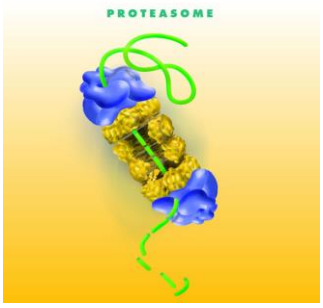


Clinical notes:

1. In some cases, lysosomes release their contents extracellularly, and their enzymes act in the extracellular milieu. An example is the destruction of bone matrix by the collagenases synthesized and released by osteoclasts during normal bone tissue formation.
2. Lysosomal enzymes acting in the extracellular milieu also play a significant role in the response to inflammation or injury.
3. Diseases categorized as lysosomal storage disorders resulted from defects in one or more of the digestive enzymes present in lysosomes.
4. In cells that must digest the substrate of the missing or defective enzyme following autophagocytosis, the lysosomes cannot function properly. Such cells accumulate large secondary lysosomes or residual bodies filled with the indigestible macromolecule. The accumulation of these vacuoles may eventually interfere with normal cell or tissue function, producing symptoms of the disease.

Proteasomes

Proteasomes are multiple protease complexes that digest proteins. The proteasomes deal primarily with proteins as individual molecules, whereas lysosomes digest bulk material introduced into the cell or whole organelles and vesicles.



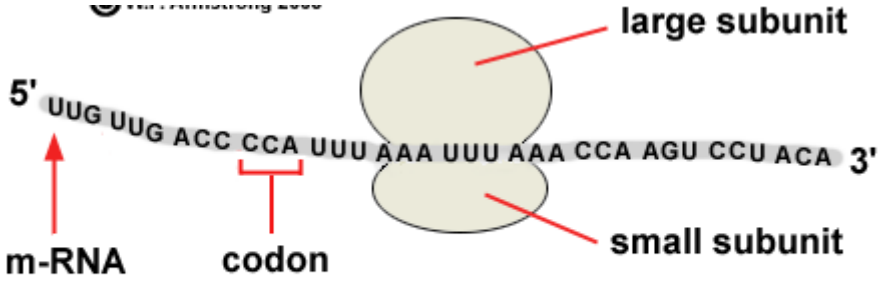
Protein degradation by proteasomes includes:

1. remove excess enzyme and other proteins that become unnecessary to the cell after they perform their normal functions.
2. remove proteins that were incorrectly folded.
3. proteins encoded by virus also destroyed.

Clinical notes:
Failure of proteasomes or other aspects of a cell's protein quality control can allow large aggregates of protein to accumulate in affected cells. Such aggregates may adsorb other macromolecules to them and damage or kill cells.
Aggregates released from dead cells can accumulate in the extracellular matrix of the tissue. In the brain this can interfere directly with cell function and lead to neurodegeneration, *Alzheimer disease* and *Huntington disease* are two neurologic disorders caused initially by such protein aggregates.

Non membrane bounded organelles
Ribosomes:

Ribosomes are small particles about 20*30 nm in size. They are not membrane-bound and occur in all cells. They are composed of 4 types of ribosomal RNA (rRNA) and almost 80 different proteins.
Ribosomes are composed of 2 different sized subunits. Ribosomes are basophilic because of the presence of numerous phosphate groups in rRNA. Ribosomes are held together by a strand of messenger RNA (mRNA) to form polyribosomes (polysomes) and often are cluster on the endoplasmic reticulum.



Ribosome Moving Along m-RNA Strand

Ribosomes are located in 4 places within the cytoplasm:

1. free ribosomes are found suspended in cytosol and synthesize proteins that will be used in the cell (except for membrane proteins).
2. bound ribosomes are found attached to the outer surface of the membranous endoplasmic reticulum. The areas of the ER that have attached ribosomes are called rough ER.
3. Nuclear envelope, which is an extension of the ER.
4. Inside mitochondria.

The function of a ribosome is to convert the genetic code into a sequence of amino acids that form a specific protein. Ribosomes are involved in protein synthesis. It creates protein for the cell.