G. The lysosomal system: structure and function

The lysosome is an intracellular organelle that plays a role in the degradation, recycling, and renewal of cell components. The lysosome is a waste processing factory. Lysosomes are not visible under an optical microscope; an electron microscope is required to observe them.

I. Structural characteristics of lysosomes

I.1. Shape

Lysosomes are spherical or oval intracellular organelles, generally between 0.1 and 0.2 µm in diameter, bounded by a plasma membrane and containing a set of hydrolytic enzymes. They are present in all eukaryotic cells except red blood cells. There are primary lysosomes (those that have just been synthesized) and secondary lysosomes (those that contain decomposing structures).

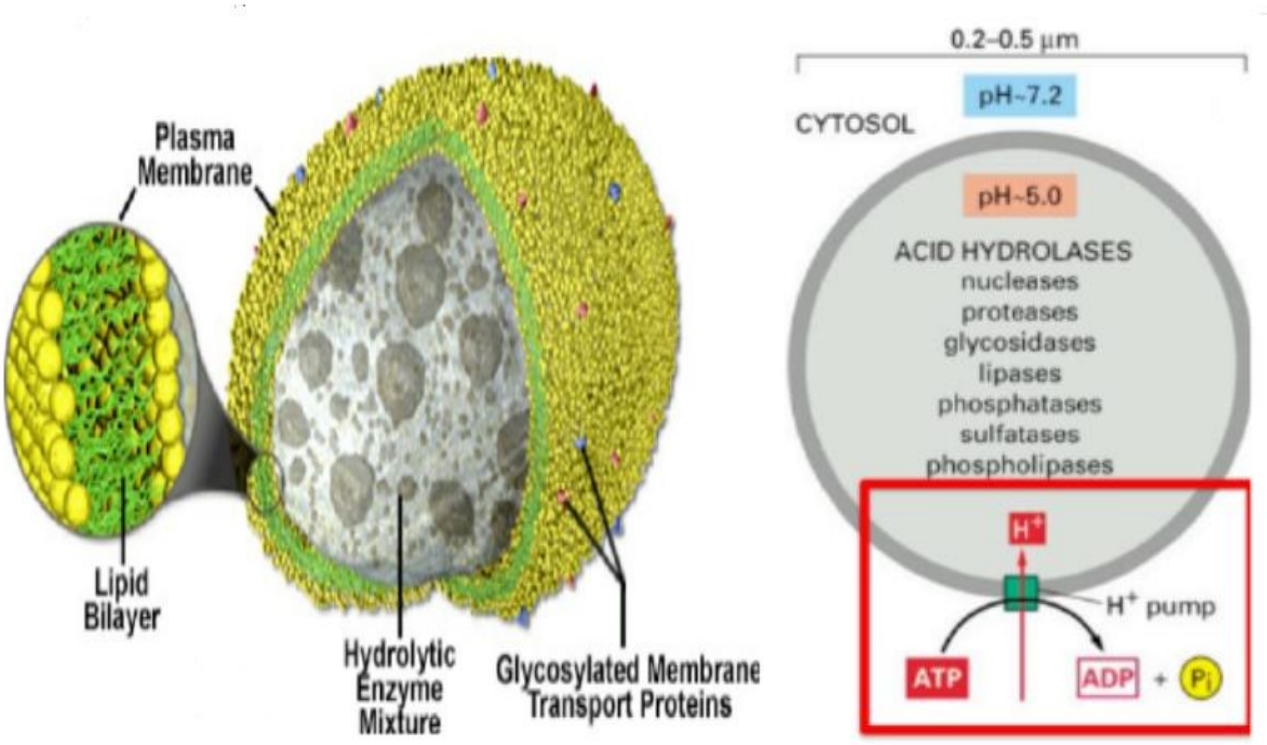

Figure III. 31. Lysosome structure **[39].**

I.2. Chemical composition

The lysosomal membrane is composed of lipids and around thirty different proteins (MW between 20 and 200 kDa), mainly glycoproteins. These include:

- Structural glycoproteins, some of which are used as markers: Lamp1, Lamp2, Lamp3 (lysosome-associated membrane protein).

- Enzymatic glycoproteins, the number of which varies from one cell type to another.

- ATPase/H+ dependent (proton pump), which maintain an acidic pH inside the lysosome.

- Permeases: allowing molecules destined for degradation to enter the lysosomal lumen (import permeases) and export permeases: ensuring the exit of catabolism products.

The lysosomal matrix contains more than 60 different hydrolases. These are soluble enzymatic glycoproteins. They act in an acidic environment at a pH of 4-5 and are inactive at a pH of 7.

- **Lysosomal enzymes : acid hydrolases**

Lysosomes contain digestive enzymes (acid hydrolases) to digest macromolecules. To function properly, digestive enzymes require the acidic environment of the lysosome. For this reason, if acid hydrolases were to leak into the cytosol, their potential danger to the cell would be reduced because they would not be at their optimum pH. All of these enzymes are produced by the endoplasmic reticulum and transported and processed by the Golgi apparatus. Each acid hydrolase is then targeted to a lysosome. The lysosome itself is apparently protected from digestion by its unique internal three-dimensional structures, which prevent enzymatic action. Some important enzymes in lysosomes are:

-Lipases, which break down lipids into fatty acids;

-Glycoside hydrolases, which break down sugars;

-Proteases, which break down proteins into peptides, which are then broken down by peptidase into tripeptides, dipeptides, and then amino acids;

-Nucleases, which break down nucleic acids into nucleosides.

The lysosome therefore contains all the materials necessary for the breakdown of a cell.

- **How can the highly acidic pH of lysosomes be explained?**

This is explained by the presence of proton pumps. There are more protons inside the lysosome than there are in the cytosol, and we still want to continue bringing in protons, H+ ions (against the concentration gradient) using energy (hydrolysis of ATP into ADP + Pi), which will strengthen the concentration gradient and maintain a pH of 5. What enters the lysosome are lysosomal membrane proteins and lysosomal enzymes. What leaves the lysosome are the products of digestion, which are transported to the cytosol and can therefore be reused by the cell.

II. Formation

Lysosomes originate from the Golgi apparatus through the formation of vesicles. The vesicles bud off from the GA, and this is what allows the formation of more mature lysosomes. Inside, there is an accumulation of lytic enzymes, all of which are marked by Man6P (mannose-6-phosphate).

At the Golgi apparatus, Man6P is added to proteins that must be sent to the lysosome. This Man6P is captured by a membrane receptor, which will all be gathered in the same place and will allow a vesicle to bud, which will be covered by clathrin. Then the clathrin coat is opened, and the vesicle is said to be naked, which will go to the lysosome. The lysosome has an acidic pH, which allows the ligand to dissociate from the receptor. The receptors are then recycled to the AG.

There are two pathways in the formation of lysosomes:

• The endosomal pathway

This corresponds to the fusion of the primary lysosome, originating from the trans-Golgi network, with a late endosome, allowing the formation of the endolysosome, which will form the lysosome.

• The lysosomal pathway

This corresponds to the fusion of the primary lysosome with an existing lysosome.

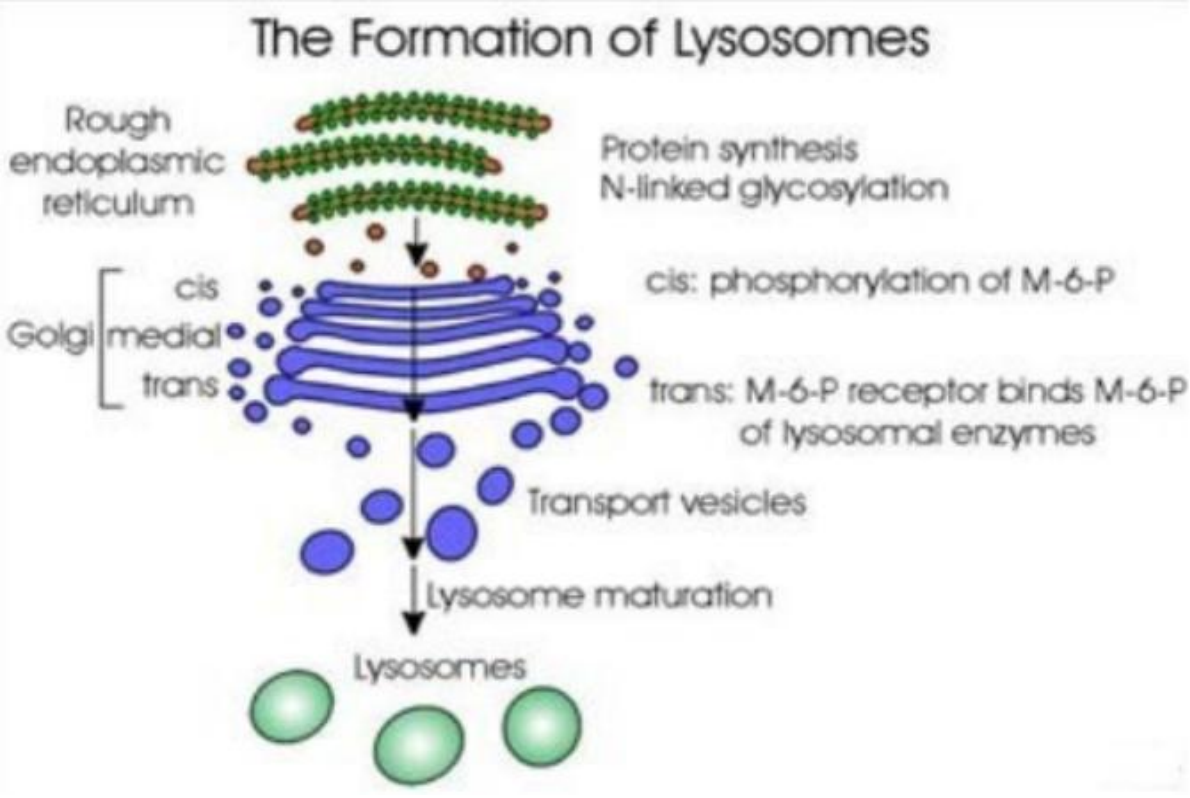

Figure III. 32. Lysosome formation **[39].**

III. Fonctions of lysosomes

The lysosome can intervene to:

- **Eliminating pathogens**: The cell is capable of capturing bacteria through a mechanism called phagocytosis. The bacteria are enveloped by a membrane, known as a phagosome. This phagosome fuses with a lysosome, and thanks to the lytic enzymes present in the latter, the bacteria can be broken down and eliminated. This is the first line of defense in our body, enabling it to eliminate a certain number of bacteria.
- **Eliminating "worn-out" organelles**: Autophagy is another degradation pathway. Mitochondria that are too old and malfunctioning are recognized as such and captured by membranes that fuse around them to form autophagosomes, which then fuse with lysosomes, allowing them to be broken down.
- **Eliminating cell waste**: Once the mitochondria and bacteria have been degraded, the waste must be eliminated, which is done by exocytosis. But from the lysosome, there is excretion into the external environment to eliminate cell waste.

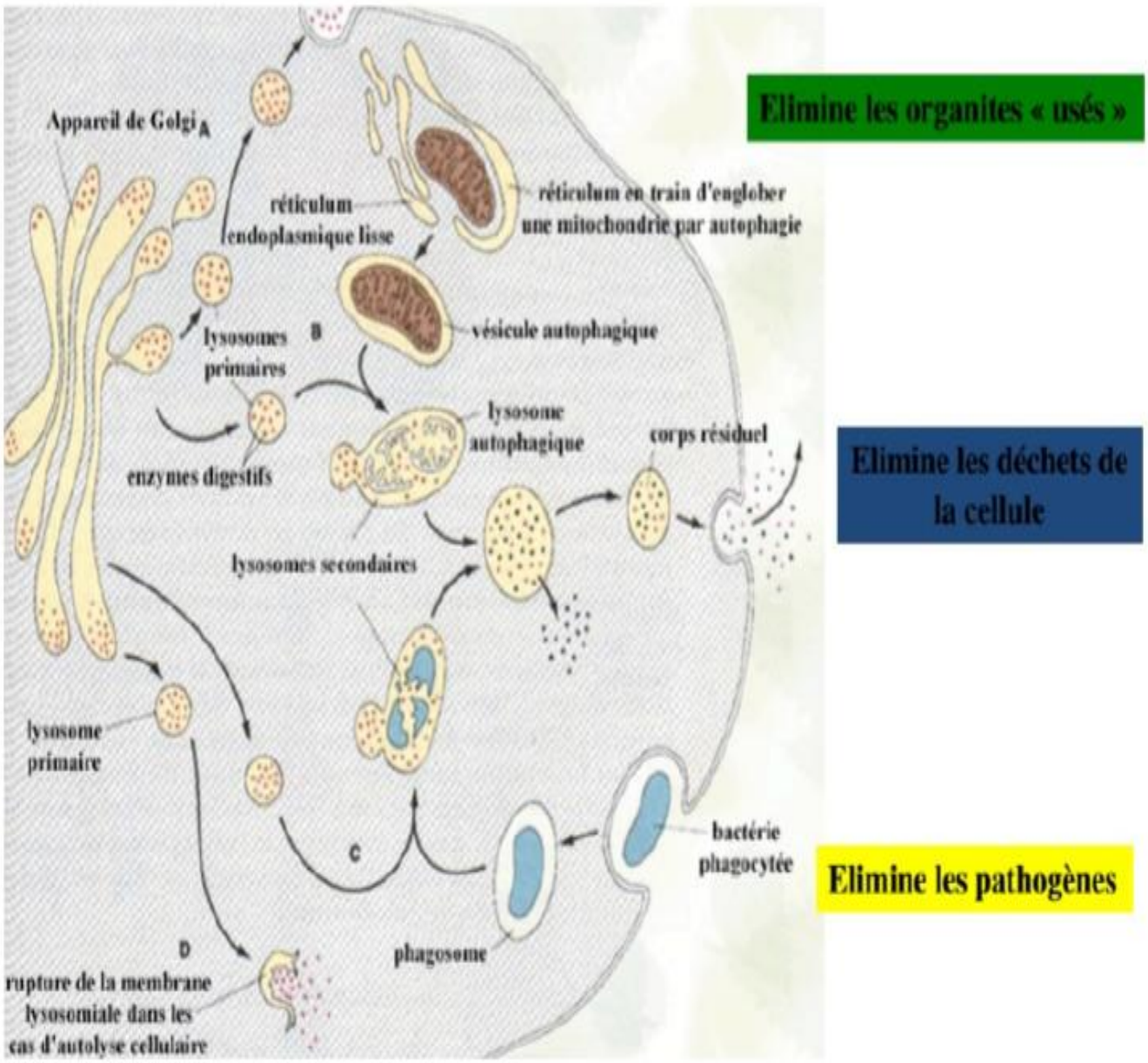

Figure III. 33. Degradation pathways **[39].**