STRUCTURE AND FUNCTIONS OF LYSOSOMES

ABOUT LYSOSOMES

Lysosomes are membrane-enclosed organelles that contain an array of enzymes capable of breaking down all types of biological polymers - proteins, nucleic acids, carbohydrates, and lipids.

Lysosomes function as the digestive system of the cell, serving both to degrade material taken up from outside the cell and to digest obsolete components of the cell itself.

In their simplest form, lysosomes are visualized as dense spherical vacuoles, but they can display considerable variation in size and shape as a result of differences in the materials that have been taken up for digestion.

Lysosomes thus represent morphologically diverse organelles defined by the common function of degrading intracellular material.

LYSOSOMAL ACID HYDROLASES

Lysosomes contain about 50 different degradative enzymes that can hydrolyze proteins, DNA, RNA, polysaccharides, and lipids.

All of the lysosomal enzymes are acid hydrolases, which are active at the acidic pH (about 5) that is maintained within lysosomes but not at the neutral pH (about 7.2) characteristic of the rest of the cytoplasm.

The requirement of these lysosomal hydrolases for acidic pH provides double protection against uncontrolled digestion of the contents of the cytosol; even if the lysosomal membrane were to break down, the released acid hydrolases would be inactive at the neutral pH of the cytosol.

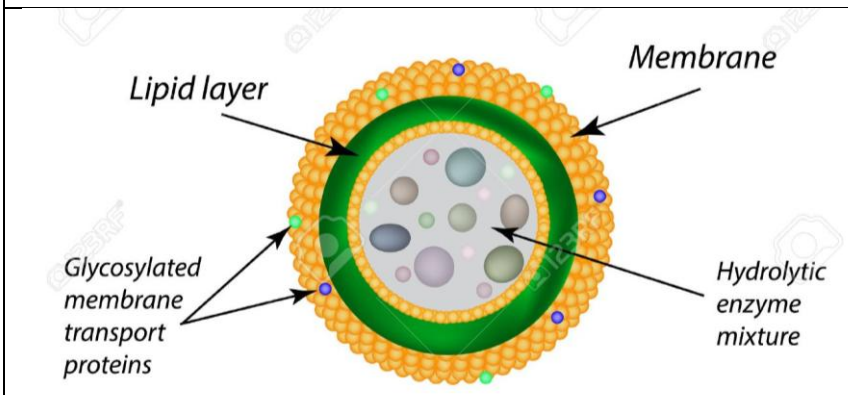
To maintain their acidic internal pH, lysosomes must actively concentrate H^+ ions (protons). This is accomplished by a proton pump in the lysosomal membrane, which actively transports protons into the lysosome from the cytosol.

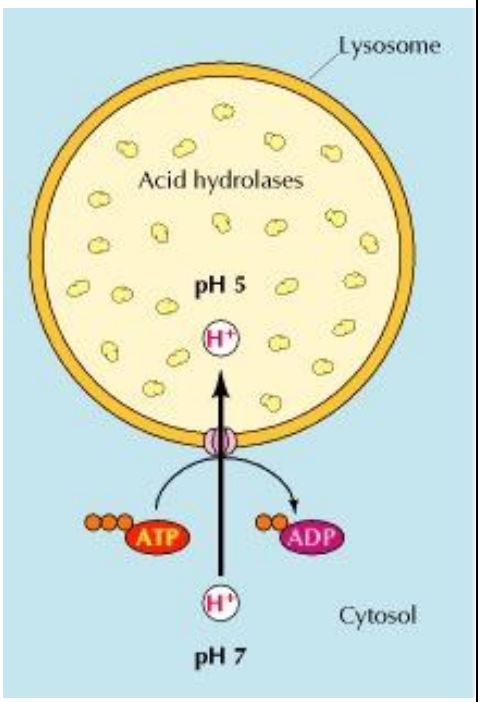
This pumping requires expenditure of energy in the form of ATP hydrolysis, since it maintains approximately a 100 fold higher H^+ concentration inside the lysosome.

LYSOSOMAL STORAGE DISEASES

Mutations in the genes that encode these enzymes are responsible for more than 30 different human genetic diseases, which are called **lysosomal storage diseases** because undegraded material accumulates within the lysosomes of affected individuals.

Most of these diseases result from deficiencies in single lysosomal enzymes. For example, Gaucher's disease (the most common of these disorders) results from a mutation in the gene that encodes a lysosomal enzyme required for the breakdown of glycolipids.





Organization of the lysosome: Lysosomes contain a variety of acid hydrolases that are active at the acidic pH maintained within the lysosome, but not at the neutral pH of the cytosol. The acidic internal pH of lysosomes results from the action of a proton pump in the lysosomal membrane, which imports protons from the cytosol coupled to ATP hydrolysis.

FORMATIONS OF LYSOSOMES

Lysosomes are formed by the fusion of transport vesicles budded from the *trans* Golgi network with endosomes, which contain molecules taken up by endocytosis at the plasma membrane.

The formation of lysosomes thus represents an intersection between the secretory pathway, through which lysosomal proteins are processed, and the endocytic pathway, through which extracellular molecules are taken up at the cell surface.

Material from outside the cell is taken up in clathrin-coated endocytic vesicles, which bud from the plasma membrane and then fuse with early endosomes.

Membrane components are then recycled to the plasma membrane and the early endosomes gradually mature into late endosomes, which are the precursors to lysosomes.

One of the important changes during endosome maturation is the lowering of the internal pH to about 5.5, which plays a key role in the delivery of lysosomal acid hydrolases from the *trans* Golgi network.

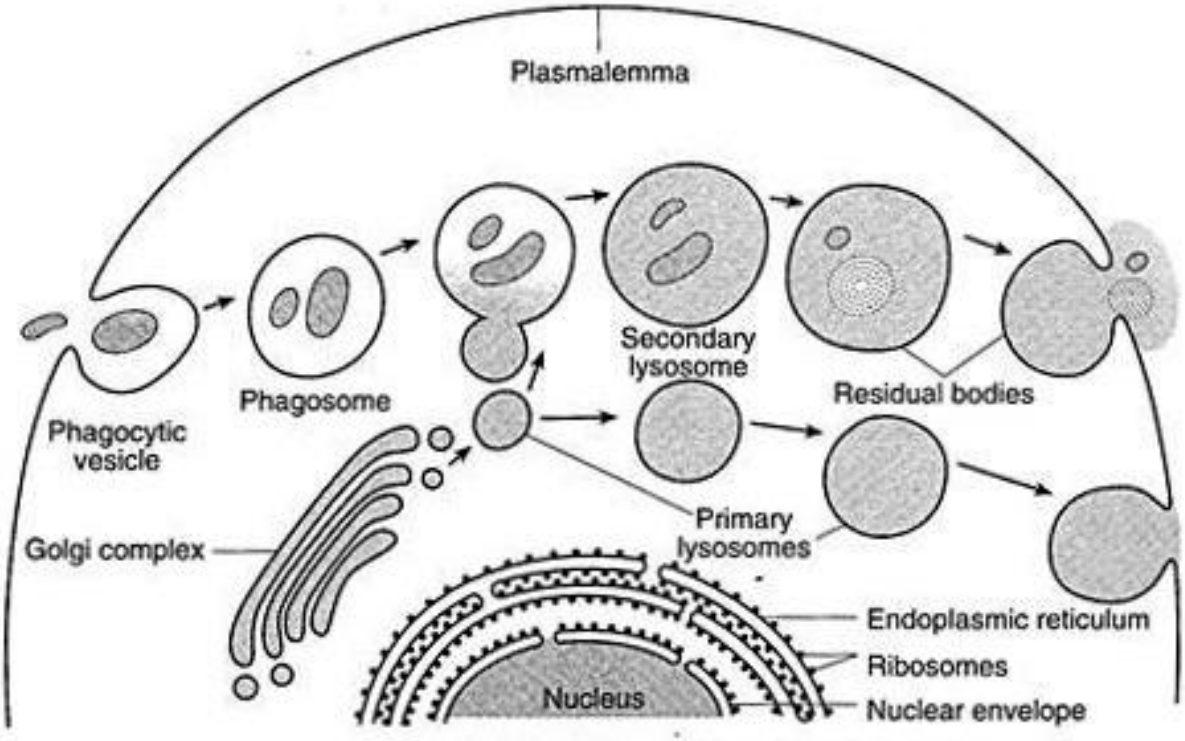


Fig. 2.61: Diagram showing the origin and different phases of lysosomes

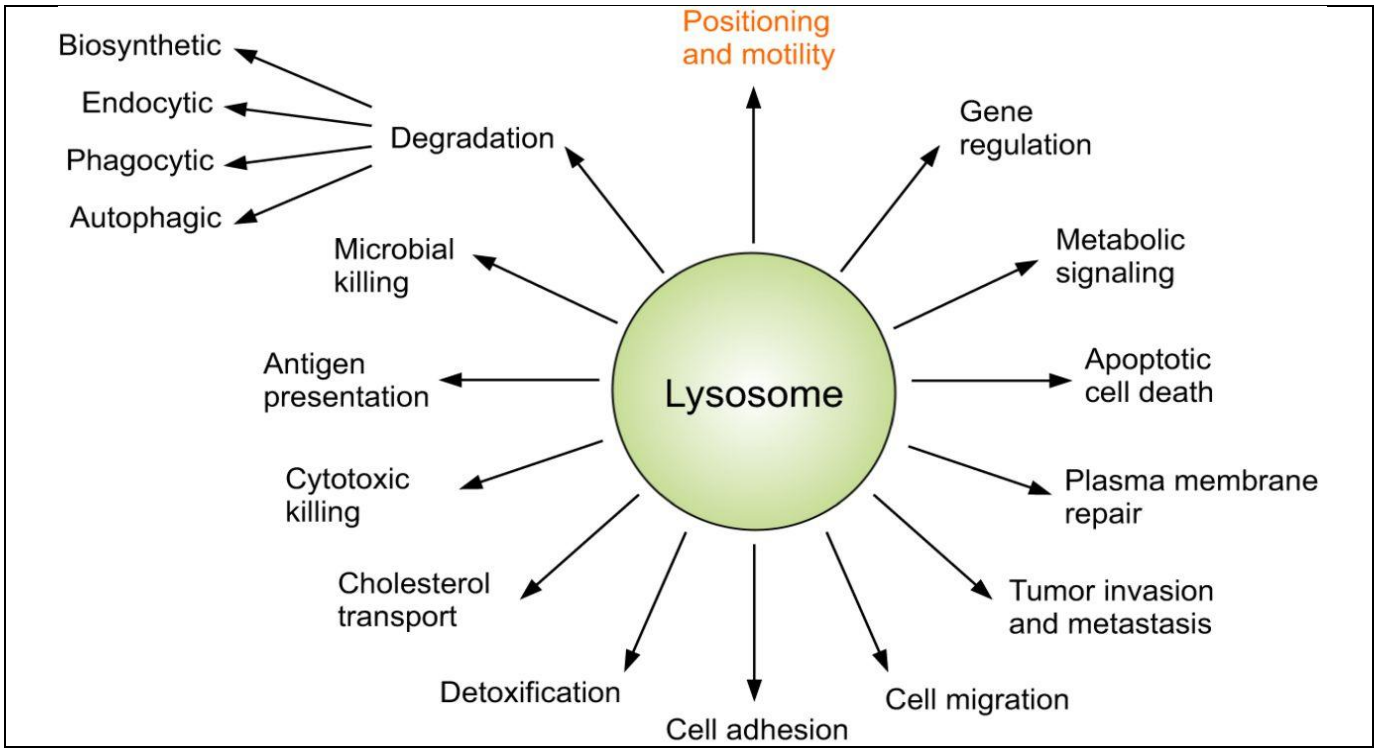
FUNCTION OF LYSOSOMES

Lysosomes digest material derived from two other routes: phagocytosis and autophagy. 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, since their size and shape is determined by the content of material that is being digested.

Lysosomes are also responsible for autophagy, the gradual turnover of the cell's own components. The first step of autophagy appears to be the enclosure of an organelle (e.g., a mitochondrion) in membrane derived from the ER. The resulting vesicle (an **autophagosome**) then fuses with a lysosome, and its contents are digested.


Positioning
and motility
Biosynthetic
Endocytic
Phagocytic
Autophagic
Degradation
Gene
regulation
Microbial
killing
Metabolic
signaling
Antigen
presentation
Lysosome
Apoptotic
cell death
Cytotoxic
killing
Plasma membrane
repair
Cholesterol
transport
Tumor invasion
and metastasis
Detoxification
Cell adhesion
Cell migration