CELL BIOLOGY

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Lecture 9: Lysosomes, Peroxisome, and glyoxisomes 29/11/2021

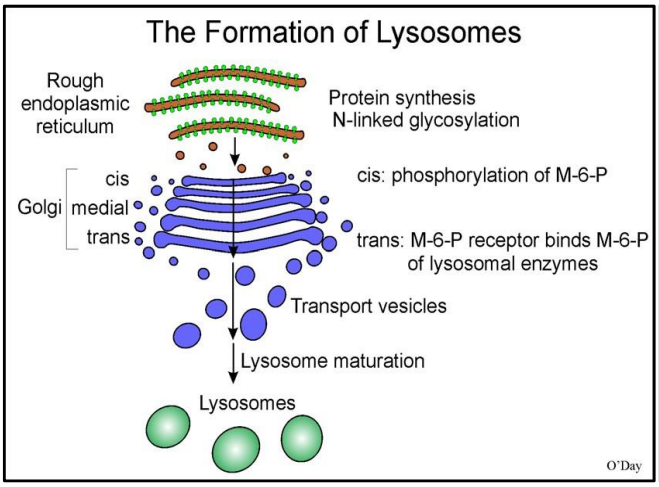
Lysosomes

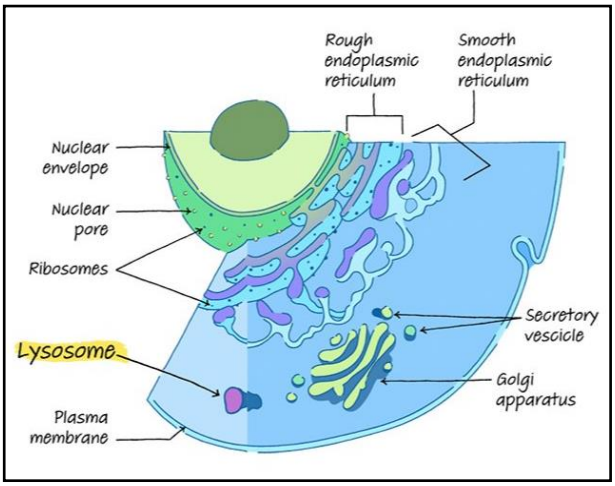
- The lysosomes are one of the simplest cellular organelles found in the cytoplasm of eukaryotic cells.
- Basically it is a bag of digestive enzymes surrounded by a single biomembrane. Lysosomes are organelles containing digestive enzymes (acid hydrolases).
- It acts as the "garbage disposal" of the cell by breaking down cell components that are no longer needed as well as molecules or even bacteria that are ingested by the cell.
- Lysosomal enzymes are capable of digesting essentially every type of biological molecule through phagocytosis or pinocytosis. Many of the products of lysosomal digestion, such as amino acids and nucleotides, are recycled back to the cell for use in the synthesis of new cellular components.
- The size of lysosomes varies from 0.1 µm to 1.2 µm With a pH ranging from 4.5–5.0, the interior of the lysosomes is acidic compared to the slightly basic cytosol (pH 7.2).

Lysosomal Biogenesis: The Formation of Lysosomes

The lysosomal enzymes are synthesized in the endoplasmic reticulum.

The enzymes are passed on to the Golgi apparatus where the lysosomes are produced.



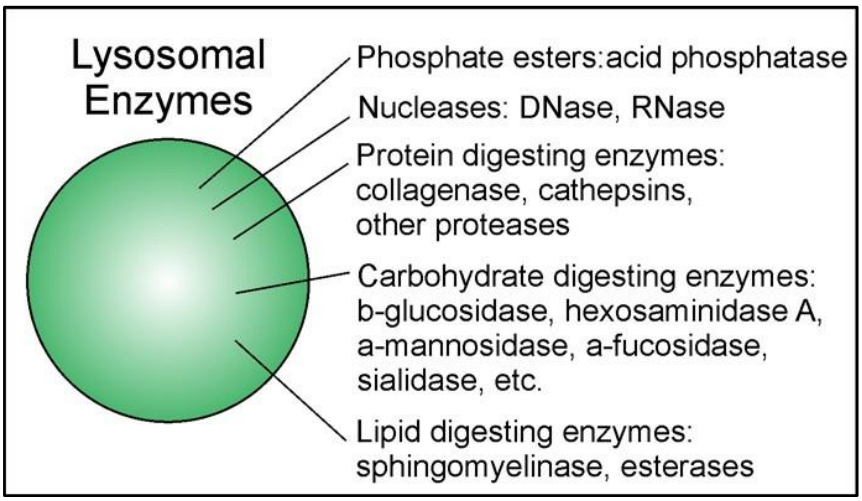


The Lysosomal Enzymes

The following picture shows the diversity of lysosomes enzymes that are capable of digesting almost all biological molecules.

They contain over 3 dozen different kinds of hydrolytic enzymes including

- **Phosphatase , Nucleases, Proteases, Polysaccharidase, Lipases**



The enzymes are kept inside by the lysosomal membrane. These enzymes remain inactive inside the lysosomes. When the pH of the interior lysosomes changed to acidic pH 4.8, enzymes become active. At pH 4.8, the interior of the lysosomes is acidic compared to the slightly alkaline cytosol (pH 7.2).

The lysosome maintains this pH differential by pumping protons (H+ ions) from the cytosol across the membrane via proton pumps and chloride ion channels.

The lysosomal membrane protects the cytosol, and the rest of the cell, from the degradative enzymes within the lysosome. The cell is additionally protected from any lysosomal acid hydrolases that leak into the cytosol as these enzymes are pH-sensitive and function less well in the alkaline environment of the cytosol.

All the enzymes in the lysosome work best at an acid pH. This reduces the risk of their digesting their own cell if they should escape from the lysosome.

Types of lysosomes

A newly formed lysosome that has not yet been engaged in any cellular activity is called a primary lysosome. All others are classed as secondary lysosomes (e.g., digestive vacuole, residual vacuole, autophagic vacuole, etc.)

1) **Primary lysosomes**: these are the lysosomes that are not involved in digestion yet, they are also called virgin lysosomes
2) **Secondary lysosomes**: when primary lysosomes fuse with a phagosome, the whole vacuole is called secondary lysosome, the enzymes of the primary lysosome will release into the lumen of phagosome and start digest its components
3) **Autolysosomes**: internal digestion of aged or unwanted cellular organelles such as mitochondria and endoplasmic reticulum
4) **Residual bodies**: the remaining vacuole after digestion of their content by lysosomal enzymes are called residual bodies, it takes many shapes, the most common are the whorls shape.

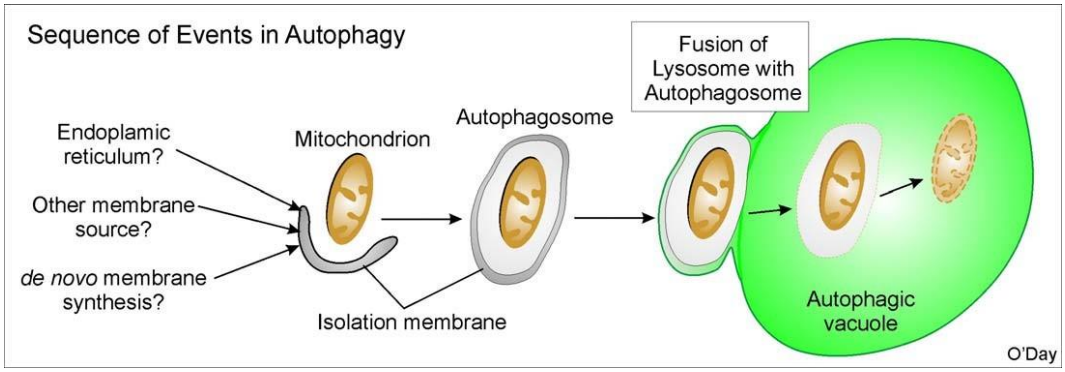
Lysosomes & Cell Function

These are not the only functions of lysosomes as new responsibilities for this organelle are being discovered including metal ion homeostasis and cell membrane repair.

1. Digestion of Ingested Materials - Cells ingest materials by various endocytotic means including the classic phagocytosis ("cell eating") and pinocytosis ("cell drinking"). Inside the cell, the material that is taken up is enclosed in an endosome (phagosome or pinosome, respectively). Inside the cell the endosome fuses with a primary lysosome to form a digestive vacuole. In the digestive vacuole the hydrolases of the lysosome will act on the ingested material to break it down. After digestion is complete, the vacuole is called a residual vacuole because it is full of residual, indigestible components. The contents of the residual vacuole are released outside of the cell by exocytosis.

2. Cell Death - Lysosomes mediate events in the controlled or programmed death of cells called apoptosis. They also come into play during necrosis, the pathologic death of cells and tissues. For example, meat becomes tenderized after the death of the animal because the lysosomes break down releasing their enzymes into the muscle causing the digestion of the contractile and other muscle proteins.

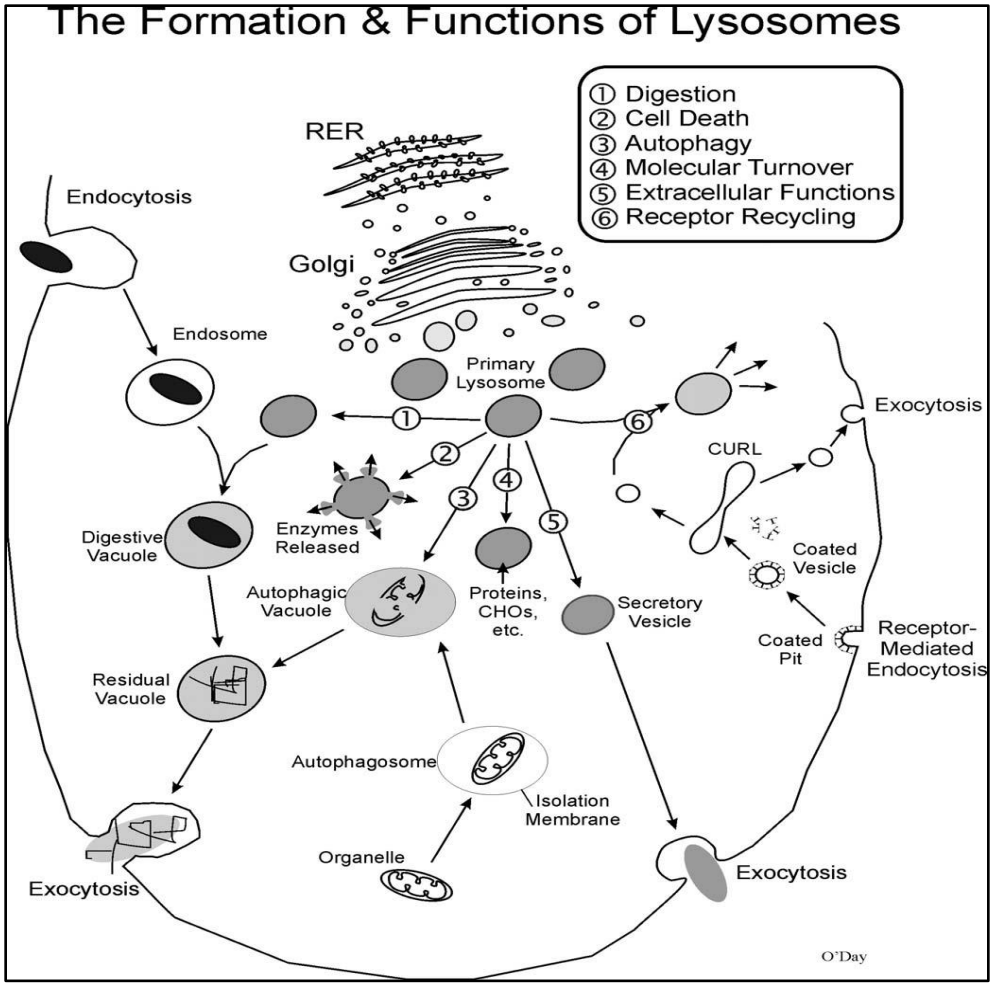
3. Autophagy - The survival of cells requires that cellular constituents are constantly turning over. New molecules and structures are made while old unnecessary or worn out components are removed. During starvation, cells use autophagy to break down cellular components to provide energy for their survival. In the case of organelles, the mitochondrion, for example, is separated from other cellular constituents by an isolation membrane to become an autophagosome. The autophagosome fuses with primary lysosomes to form an autophagic vacuole within which the mitochondrion is digested. The resulting residual vacuole is exocytosed. The following picture shows the sequence of events in digesting mitochondria.



4. Protein Turnover - In this situation, molecules are digested by lysosomal enzymes. The exact ways in which the different types of molecular turnover occur are under active investigation. But this process removes old, abnormal or unnecessary molecules allowing cells to alter their physiology or behaviour. Some of the molecules enter the digestive pathway via receptor mediated endocytosis as mentioned below and discussed in detail in a future lecture.

5. Extracellular Functions - Lysosomal enzymes have responsibilities that lie outside of the cell as well they can digest extracellular components or modify the cell surface. For example, high levels of secretion of glycosidases are linked to some of the changes in cell adhesion molecules that underlie the behaviour of some cancer cells.

6. Receptor-Mediated Endocytosis - Lysosomes play an important role in the uptake and modification of critical molecules such as cholesterol. They also mediate events of receptor recycling and the shutting down of events of cell communication.



Why doesn't the lysosome digest itself?

Since the lysosome is full of digestive enzymes that can digest essentially all cellular components, why doesn't the lysosome digest itself? This is because the inner leaflet of the lysosomal membrane is coated with an extensive glycocalyx (like that present in the intestinal epithelium to prevent its digestion).

Role of Lysosome in Disease

Lysosomes play a role in both the *fight against* diseases and in the *cause* of disease. When foreign pathogens such as bacteria enter a cell, the lysosomes can help neutralize them by digesting them. In this way they help with an organism's immune response. When lysosomes don't work properly, they can cause disorders called lysosomal storage diseases.

Lysosomal Storage Diseases

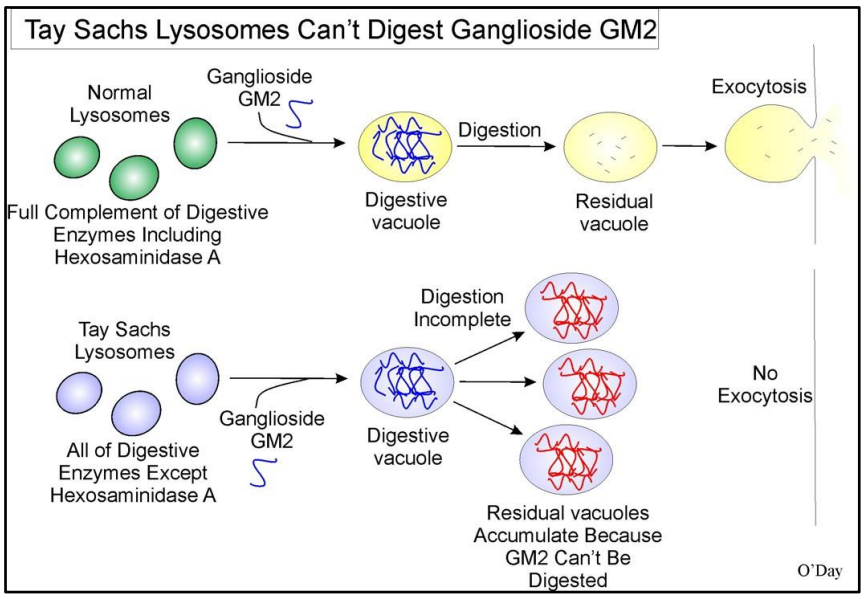
Are genetic disorders in which a genetic mutation affects the activity of one or more of the acid hydrolases enzymes of the lysosome.

In such diseases, the normal metabolism of specific macromolecules (proteins, polysaccharides, lipids) is blocked and the macromolecules accumulate inside the lysosomes, causing severe physiological damage.

-Hurler syndrome, which involves a defect in the metabolism of mucopolysaccharides, is a lysosomal storage disease.

-Tay-Sachs disease and **Gaucher's disease** — both caused by a failure to produce an enzyme needed to break down **sphingolipids** (fatty acid derivatives found in all cell membranes).

-Mucopolysaccharidosis I (MPS-I). Caused by a failure to synthesize an enzyme (α-L-iduronidase) needed to break down proteoglycans like heparan sulfate.



Secretory Lysosomes

In some cells, lysosomes have a secretory function — releasing their contents by exocytosis.

- Cytotoxic T cells (CTL) secrete perforin from lysosomes.
- Mast cells secrete some of their many mediators of inflammation from modified lysosomes.
- Melanocytes secrete melanin from modified lysosomes.
- The exocytosis of lysosomes provides the additional membrane needed to quickly **seal wounds** in the plasma membrane.

Peroxisomes

Peroxisomes are about the size of lysosomes (0.5–1.5 µm) and like them are bound by a single membrane. They also resemble lysosomes in being filled with enzymes.
However, peroxisomes bud off from the endoplasmic reticulum, not the Golgi apparatus (that is the source of lysosomes). Peroxisomes are also called **microbodies**.

Some of the functions of the peroxisomes in the human liver:

- Breakdown (by oxidation) of excess fatty acids.
- Breakdown of hydrogen peroxide (H_2O_2), a potentially dangerous product of fatty-acid oxidation.
- Participates in the synthesis of cholesterol. One of the enzymes involved, HMG-CoA reductase, is the target of the popular cholesterol-lowering "statins".
- Participates in the synthesis of bile acids.
- Participates in the synthesis of the lipids used to make myelin.
- Breakdown of excess purines (AMP, GMP) to uric acid.

Glyoxysomes

Are specialized peroxisomes found in plants (particularly in the fat storage tissues of germinating seeds) and also in filamentous fungi. Glyoxysomes (as all peroxisomes) contain enzymes that initiate the breakdown of fatty acids and additionally possess the enzymes to produce intermediate products for the synthesis of sugars by gluconeogenesis. The seedling uses these sugars synthesized from fats until it is mature enough to produce them by photosynthesis.
Glyoxysomes also participate in photorespiration and nitrogen metabolism in root nodules.