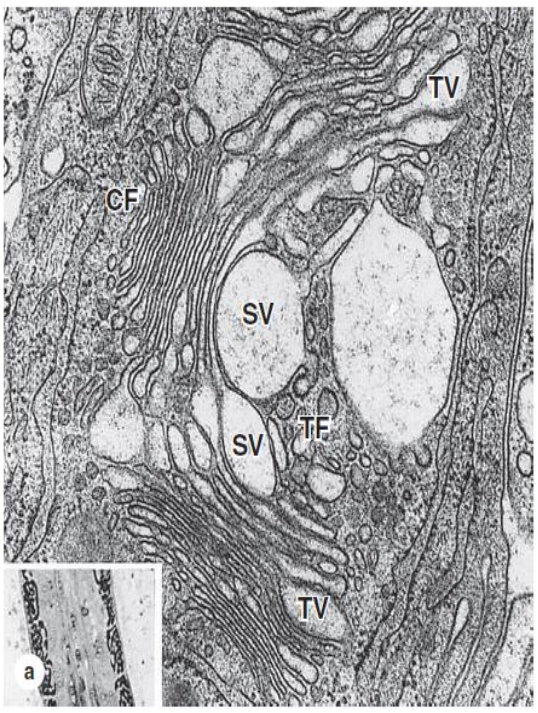
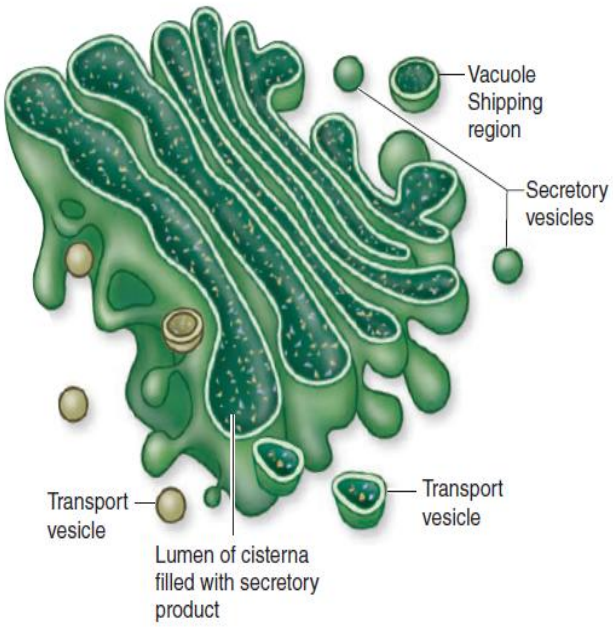
❖ Golgi apparatus

- The Golgi apparatus is a highly plastic, morphologically complex system of membrane vesicles and cisternae in which proteins and other molecules made in the RER undergo further modification and sorting into specific vesicles destined for different roles in the cell.
- Composed of smooth membranous saccules (cisternae) containing enzymes (Cisternae enzyme) for completes posttranslational modifications (modify, sort and package proteins also add sugar to protein and lipid to form glycoproteins, glycolipids and lipoproteins) of proteins synthesized in the RER and then packages and addresses these proteins to proper destinations.
- Golgi apparatus generally shows two distinct sides structurally and functionally, which reflect the complex traffic of vesicles within cells. Material moves from the RER cisternae to the Golgi apparatus in small, membrane-enclosed carriers called transport vesicles that are transported along cytoskeletal polymers by motor proteins. The transport vesicles merge with the Golgi-receiving region, or ***cis face***. On the opposite side of the Golgi network, at its shipping or ***trans face***, larger saccules or vacuoles accumulate, condense, and generate other vesicles that carry completed protein products to organelles away from the Golgi
- Golgi apparatus highly developed in secretary cells. Such as mucus-secreting goblet cells, the Golgi apparatus occupies a characteristic position between the nucleus and the apical plasma membrane
- One of Golgi membrane unique proteins important for directed vesicle fusion include golgins, which interact with enzymes; receptors and other binding proteins; and fusion promoting proteins to specify, organize, and shape Golgi membranes. Depending on their protein contents and activity of these proteins, vesicles are directed toward different Golgi regions and they give rise to lysosomes or secretory vesicles for exocytosis.





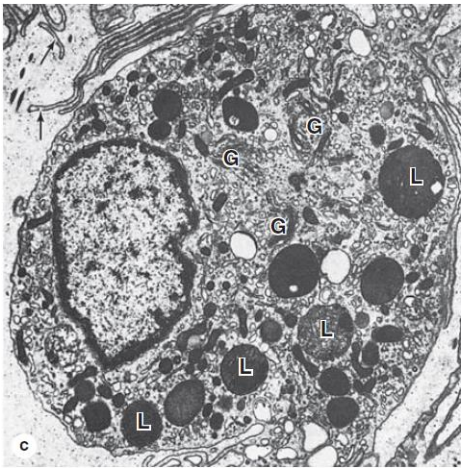
TEM of the Golgi apparatus

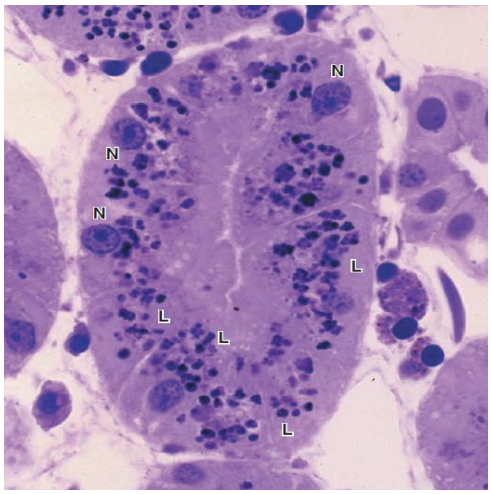
❖ Lysosomes

- Lysosomes are spherical membrane limited vesicles that function as sites of intracellular digestion, that contain about 40 different digestive enzymes called hydrolytic enzymes such as proteases, nucleases, phosphatase, phospholipases, sulfatases, and β-glucuronidase.

- Produced by the Golgi apparatus, Lysosomal hydrol**ases** are synthesized and segregated in the RER and then transferred to the Golgi apparatus, where the hydrolytic enzymes are further modified and packaged in vacuoles that form lysosomes.
- Present in all cells and particularly abundant in cells with phagocytic activity (eg, macrophages, neutrophils) because lysosomal enzymes are capable of breaking down most macromolecules

L.M. Lysosomes are not well shown on H&E-stained cells but can be visualized by light microscopy after staining with toluidine blue.
E.M. they appear as homogenous membrane bound vesicles, trilaminar unit membrane, variable in size, number, shape and homogeneity, which are usually spherical, range in diameter from 0.05 to 0.5 μm and present a uniformly granular, electron-dense appearance in the TEM





The functions of lysosome

1. Digestion of exogenous macromolecules like pathogens(bacteria, virus,…ect) by phagocytosis and LDL by receptor mediated endocytosis
2. Maintain cell health by remove all old endogenous macromolecules, excess or worn-out cell parts by autophagy.
3. Have important role in post mortum autolysis.

✓ **Exogenous macromolecules** taken from outside the cell by **endocytosis** digested when the membrane of the **phagosome** or **pinocytotic vesicle** fuses with a lysosome. The composite, active organelle is now termed a **secondary** or **heterolysosome**. Heterolysosomes are generally somewhat larger and have a more heterogeneous appearance in the TEM because of the wide variety of materials they may be digesting. During this digestion of macromolecules, released nutrients diffuse into the cytosol through the lysosomal membrane. Indigestible material is retained within a small vacuolar remnant called a residual body. In

some long-lived cells (eg, neurons, heart muscle), residual bodies can accumulate over time as granules of lipofuscin.

- ✓ Besides degrading exogenous macromolecules, lysosomes also function in the removal of excess or nonfunctional organelles and other cytoplasmic structures (**endogenous macromolecules**) in a process called **autophagy**. A membrane from SER forms around the organelle or cytoplasmic portion to be removed, producing an **autophagosome**. These then fuse with lysosomes that digest the enclosed cytoplasm. Autophagy is enhanced in secretory cells that have accumulated excess secretory granules and in times of nutrient stress, such as starvation. Digested products from autophagosomes are reused in the cytoplasm.

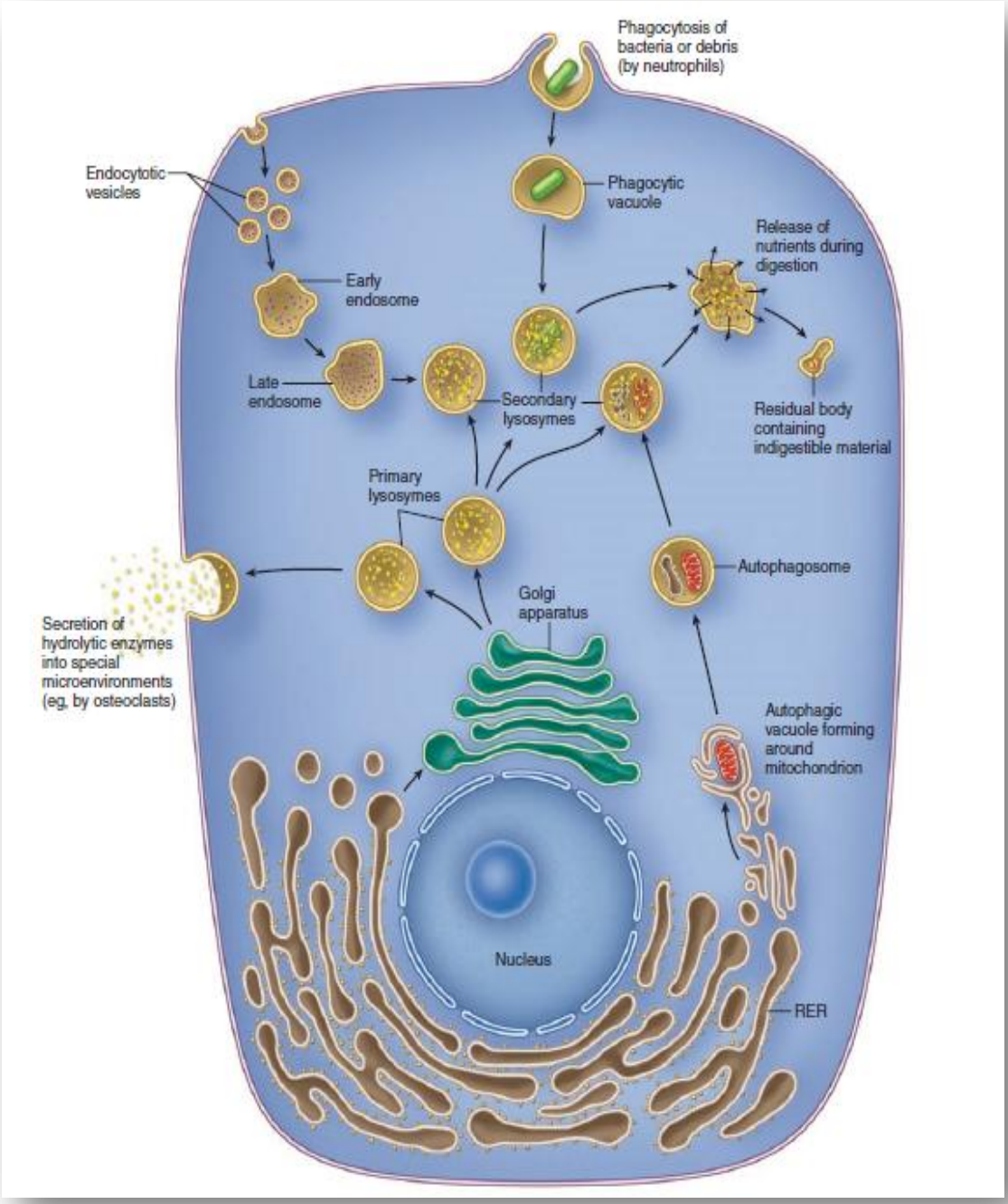


Figure show the endogenous and exogenous digestion by lysosome

Medical application

Diseases categorized as **lysosomal storage disorders** stem from defects in one or more of the digestive enzymes present in lysosomes, usually due to a mutation leading to a deficiency of one of the enzymes, or defects due to faulty posttranslational processing. 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.

Tay-Sachs disease is a rare disorder caused by the absence of an enzyme (GM2-gangliosidase) that helps break down fatty substances. These fatty substances, called gangliosides, build up to toxic levels in the child's brain and affect the function of the nerve cells.

Gaucher disease caused by the faulty of Glucocerebrosidase enzyme that lead to buildup of certain fatty substances in certain organs, particularly in spleen and liver.

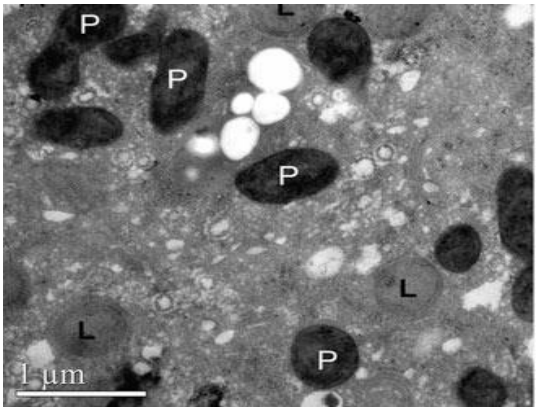
❖ Peroxisome

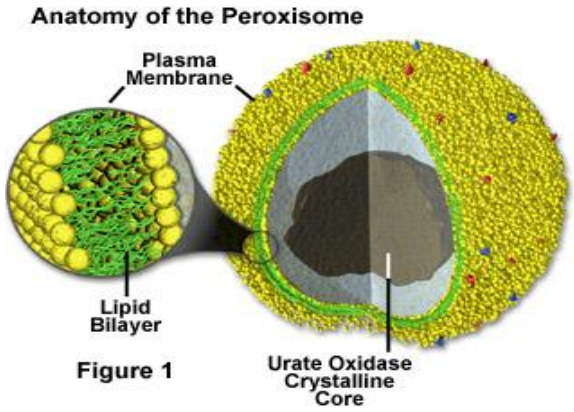
- spherical organelles enclosed by a single membrane and named for their enzymes producing and degrading hydrogen peroxide, H_2O_2
- Similar to lysosomes but containing no hydrolytic enzymes and containing several types of **oxidases and catalases** and other metabolic enzymes.
- The peroxisome enzymes are synthesized on free cytosolic polyribosomes.

Oxidases are enzymes that oxidize various organic substances by removing hydrogen atoms that are transferred to molecular oxygen (O_2), producing hydrogen peroxide (H_2O_2), a highly toxic product that is potentially damaging to the cell.

Peroxidases such as **catalase** immediately eliminate excess hydrogen peroxide by breaking it down into water and oxygen molecules.

- These enzymes also have an important role in fatty acid oxidation to produce acetylcholine that is very important in making lipids and cholesterol, like plasmalogen (white matter of the brain) and steroid hormones. Another function is alcohol metabolism, which inactivates various potentially toxic molecules, including some prescription drugs. So that the peroxisome protects the cell from the cytotoxic product because the degradation of hydrogen peroxide occurs in the same organelle.
- Very abundant in the cells of the liver and kidney.





The structure of peroxisome under TEM

- Peroxisomes form in two ways:

1. Budding of precursor vesicles from the ER
2. Growth and division of preexisting peroxisomes.

Medical application

Deficiencies of peroxisomal enzymes cause **Zellweger syndrome** that affects the structure and functions of several organ systems.

❖ Proteasomes

- Proteasomes are very small abundant protein complexes not associated with membrane, each approximately the size of the small ribosomal subunit. Composed of three subunits: two regulatory particles and one core particle.
- They function to degrade denatured or otherwise nonfunctional polypeptides that attached to **Upiquitin protein** by ATP dependent pathway.
- They function to degrade excess enzyme, denatured or otherwise nonfunctional polypeptides also remove proteins no longer needed by the cell and provide an important mechanism for restricting activity of a specific protein to a certain window of time. Destroy protein infected by viruses. Whereas lysosomes digest organelles or membranes by autophagy, proteasomes deal primarily with free proteins as individual molecules.

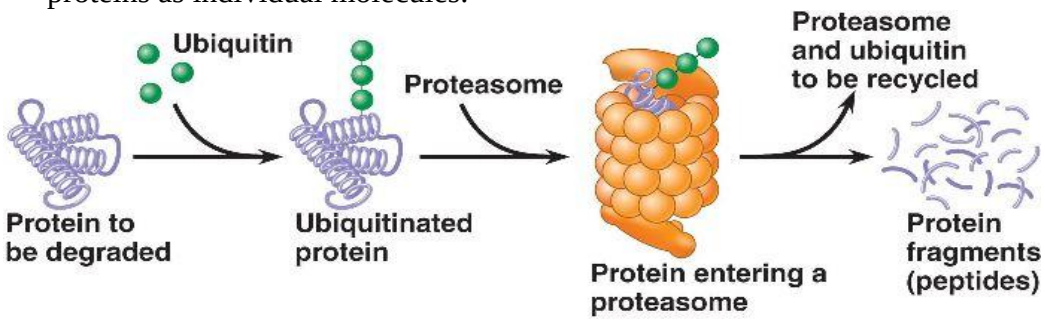


Figure: Diagram of proteasome and Upiquitin pathway

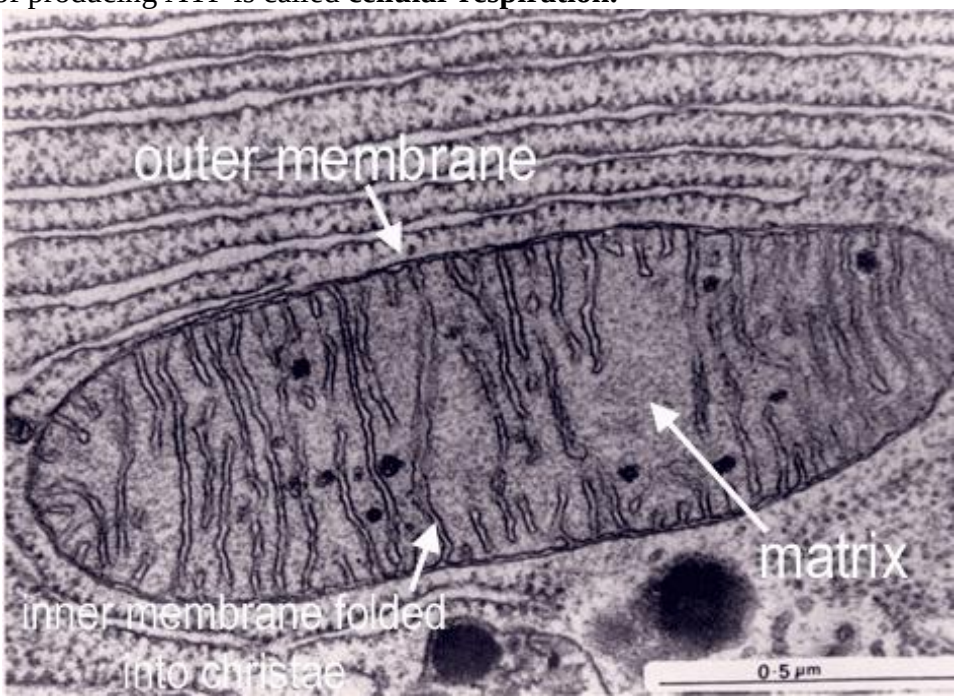
Medical application

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.

❖ Mitochondria

- Mitochondria (singular, **mitochondrion**) are membrane-bounded organelles
- They are usually elongated structures appears under L.M. as spheres, ovoids, or thread like bodies
- They are highly plastic, rapidly changing shape, fusing with one another and dividing, and are moved through the cytoplasm along microtubules.
- The number of mitochondria is related to the cell's energy needs: cells with a high-energy metabolism (eg, cardiac muscle, liver cells and cells of kidney tubules) have abundant mitochondria, whereas cells with a low-energy metabolism have few mitochondria such as small lymphocyte
- Mitochondria are often called the **powerhouses** of the cell. Just as a powerhouse burns fuel to produce electricity, the mitochondria convert the chemical energy of glucose products into the chemical energy of ATP molecules. In the process, mitochondria use up oxygen and give off carbon dioxide. Therefore, the process of producing ATP is called **cellular respiration.**



TEM of Mitochondria

The structure of mitochondria under E.M.: each mitochondrion consists of:

1. **Outer membrane:** is smooth membrane surrounded that allows entry of molecules and contain enzyme involved in mitochondrial lipid synthesis.
2. **Intermembrane space:** Because of channels in the outer membrane of the mitochondria, the content of the intermembrane space is similar to that of the content of the cytoplasm.
3. **Inner membrane:** exhibit numerous folds called **cristae** which maximize internal surface area of mitochondria and contain most of the respiratory chain enzymes and ATP synthase which is responsible for cell respiration (oxidative phosphorylation) and production of cell ATP.

✓ Shape of cristea different according type of cells;

1. In protein secreting cells cristea project into the interior of the organelle like shelve.
2. In steroid secreting cells such as the adrenal cortex or interstitial cells in the testes, the mitochondria cristea are tubular.

4. **Mitochondrial matrix:** the matrix is the space within the inner membrane; contain enzymes for Krebs cycle, mitochondrial DNA **(circular DNA),** special ribosome, tRNase and enzymes for gene expression.
   - *Mitochondrial DNA* is double stranded and has a circular structure very similar to bacterial chromosomes, mitochondrial DNA synthesis and duplication is independent of nuclear DNA replication.
   - *Mitochondrial ribosome* is smaller than cytosolic ribosome.
   - *tRNases* are enzymes that degraded the tRNA.

✓ The structure of a mitochondrion supports the hypothesis that they were originally prokaryotes engulfed by a cell ☺☺☺☺

➢ **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 mitochondria must first replicate the DNA.

➢ **Function of mitochondria**

1. Mitochondria are primary sites for ATP synthesis (site of Krebs cycle**)** from organic material so that known as powerhouse of the cell.
2. Cell respiration.
3. Maintain body heat because some energy dissipated as heat.
4. They have key role in apoptosis programmed cell death.
5. 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.
6. Heme synthesis occurs partly in the mitochondria and partly in the cytosol, Heme is an essential prosthetic group in proteins that is necessary as a subcellular compartment to perform diverse biological functions like hemoglobin and myoglobin. The major tissues for heme synthesis are bone marrow by erythrocytes and the liver by hepatocytes.
7. Other metabolic reactions happened in mitochondria include gluconeogenesis and ketogenesis

Medical application

A maternally-inherited mutation in the mitochondrial genome is leading to defective synthesis of respiratory chain proteins which can produce structural abnormal in muscle fibers especially skeletal muscle fibers are very sensitive to mitochondrial defect (muscular dysfunction) and other cells. (**This called mitochondrial disorders).**