

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ
الَّذِي عَلَّمَ بِالْقَلَمِ ۖ عَلَّمَ الْإِنْسَانَ مَا لَمْ يَعْلَمْ ۝

🧬 CYTOLOGY

MID | Lecture #3

Golgi apparatus & vesicular transport

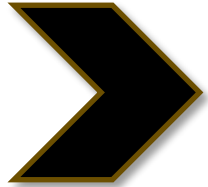
Reviewed by:

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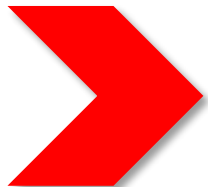
Black: the original slides



Orange: the doctor's explanation/words



Gray: additional information and explanation



Red: important information



Lecture 2: Golgi apparatus and vesicular transport

Prof. Mamoun Ahram
School of Medicine
Second year, First semester, 2026-2027

Functions of the Golgi apparatus

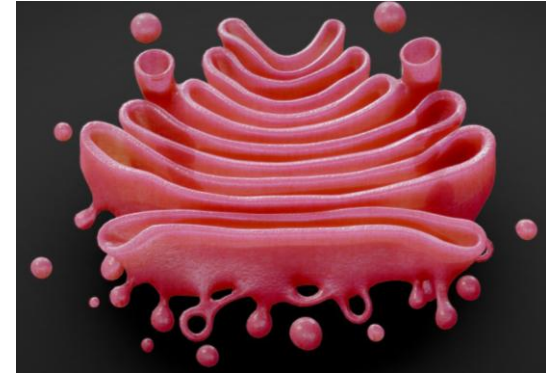


- Further protein processing (starts in the er and ends in the golgi apparatus with the help of additional enzymes and proteins) and modification.
- Synthesis of glycolipids, sphingomyelin and ceramides (structure not included just the name).
- Protein sorting, proteins moving from golgi apparatus to different places in the cell :
 - Secretion outside the cell.
 - Plasma membrane (plasma proteins, receptors).
 - Endosomes and lysosomes (mentioned later on the lecture).
- When sugar is added to the ceramide, it turns into Glycolipids :
 - 1: Cerebroside glucose or galactose.
 - 2: Globoside 2 or more sugar molecules (lactose).
 - 3: Ganglioside 3 or more sugars one of them being sialic acid.

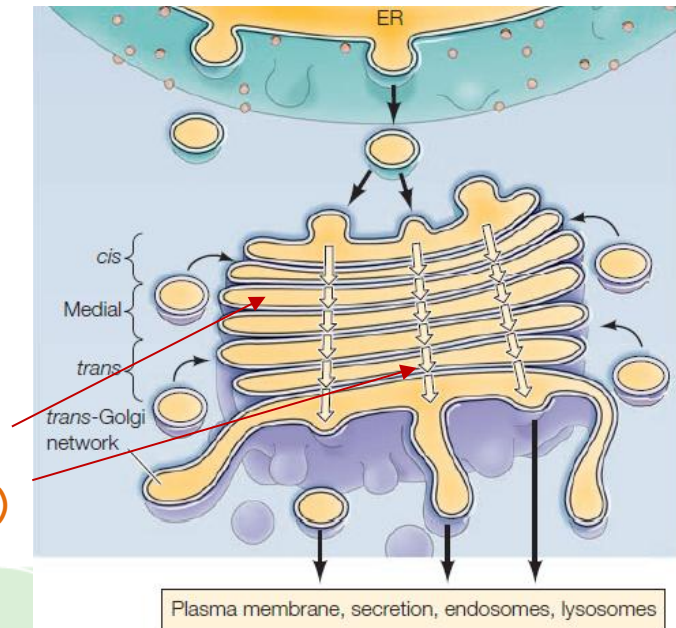
Structure of the Golgi



- The Golgi apparatus consists of a stack of flattened sacs (cisternae) of three regions: *cis* (close to ER, first one), medial, and *trans* (further to ER, last one) compartments and the *trans*-Golgi network. (the doctor didn't mention it, however its the part of the Golgi apparatus that sorts, packages, and sends proteins and lipids to their correct destinations inside or outside the cell).
- Proteins are carried through the Golgi apparatus in the *cis-to-trans* direction.
- Transport vesicles carry the Golgi proteins back to earlier compartments for reuse. (from *trans-to-cis*)

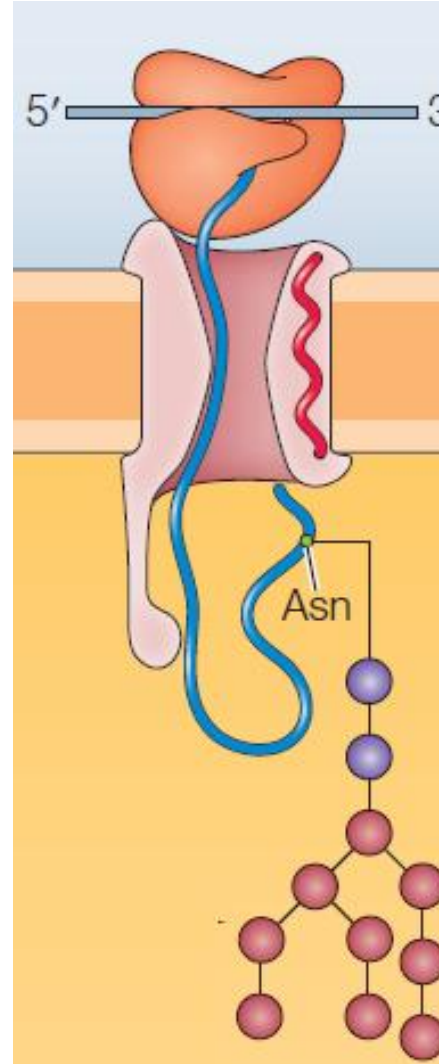


Cisternae
(flattened sacks)

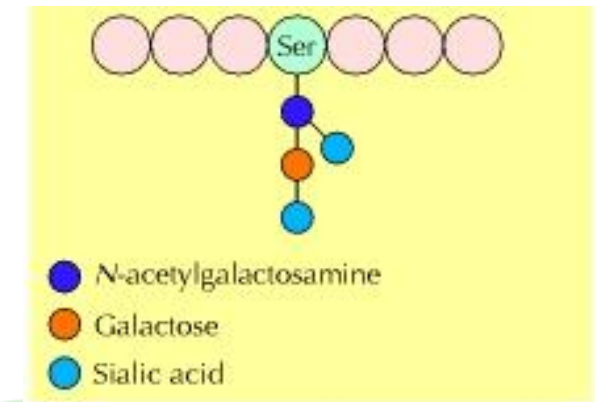


Processing of N-linked oligosaccharides in Golgi

The N-linked oligosaccharides, which are added to **asparagine** residues of glycoproteins in the ER and transported from the ER, are **further modified enzymatically in the Golgi**.



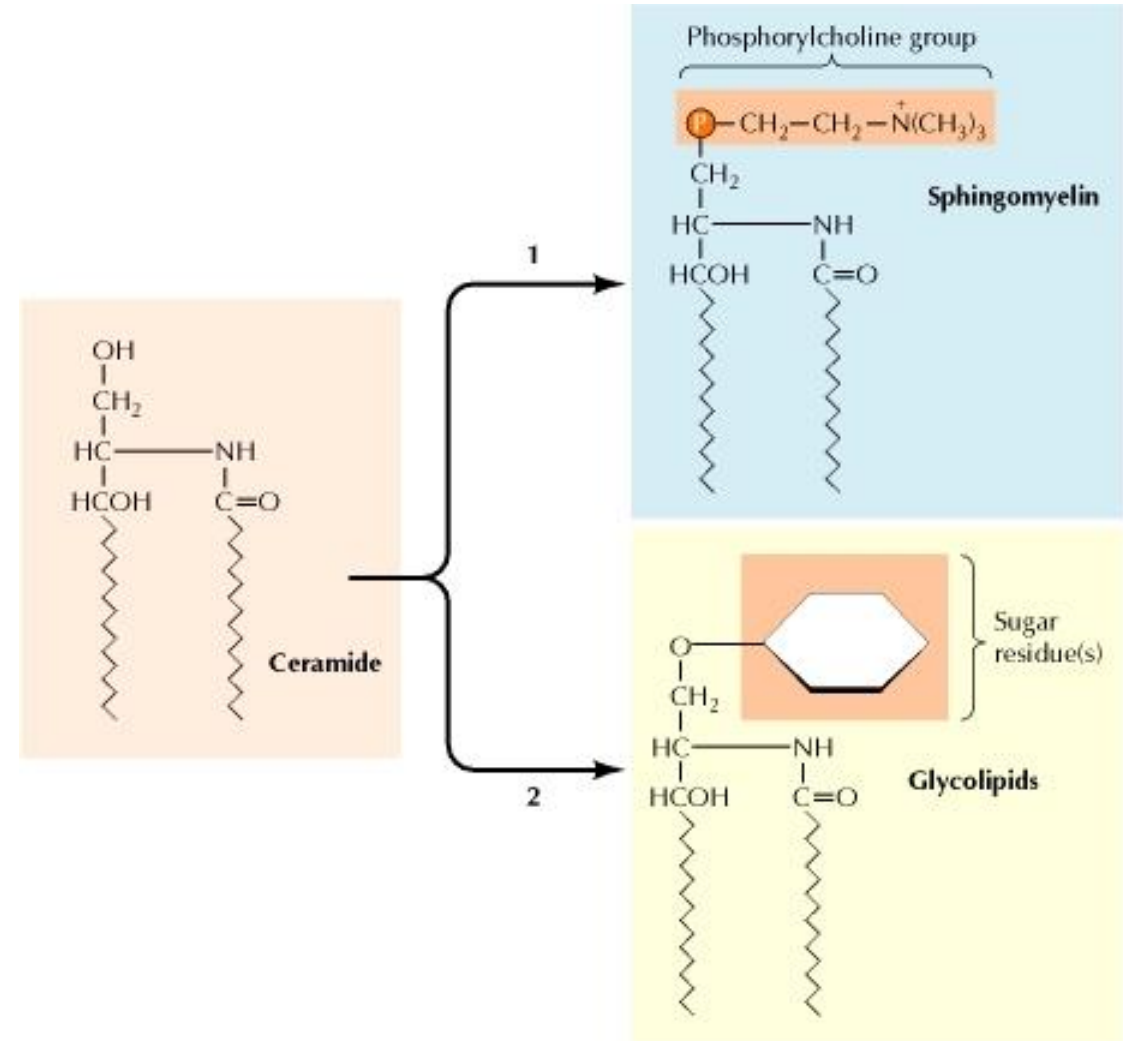
*Proteins can also be modified by the addition of carbohydrates to the **hydroxyl side chains of serine and threonine** residues, hence called **O-linked sugars**. These sugars are synthesized in the Golgi Apparatus*



Lipid and Polysaccharide Metabolism in the Golgi



- The glycerol phospholipids, cholesterol, and ceramide are synthesized in the ER.
- Ceramide is then converted either to sphingomyelin **by the addition of phosphocholine** (a phospholipid) or to glycolipids **by adding sugars** in the Golgi apparatus.

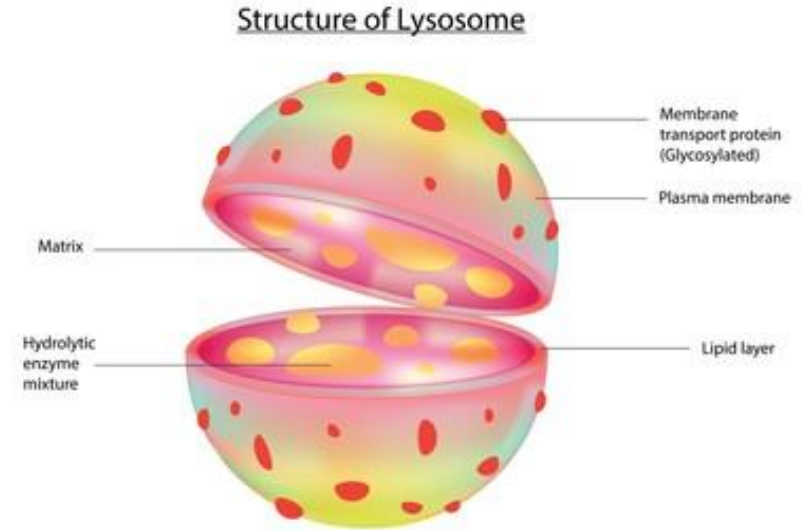


Lysosomes



Structure

- Lysosomes are membrane-enclosed (single bi-layer membrane) organelles that contain various hydrolase enzymes that break down all types of biological macromolecules (lyses, breaking down)
- Lysosomes degrade material taken up from outside and inside the cell.
- Lysosome contains hydrolytic enzymes, which uses water to break down molecules such as sugars, lipids, proteins, and peptides.

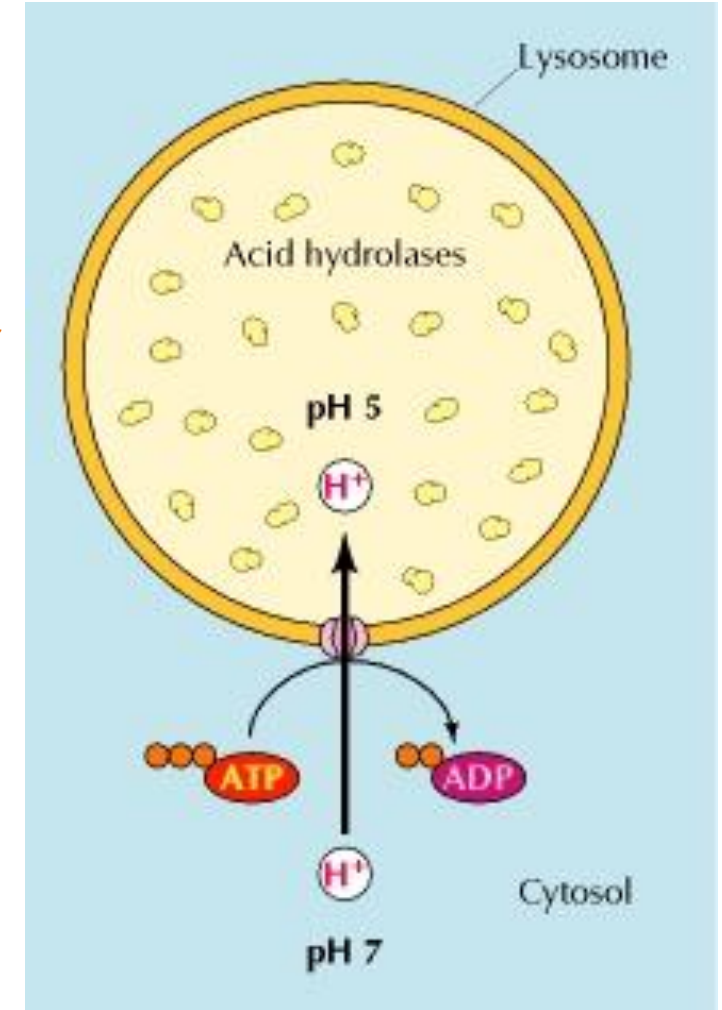


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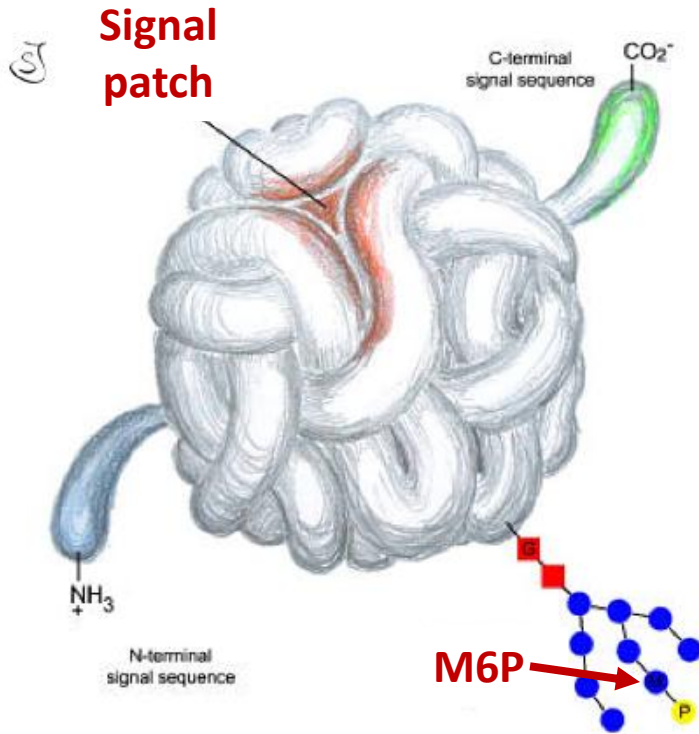


Lysosomal enzymes

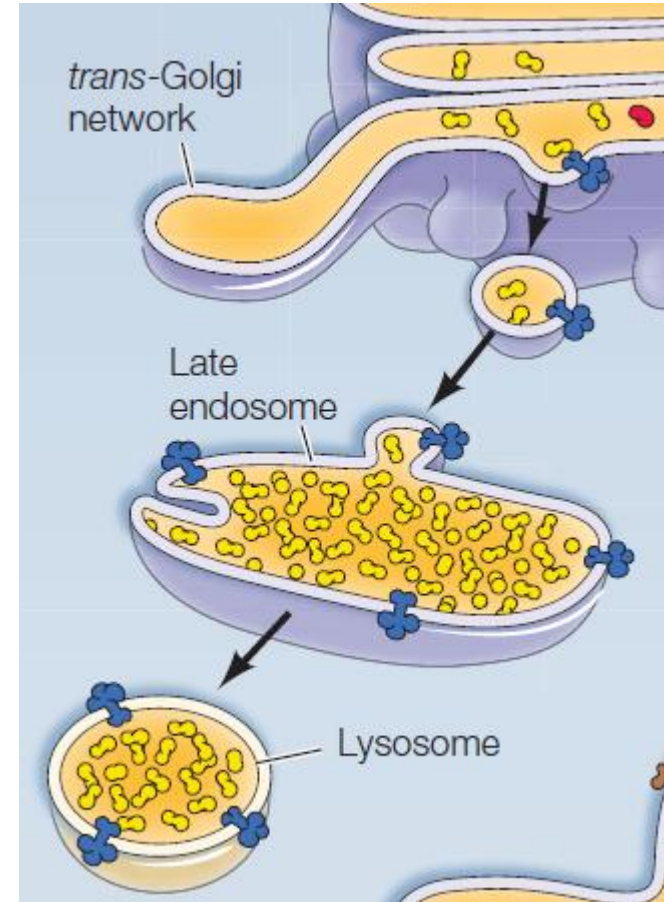
- Lysosomes contain ~60 different acid hydrolases.
- The enzymes are active at the acidic pH (about 5) that is maintained within lysosomes. *why? 1- So it can denature proteins to lose their 3d structure since the bonds are weak at low Ph levels, making it accessible for the hydrolases to cut up the degraded proteins. 2- to protect the cell, how? If the lysosomes bust, the hydrolases will be inactive due to their property of needing a low Ph space to operate*
- Levels of cell protection from these hydrolases:
 - Containment
 - Inactive if released
- **IMPORTANT: An ATP-dependent proton pump maintains the lysosomal pH.**



Targeting of lysosomal proteins to the lysosomes



Proteins destined to lysosomes have a signal patch (a three-dimensional structural determinant), which is recognized by modifying enzymes that add mannose-6-phosphate to the proteins.



Luminal lysosomal proteins bind to a mannose-6-phosphate receptor in the Golgi and are transported to vesicles known as the late endosome, which mature into lysosomes.

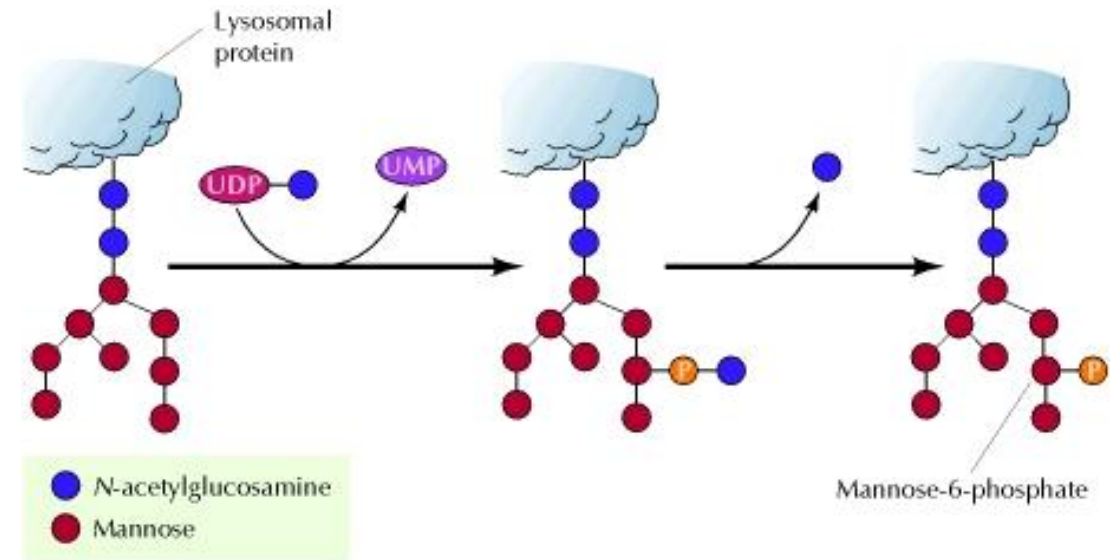


- How do cells know that the protein must be targeted to the lysosome? There's a code, phosphorylated mannose. Proteins have a single patch (3d structure within the proteins that indicates which pathway it takes.
- There's a receptor in the Golgi apparatus it's a mannose-6-phosphate receptor, proteins that have a phosphorylated mannose binds to the receptor forming a vesicle and moving to the endosomes.
- Endosomes then mature into lysosomes. The Ph inside endosomes is about 6-6.5 .

I-cell disease

also called mucopolidosis IIA, or mucopolidosis II alpha/beta: ML-II α / β

- Defective targeting of lysosomal enzymes from Golgi to the lysosomes
- A deficiency in the tagging enzyme that phosphorylates mannose.
- So, proteins can't move from Golgi to lysosomes leading to I-cell disease severely affecting the CNS
- Features: severe psychomotor retardation that rapidly progresses leading to death between 5 and 8 years of age.



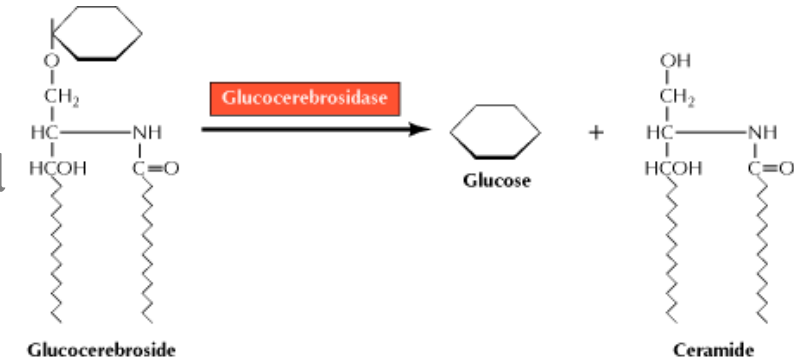
Many in-born Metabolic diseases (defective degradation/synthesis) have a symptom of **mental retardation** since neurons are delicate.

Glucocerebroside

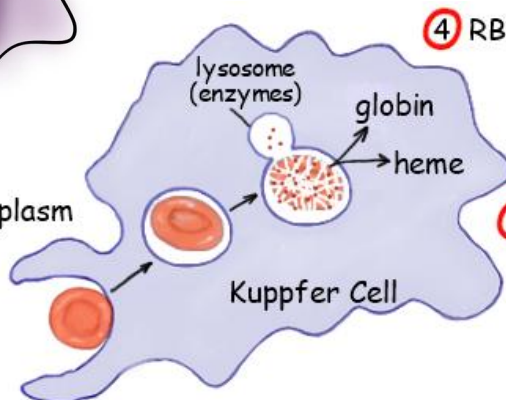


- Glucocerebroside is a glycosphingolipid (a monosaccharide attached directly to a ceramide unit (a lipid))
- It is a byproduct of the normal recycling of red blood cells, which are phagocytosed (eaten up) by macrophages, degraded, and their contents recycled to make new cells.

Just to remember: Kupffer cells are specialized macrophages located in the liver that perform phagocytosis of bacteria, cellular debris, and old red blood cells, contributing to immune defense and clearance of foreign particles from the blood.



② RBC moved into cytoplasm inside a vacuole;



④ RBC hemoglobin broken down into heme and globin;

③ lysosome fuses with vacuole to release enzymes used to break down RBC;

① red blood cell (RBC) taken in by phagocytosis by Kupffer cell;

Glucocerebroside



Glucocerebroside is a molecule found in the plasma membrane . It is a sphingolipid (a lipid that has sphingosine as a backbone instead of glycerol).

- **Cerebroside** is made of **ceramide** attached to 1 monosaccharide (glucose or galactose).
- **Globoside** is made of **ceramide** attached to 2 monosaccharides or more. Addition of **sialic acid** gives **ganglioside**.

In **lysosomes**, there is an enzyme called **glucocerebrosidase** which converts Glucocerebroside into free glucose and ceramide

Macrophages during phagocytosis of RBCs (hemolysis) encounter high amounts of glucocerebrosides. So **defective glucocerebrosidase** leads to the **accumulation of glucocerebrosides** leading to several symptoms including mental retardation. This process also occurs in the neural cells in the CNS



Lysosomal storage diseases In-born errors of metabolism

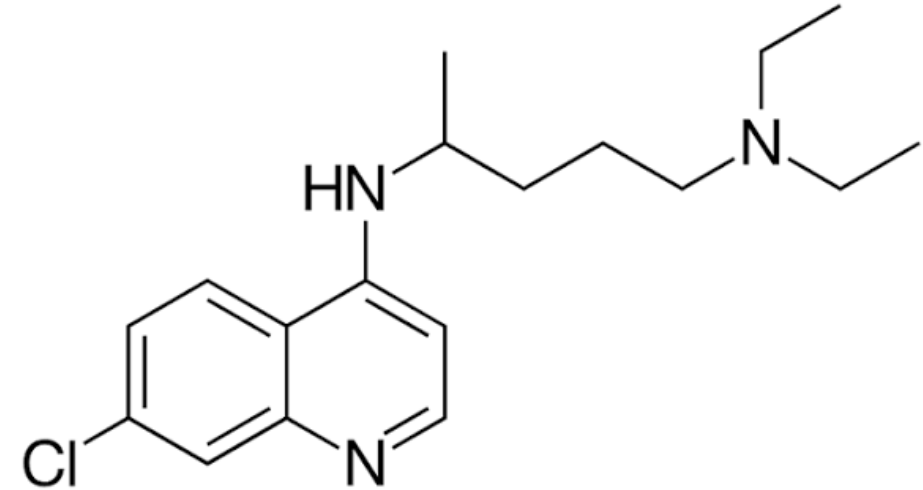
There are a group of diseases in which some **hydrolytic enzymes in the lysosome** are defective leading to accumulation of molecules in the lysosome.

Mental retardation is associated with those diseases

- Gaucher disease (glucocerebrosidase deficiency) **(most common metabolic syndrome)→all of those diseases are very rare but this one is the most common of them.**
- Glycolipidoses (sphingolipidoses) **(disease where enzymes that degrade sphingolipids are defective)**
- Oligosaccharidoses **(disease where enzymes that degrade sugars are defective)**
- Mucopolysaccharidoses: deficiencies in lysosomal hydrolases of glycosaminoglycans (heparan, keratan and dermatan sulfates, chondroitin sulfates).
 - They are chronic, progressively debilitating disorders that lead to severe psychomotor retardation and premature death.

Targeting malarial lysosomes

- Antimalarial drugs like chloroquine and pyronaridine act as weak bases that raise the acidic pH of the malaria parasite's digestive vacuoles.
- The pH elevation prevents the proper neutralization of the toxic free heme produced during hemoglobin breakdown and the parasite is effectively poisoned and killed by its own accumulated metabolic waste products.



The general mechanism of vesicular transport

Proteins go into the ER with the help of signal peptides then these proteins go into either the nuclear membrane, peroxisomal membrane, or the golgi apparatus.. From the golgi it goes into either the plasma membrane, extracellular milieu (specific region outside the cell), endosomes and lysosomes, or secretory vesicles.

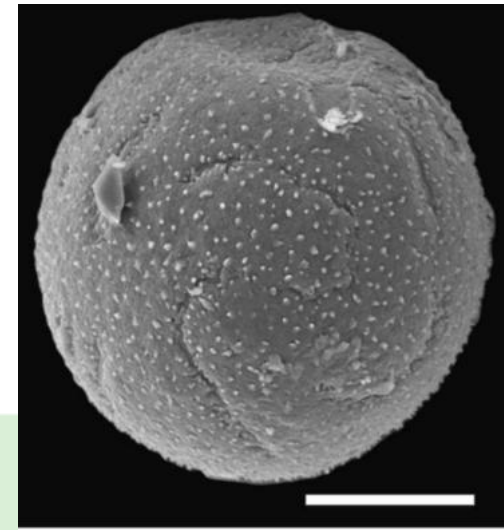
The general mechanisms for transport of proteins is through vesicles which is **selective**



What are transport vesicles?

- Vesicular transport is the movement of molecules in bags (or sacs) called transport vesicles in and out of cells or within cells.
 - Examples: (1) the transport of materials taken up from outside the cells at the cell surface into them, or (2) the transport of lysosomal enzymes from the Golgi apparatus to the lysosomes.
- Vesicular transport is selective in terms of destination and packaging.

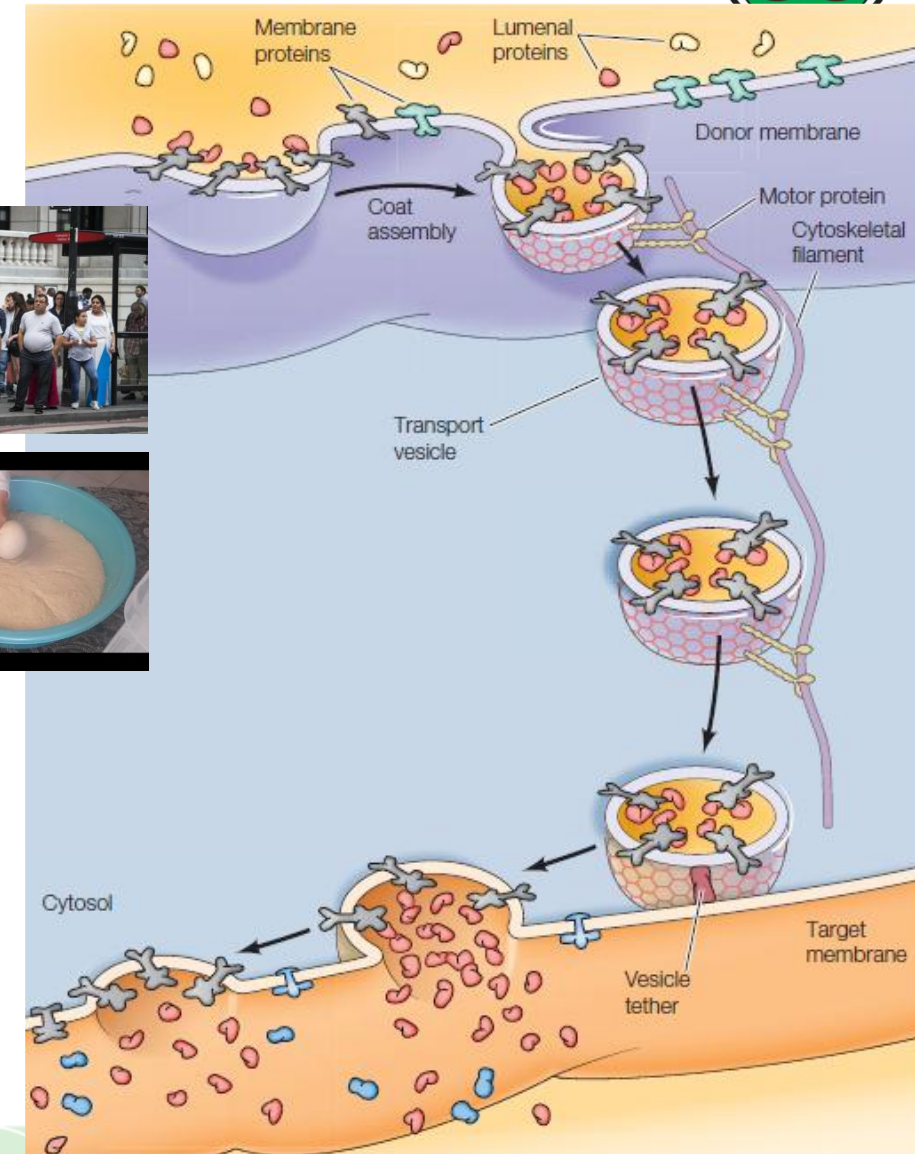
- When molecules enter the cell, they get enclosed by a vesicle. When molecules are released outside the cell the vesicle fuses into the target membrane



The general steps of vesicular transport



1. The molecules to be transported are aligned along or clustered in the membrane of the donor compartment. **all of the molecules concentrate in a certain area like bus station (they know where to cluster based on the presence of their specific receptor on the organelle's membrane)**
2. A vesicle buds from the donor membrane.
3. The bud grows and ultimately pinches off the donor membrane, yielding a transport vesicle.
4. The vesicle is transported along cytoskeletal filaments to a target membrane.
5. The vesicle fuses with the target membrane, whereupon the transmembrane proteins are incorporated into that membrane and the soluble proteins are released.

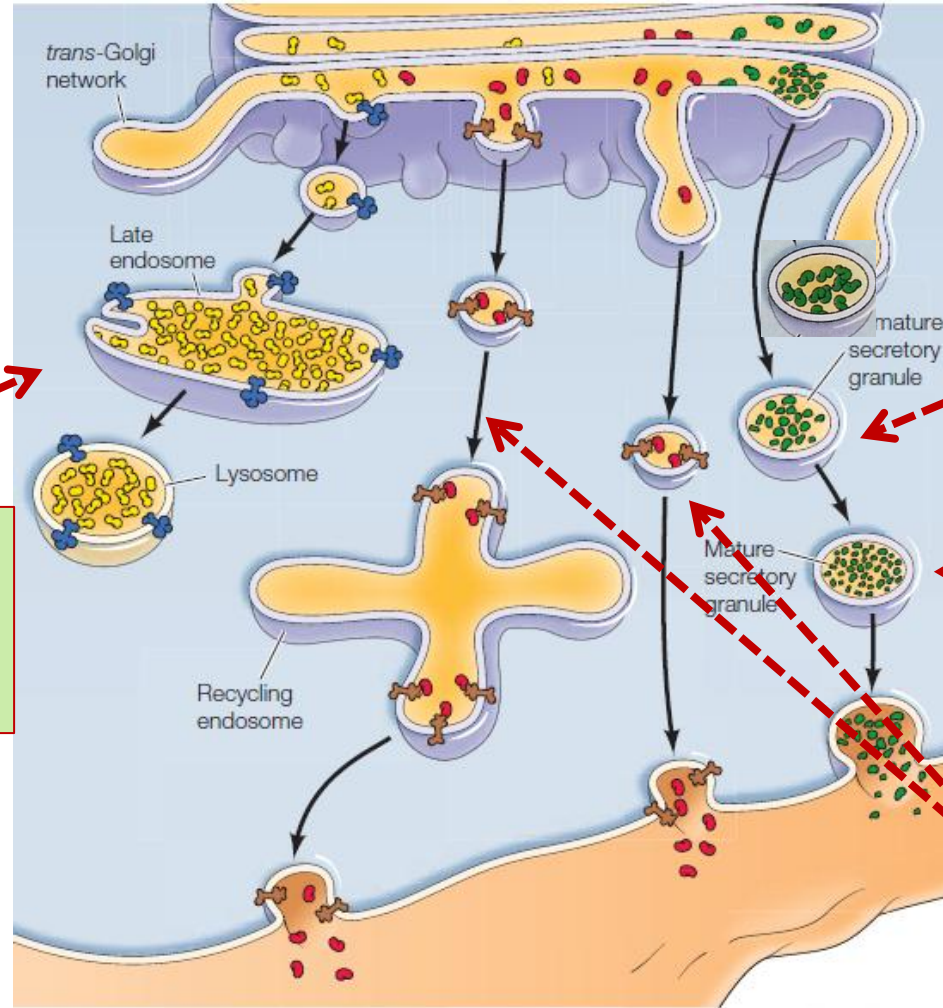


The processes of vesicular transport



The secretory pathway (exocytosis)

Secretion of molecules to the outside of the cell



Cytosis: a cellular process of moving material across membranes

Moving of molecules in the cell

Protein processing in Immature secretory vesicles

2. Regulated, signal-stimulated secretion of processed proteins from specialized vesicles (e.g., neurotransmitters and digestive enzymes)

1. Continuous, unregulated secretion directly or via recycling endosomes, which also act to recycle endocytosed proteins to the plasma membrane

Already discussed: Proteins can be targeted to late endosomes, which develop into lysosomes

Exocytosis



Exocytosis could be:

Continuous exocytosis, which has 2 types:

- 1- The vesicle moves directly from the Golgi to the Plasma membrane
- 2- The vesicle moves from the Golgi into a recycling endosomes and fuses with it. Then the recycling endosome fuses with the plasma membrane to release its contents outside the cell.

Vesicles that pinch off Golgi could fuse with late endosome, where proteins will get released from the mannose-6-phosphate receptor due to low pH found in endosomes. Then endosome then matures in to lysosome which has a lower PH.

Regulated exocytosis,

means that after pinching off the Golgi, the vesicles remain in the cytosol until a signal appears which allows them to fuse the plasma membrane and leave the cell.,like what we can observe in neurons the entry of Ca^{+2} allows the neurotransmitter vesicles to be released in the synaptic cleft.

Regulatory vesicles contain neurotransmitters or digestive enzyme (in pancreatic cells). During this regulated exocytosis, there might be intermediate vesicles where protein processing occurs

Quiz



Good luck

For any feedback, scan the code or click on it.



Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1	Slide 4 , Number 2 Slide 6	Glucoside	Globoside
V1 → V2			

Additional resources:

References Used:

Prof. Mamoun Ahram recorded lecture

Extra References for The Reader to Use:

اللهم ارزقني قوة الحفظ
وسرعة الفهم وصفاء الذهن
اللهم الهمني الصواب في
الجواب وبلغني اعلى المراتب
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