
بسم الله الرحمن الرحيم

Foundation Module

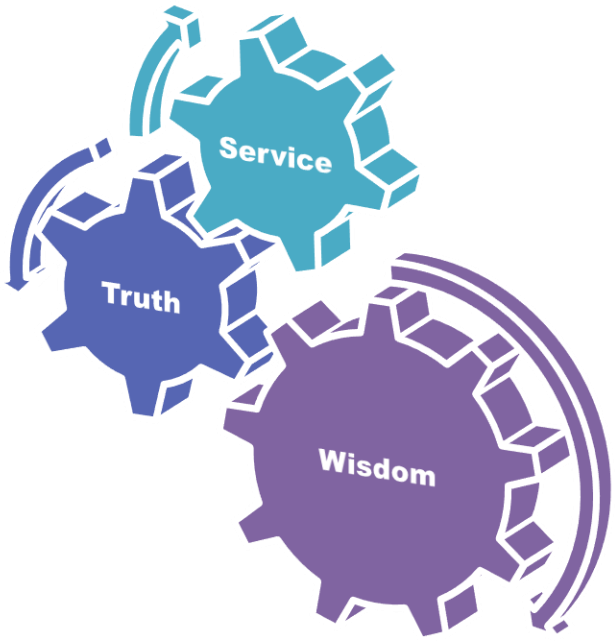
1st Year MBBS(LGIS)

Cell & Cell Organelles-2

Presenter: Dr Nayab Ramzan
Deptt of Biochemistry
RMU

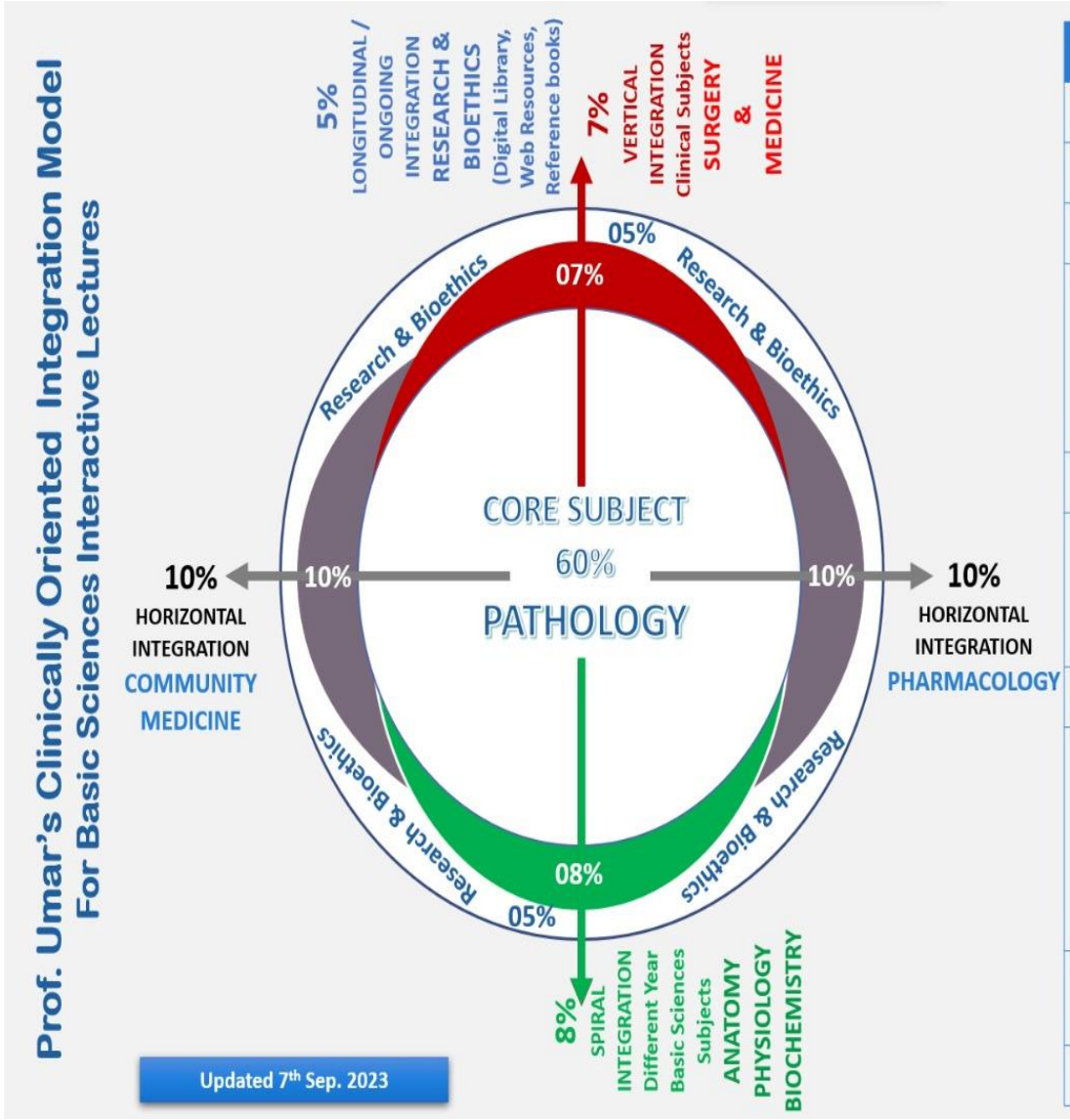
Date: 07-02-25

Motto, Vision, Dream



- To impart evidence based research oriented medical education
- To provide best possible patient care
- To inculcate the values of mutual respect and ethical practice of medicine

Professor Umar Model of Integrated Lecture



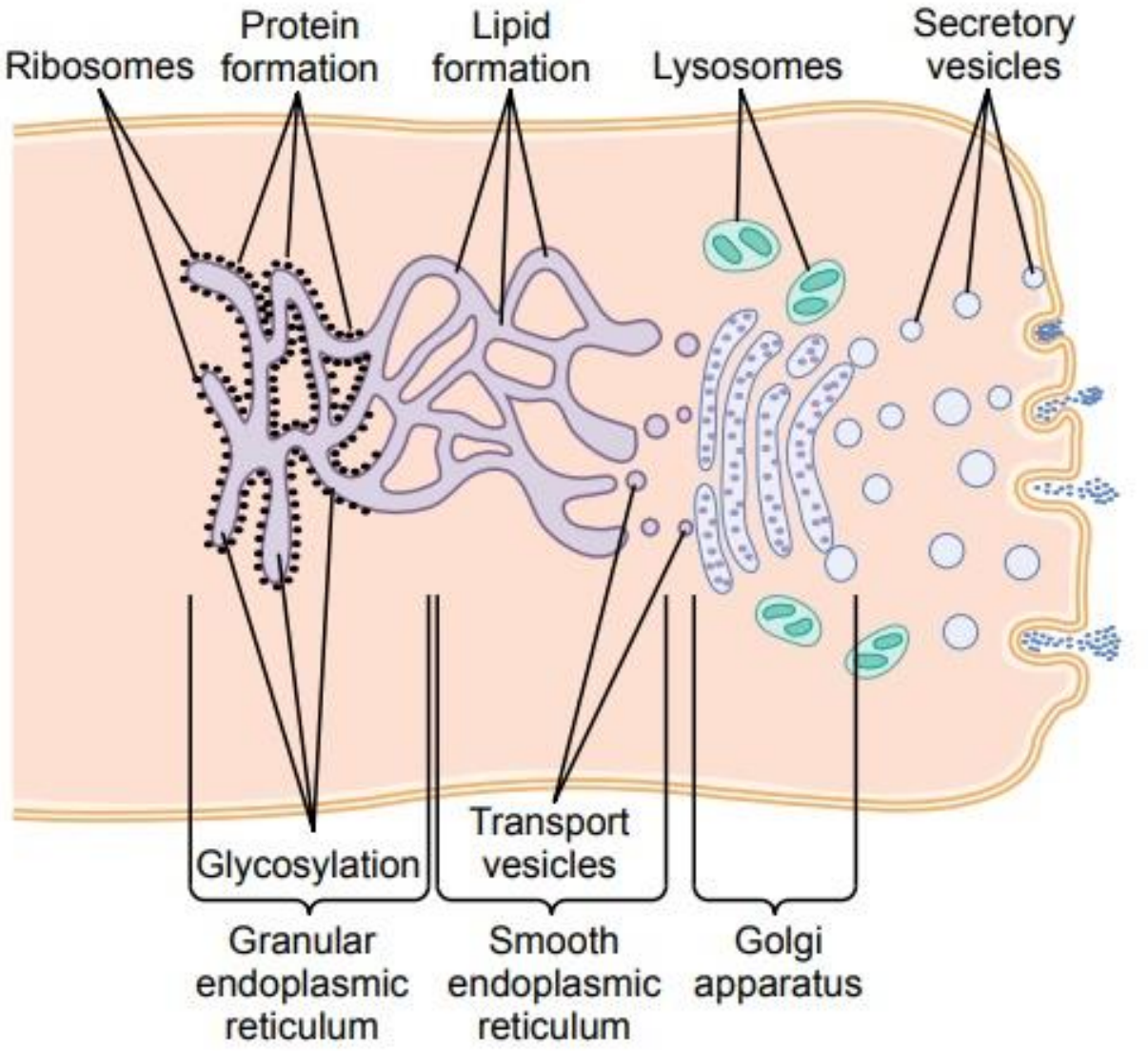
Model 3rd Year Pathology LGIS (≈30 slides)	
Core Subject – 60% (≈ 18-20 slides)	
Pathology (≈ 18-20 slides)	
Horizontal Integration – 20% (≈ 5-6 slides)	
Same Year Subjects	• Pharmacology (10%) (≈ 2-3 slides) • Community Medicine (10%) (≈ 2-3 slides)
Vertical Integration – 07% (≈ 2-3 slides)	
Clinical Subjects	• Medicine (3-5%) (≈ 1-2 slides) • Surgery (3-5%) (≈ 1-2 slides)
Spiral Integration – 08% (≈ 2-3 slides)	
Different Year Basic Sciences Subjects	• Anatomy (1-3%) (≈ 1-2 slides) • Physiology (1-3%) (≈ 1-2 slides) • Biochemistry (1-3%) (≈ 1-2 slides)
Longitudinal / Ongoing Integration – 05% (≈ 1-2 slides)	
Research & Bioethics (≈ 1-2 slides)	

Learning Objectives

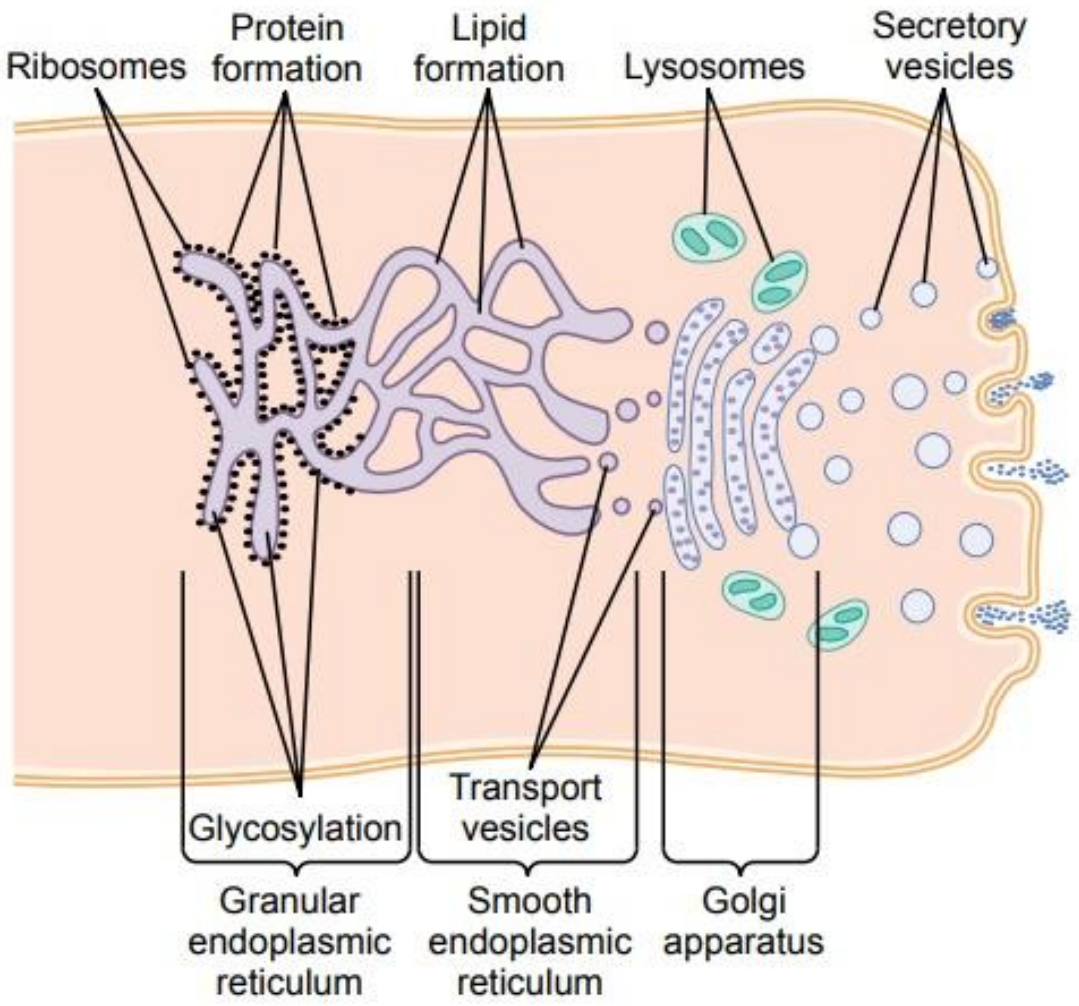
At the end of this session students should be able to

1. Explain structure, functions and marker enzymes of Endoplasmic Reticulum, Golgi apparatus, Lysosomes, Peroxisomes & Ribosomes.
2. Correlate with the clinical conditions
3. Practice the principles of bioethics & apply strategic use of A.I to the clinical conditions
4. Read relevant research articles

Cell Organelles

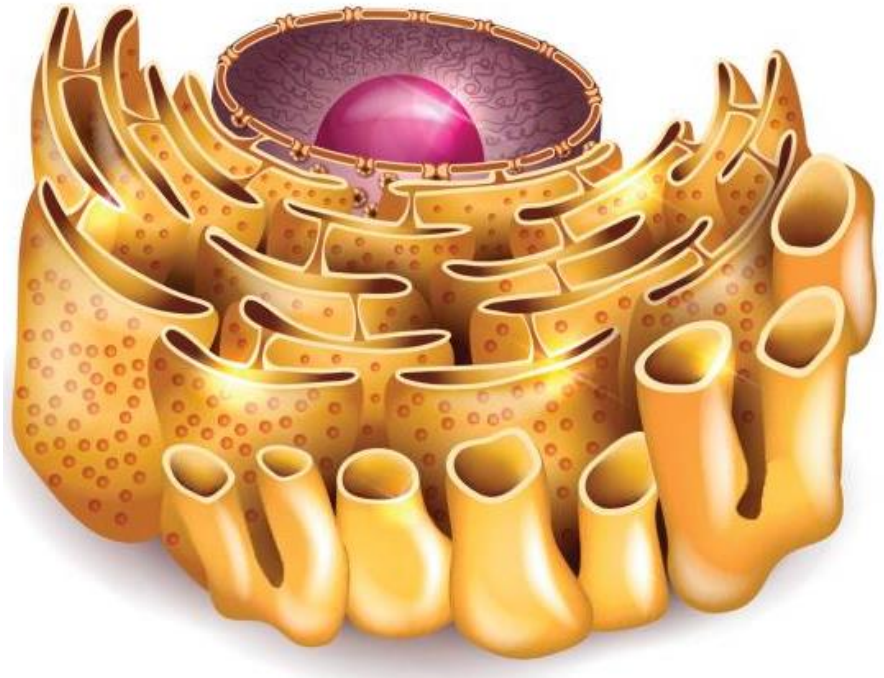


Intracellular Markers



Endoplasmic Reticulum

- Closed network of **Tubules** and **Shallow Sacs** linked with outer membrane of nucleus
- Space inside Endoplasmic Reticulum **connected** with space between two membrane surfaces of **Nuclear Envelope**
- This space is filled with watery medium called **Endoplasmic Matrix**
- The Endoplasmic Reticulum (ER)- Main Roles are **Calcium Storage**, **Protein Synthesis** and **Lipid Metabolism**.



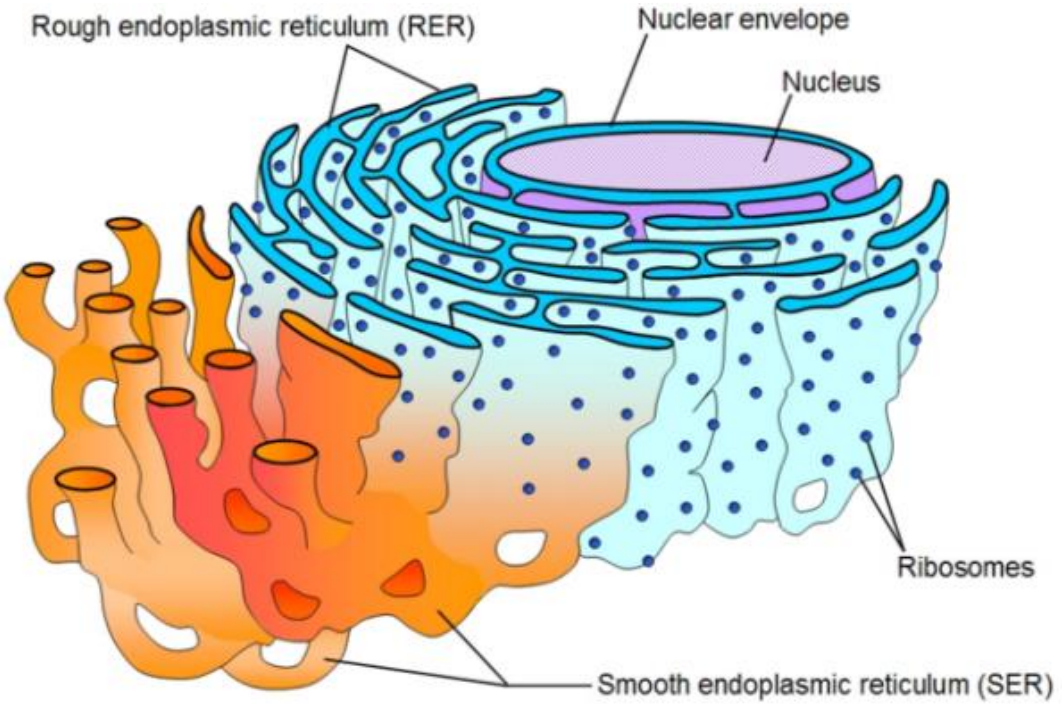
Types of ER

Rough ER

- **Ribosomes attached** to the outer surface give it a rough or granular appearance so known as **Granular** or Rough Endoplasmic Reticulum.

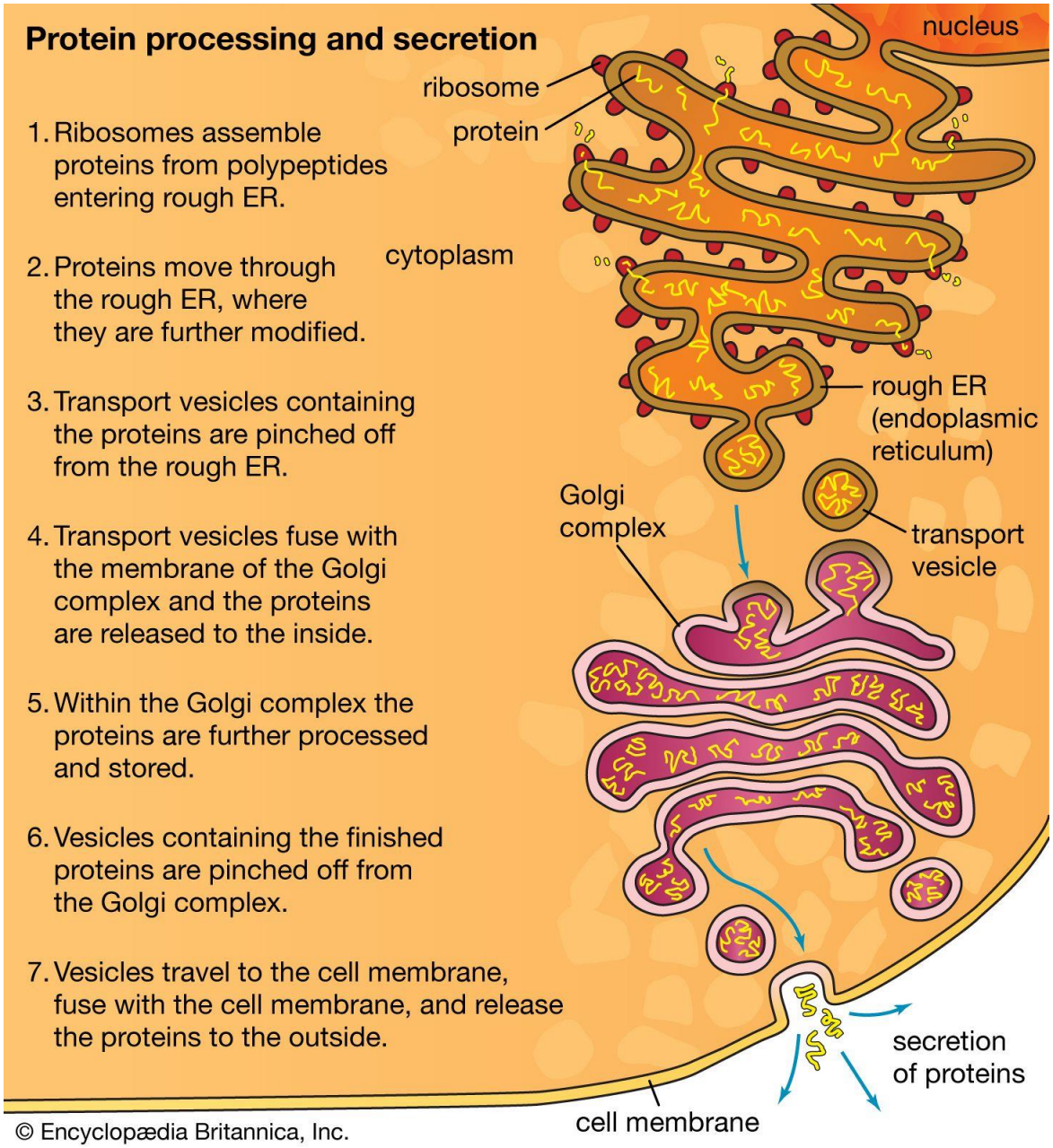
Smooth ER

- Due to **no Ribosomes** attached on the surface it is known as Smooth ER.



Functions of ER

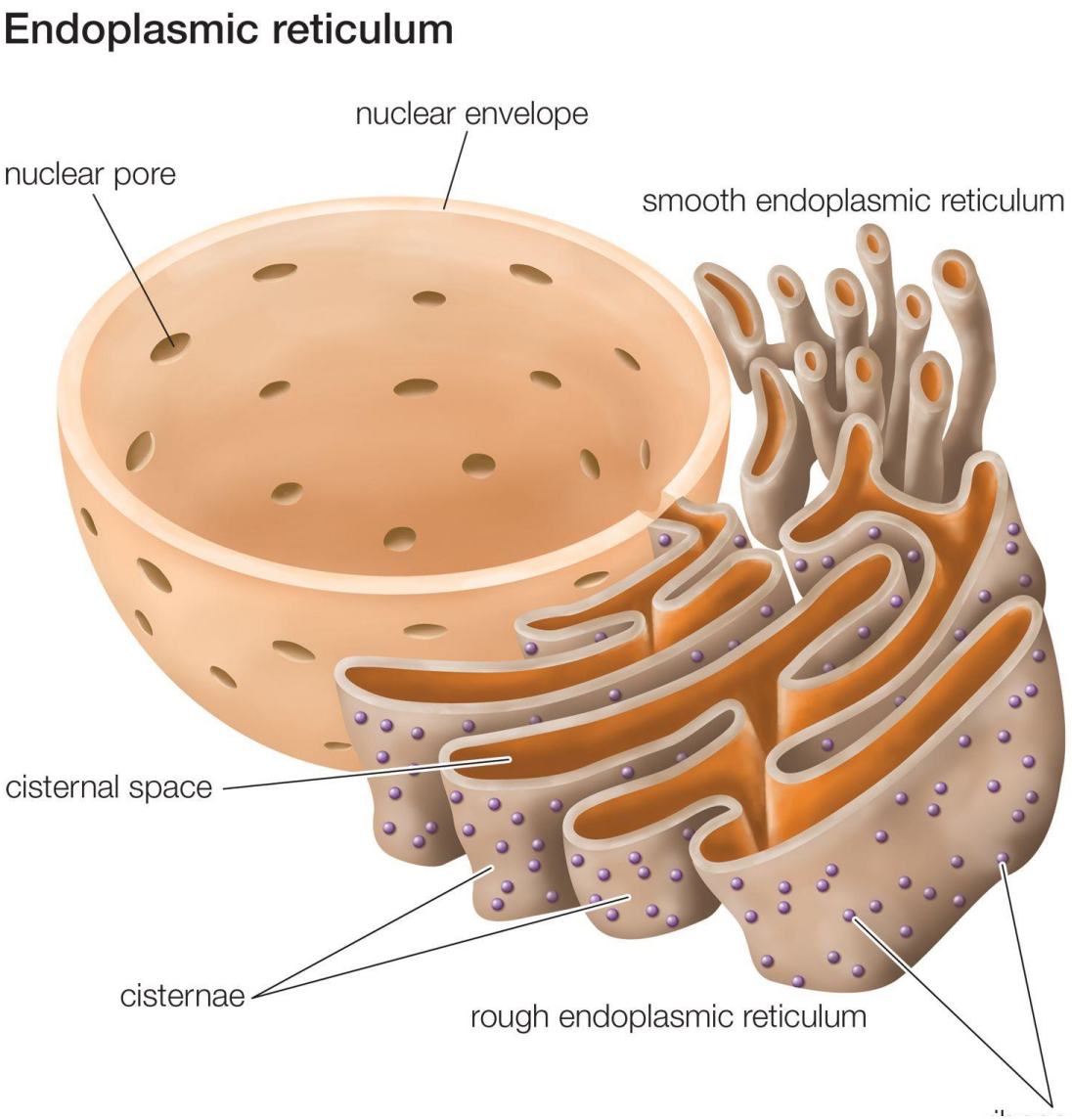
- It synthesizes CHO which along with lipids synthesize new membranes.
- Provides **Enzymes** so as to control **Glycogen Breakdown for Energy Production**
- Enzymes **cytochrome P-450** attached to the outer surface take part in **Xenobiotic Metabolism**
- SER in skeletal muscles called **Sarcoplasmic Reticulum stores Ca^{+2} ions** which take part in **Excitation- Contraction Coupling**



Core Knowledge

Functions of ER

- **Rough ER** have ribosomes which are factories for protein synthesis
- Some CHO are also synthesized within its cavities which are used for glycosylation of proteins
- **Smooth ER** takes part in synthesis of lipids especially phospholipids and cholesterol
- These lipids cause extensive growth in ER



Golgi Appt. or Golgi Complexes

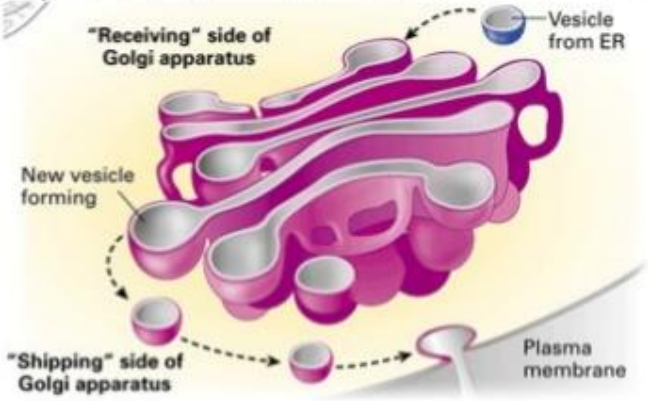
- A unique cluster of membrane vesicles known as **Dictyosomes** constitute Golgi complex-closely associated with ER

- The G.complex has **Proximal** or **CIS Compartment**, a **Median** and **Distal** or **Trans Compartment**.

- This complex is involved in **Modifying Proteins** and in **Distributing** these proteins to other regions of the cell or to the exterior.

Golgi Body Function

- Modifies proteins and lipids
- Process materials to be removed from the cell
- Make and secrete mucus
- Packages products into vesicles for transport



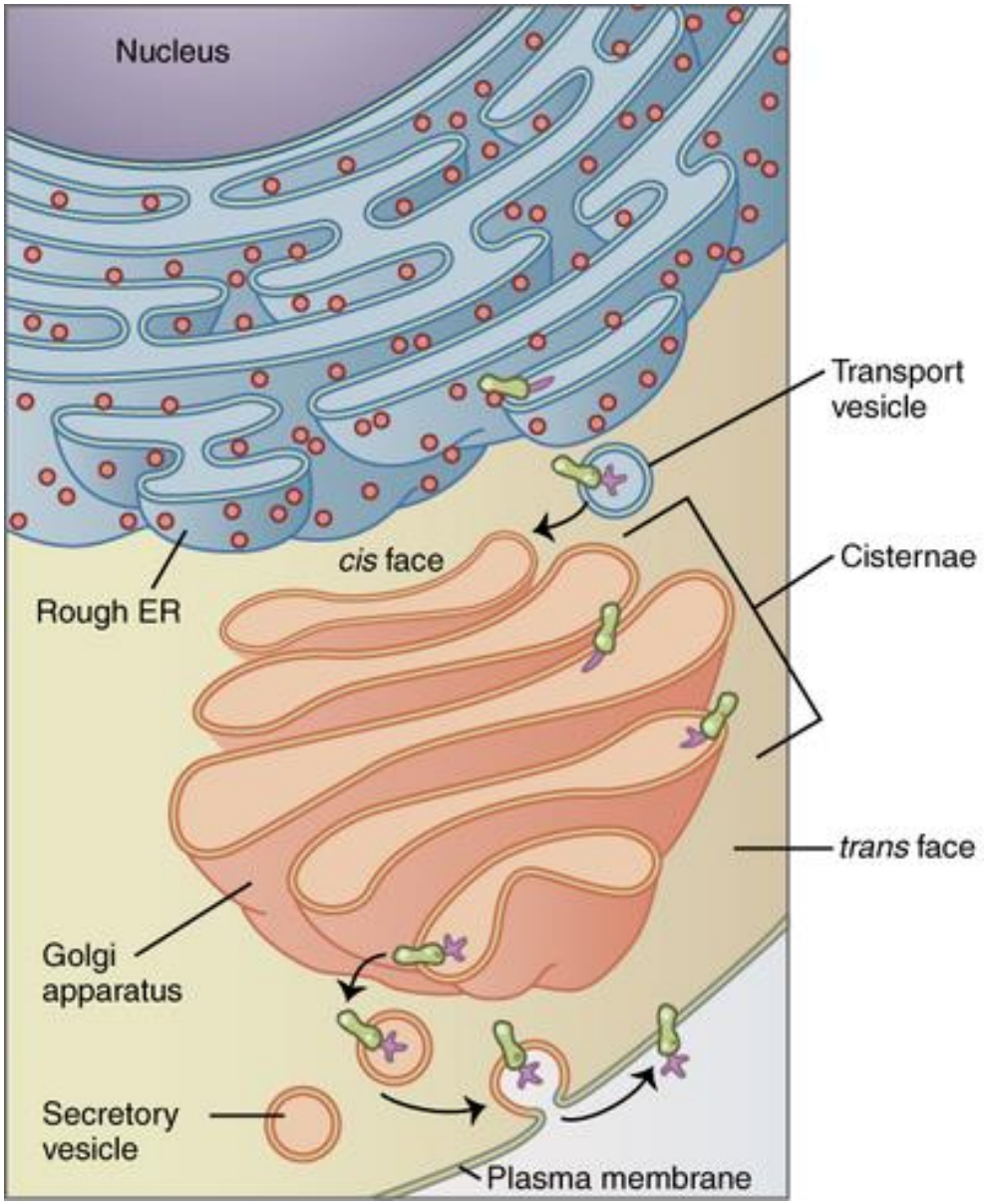
http://4.bp.blogspot.com/_rBYpndaJ_ak/S-sxGmLUOuI/AAAAAAAAAGM/oKWwbrO41-U/s1600/Golgi+apparatus.gif

Core Knowledge

Golgi Appt. or Golgi complexes

- **Small transport vesicles** continually pinch off ER and fuse with Golgi complexes. In this way, **all substances are transported from ER to Golgi complexes**

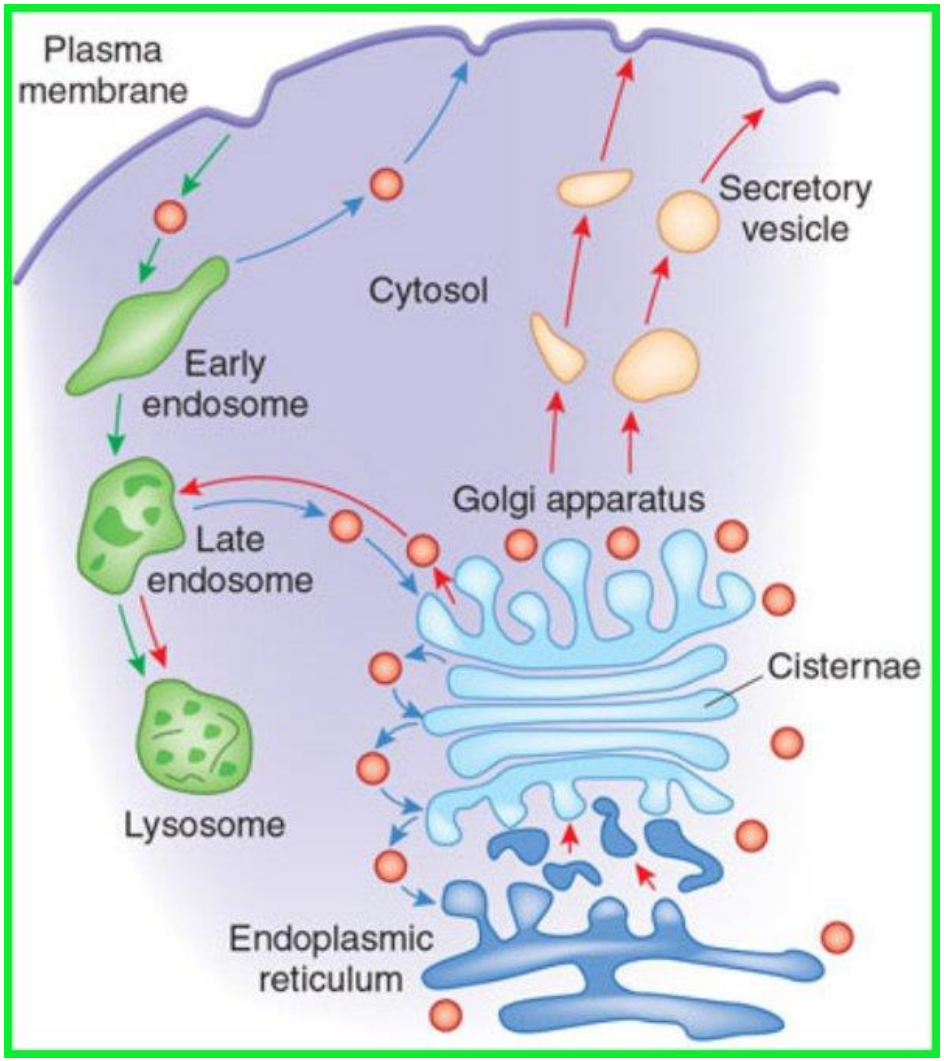
- Transported substances are **processed in lumen of median compartment** where posttranslational modifications take place



Golgi Appt. or Golgi complexes

- During this modification, CHO and lipid precursors are added to proteins to form **Glycoprotein** and **Lipoprotein** respectively

- Golgi complex can also **synthesize certain CHO which cannot be formed in ER** e.g. large saccharides polymers bound with small amount of protein like **Hyaluronic Acid** & **Chondroitin Sulphate**



Golgi Appt. or Golgi complexes

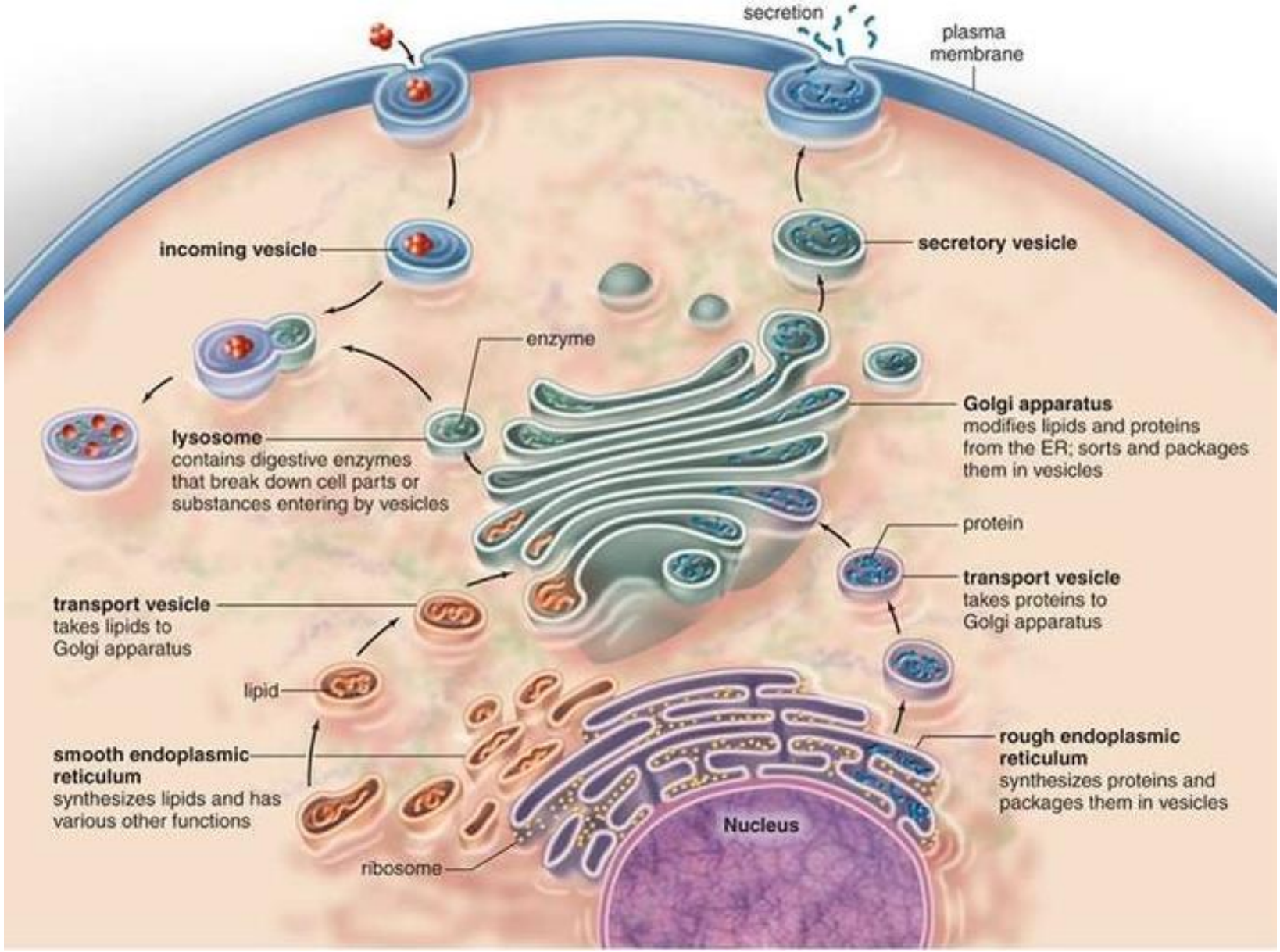
- These modified proteins are then **packaged** in vesicles. These **secretory vesicles break away from Golgi complexes at trans face** and diffuse throughout the cell

- These secretory vesicles may travel to cell membrane where they **fuse with cell membrane** and empty their substances to exterior of cell

Golgi Appt. or Golgi complexes

- Some of them fuse with mitochondria and ER so as to replenish the membranes which are used up during cellular processes
- Certain protein and enzymes are enclosed in Golgi complexes and secreted after appropriate signals e.g digestive enzymes of pancreas are produced in this way

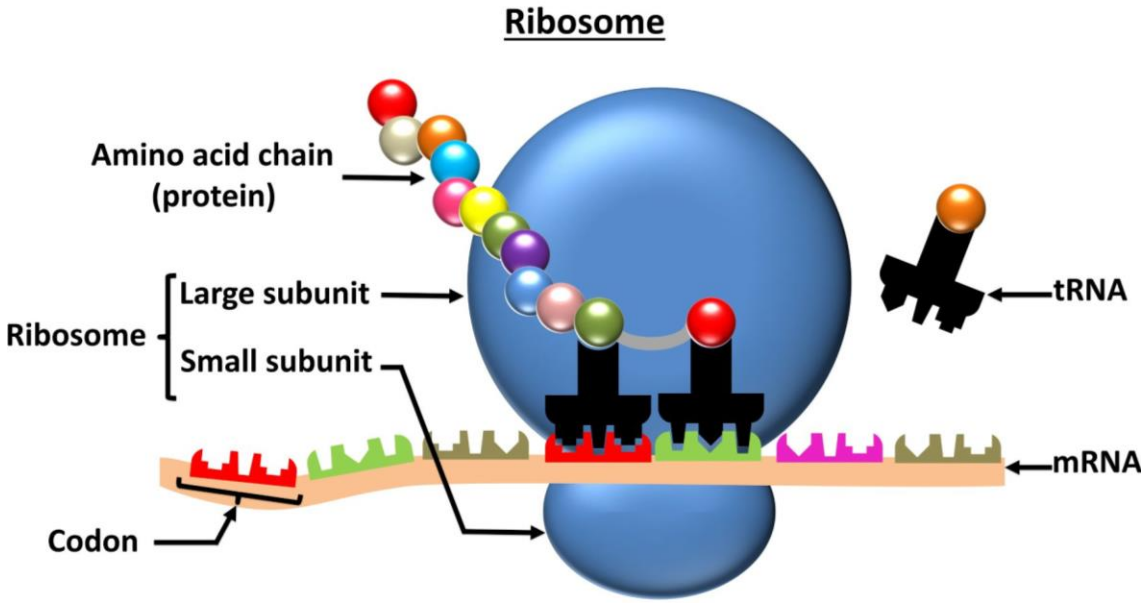
Functions of Golgi Apparatus



Core Knowledge

Ribosomes

- Site for **protein synthesis** from amino acids
- Consist of **two subunits** of different size, made up of **rRna** and large number of **proteins**
- Sedimentation coefficient of ribosomes is more significant as compared to their masses
- Sediment coefficient of eukaryotic ribosome is 80S while that of its subunits are 40S and 60S
- Smaller 40S subunit consist of 18S rRNA molecule and 33 proteins.
- The large 60S subunit contains 5S, 5.8S and 28S rRNA molecules and 47 proteins



Ribosomes

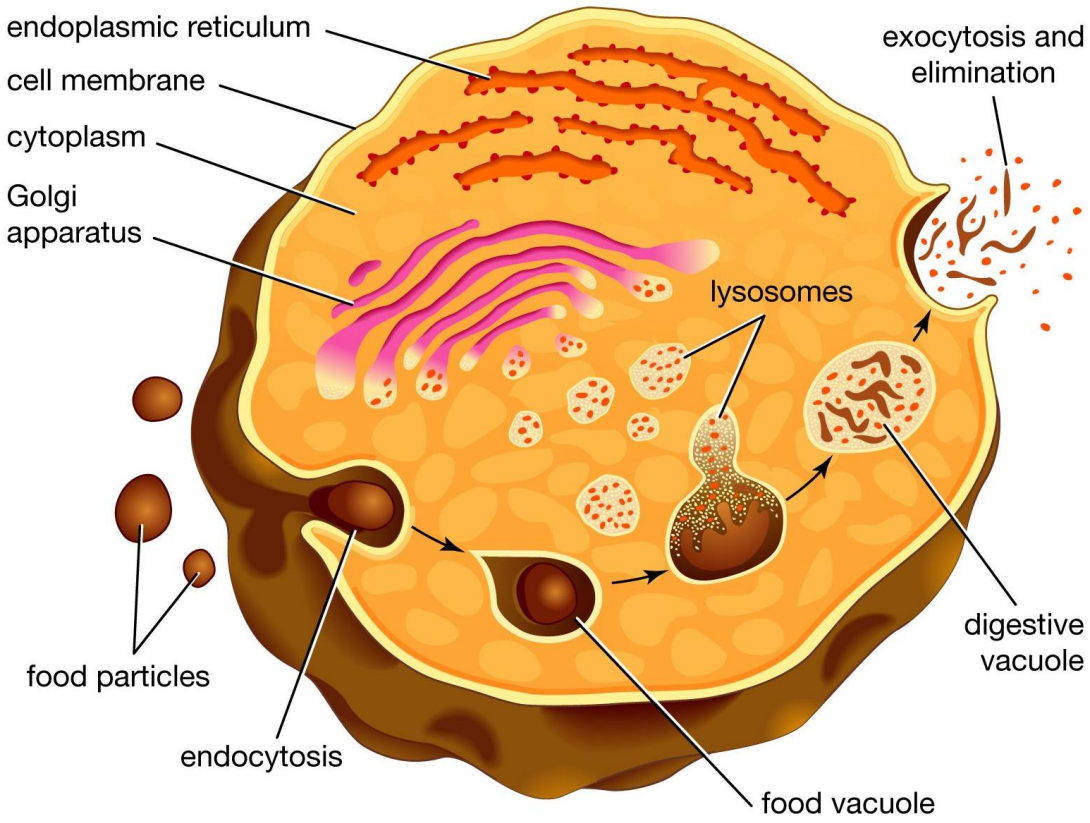
- **Subunits assemble to form complete ribosome in the presence of mRNA**
- The individual subunits are **formed in the nucleolus** and then **transported into cytoplasm** where they associate when **protein synthesis** is to be started. These subunits have separate roles in protein synthesis
- Smaller 40S subunit is site of attachment and translation of mRNA while larger 60S subunit is responsible for release of newly **synthesized protein**
- Ribosomes are found together in a linear arrangement in cells where intensive protein synthesis takes place. These ribosomes are known as **Polysomes**.

Ribosomes

- Polysomic arrangement arises because several ribosomes are translating a single mRNA molecule simultaneously
- Number of ribosomes in a polysome indicates the length of mRNA molecule associated with it and so the size of protein molecule being formed
- Ribosome occurring free in cytoplasm play a role in synthesis of protein for use outside membranous compartments. These include enzymes present in cytosol and proteins giving rise to cytoskeleton
- Some cytosol proteins can be inserted directly into mitochondrial and peroxisomal membranes

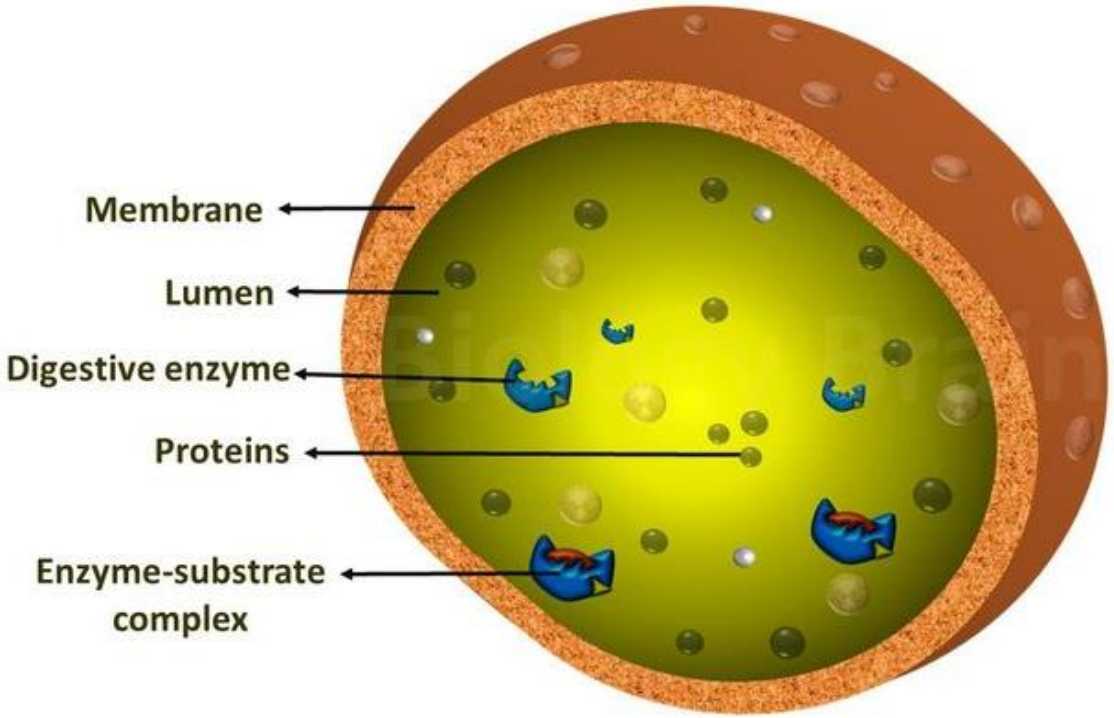
Lysosomes

- **Spherical vesicles** present in cytoplasm which are enclosed by single membrane
- This membrane contains **proton pumps** which keep internal pH of organelles near **5**
- This **acidic pH** is favorable for functions of lysosomes



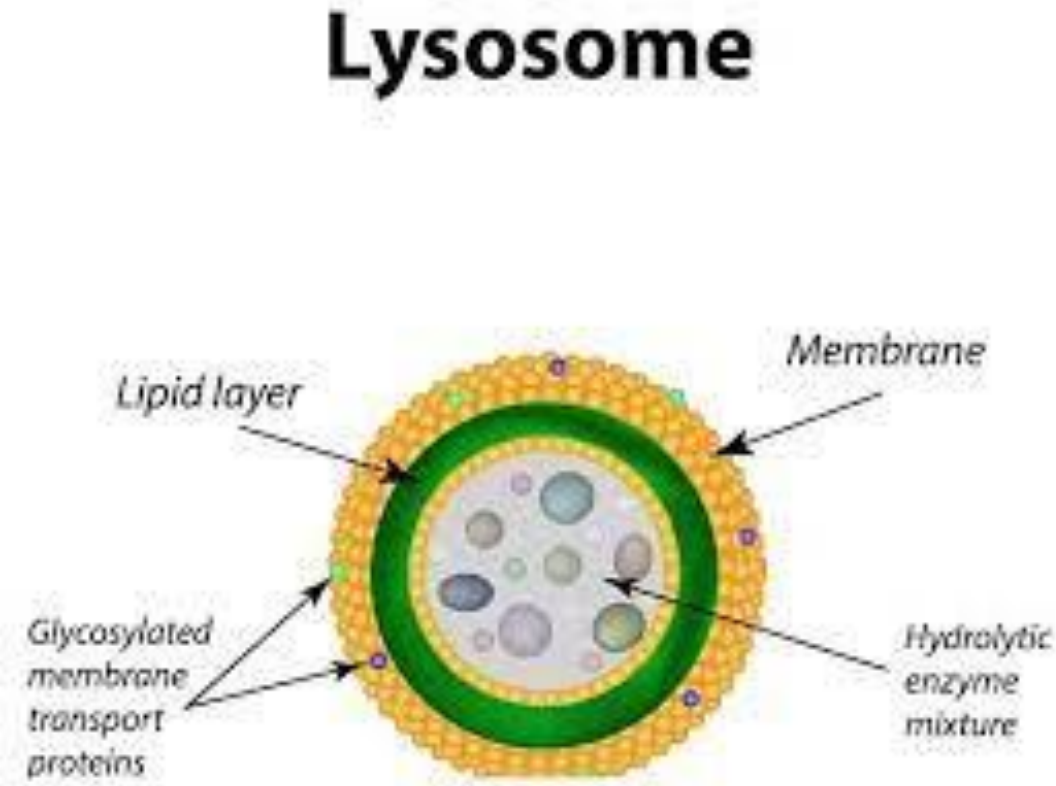
Agents in Lysosomes

- The **bactericidal agents** present in lysosomes can kill phagocytosed bacteria bef causing cellular damage.
- These include:
  - **Lysozymes**: Dissolving bacterial cell membrane
  - **Lysoferrin**: Binds iron & other substances before they can promote bacter growth
  - Acidic pH activates **Hydrolases** enzymes and inactivates bacterial metabolic systems



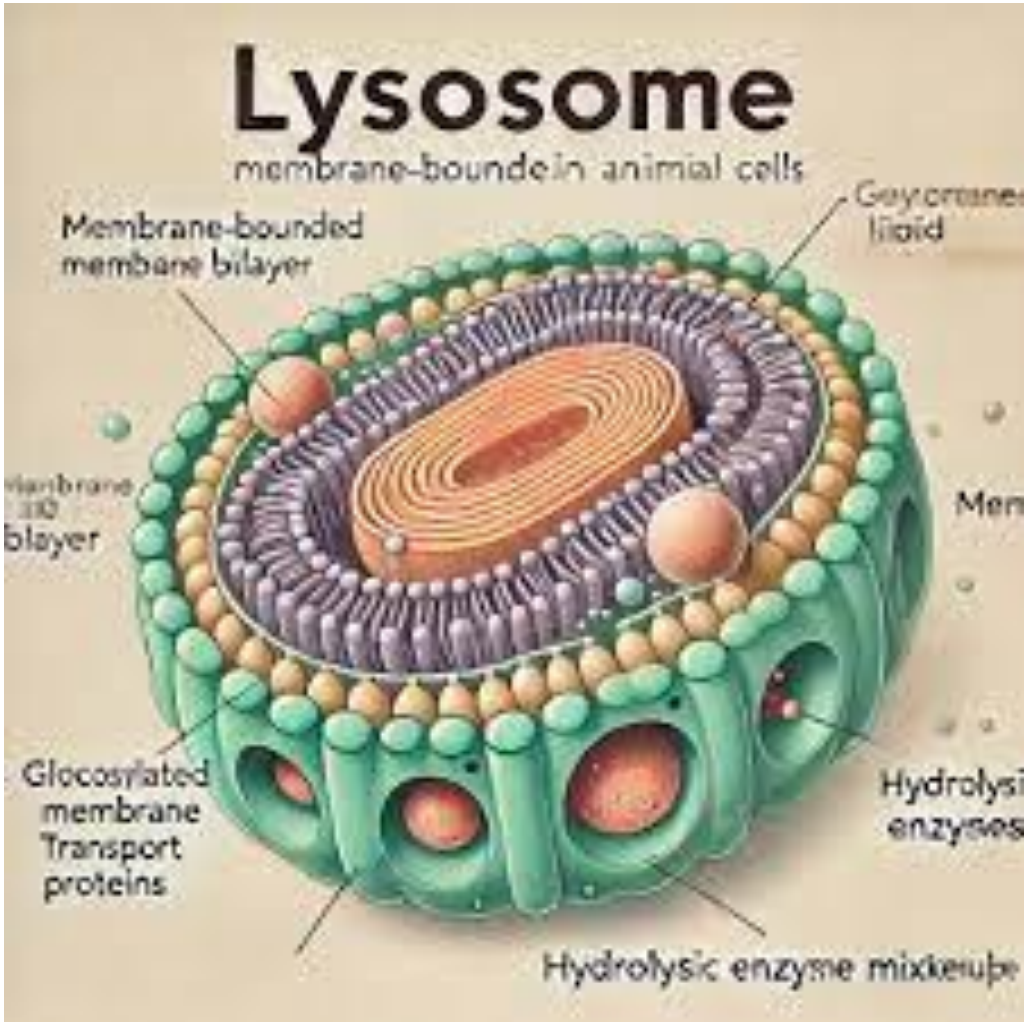
Enzymes in Lysosomes

- Enzyme groups in lysosomes are:
  - **Proteolytic enzymes**
  - **Nucleic acid hydrolyzing** enzymes
  - **Lipid hydrolyzing** enzymes
  - **Carbohydrate splitting** enzym
  - Other enzymes like acid **phosphatase** and **catalases**
  - Amino acids are produced from proteins, monosaccharides from polysaccharides and nucleotides from nucleic acid
  - The products of lysosomal digestion return to cytosol



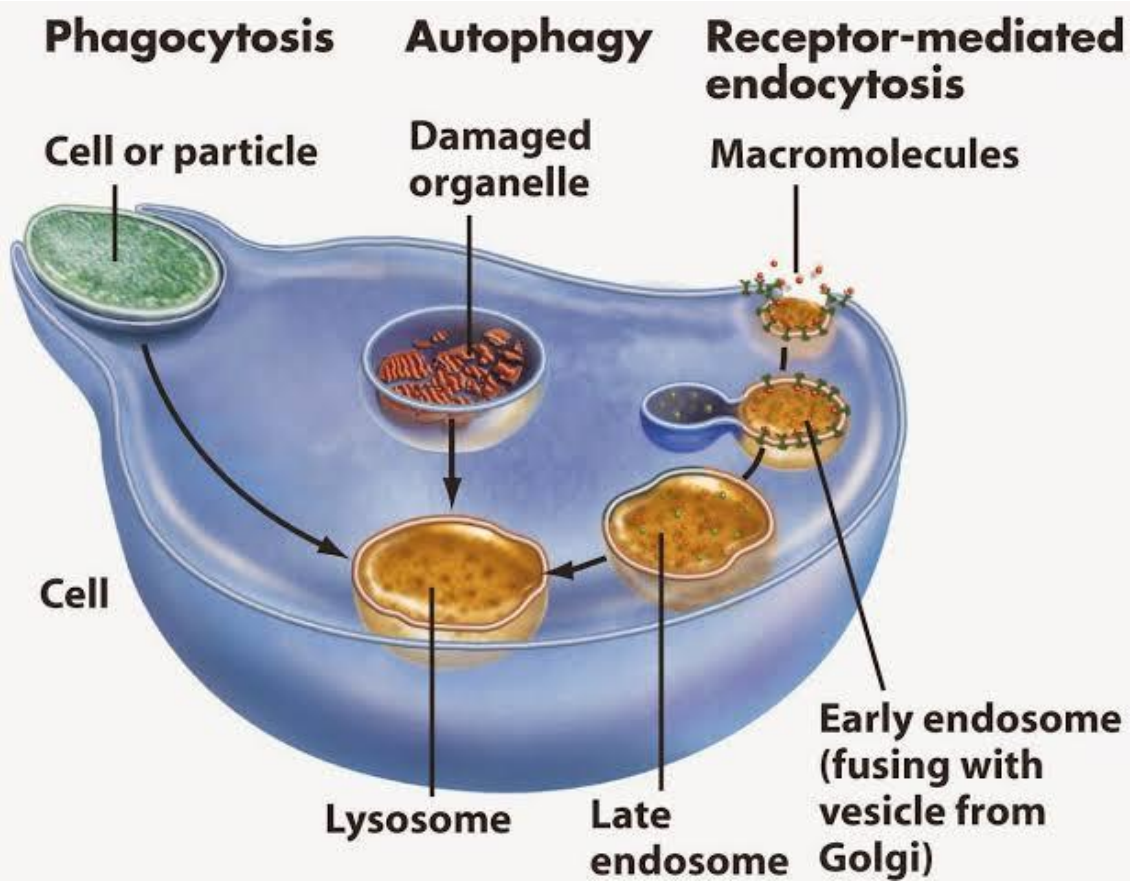
Digestion in Lysosomes

- After digestion the products cross the membrane to join their respective pools in the cytoplasm
- Membrane bound vesicles containing indigestible material known as **residual bodies**
- Sometimes residual products rich in lipids and proteins called **Lipofuscin** may accumulate in cell



Digestion in Lysosomes

- This product lipofuscin, is the **age pigment** or wear and tear pigment
- Tissues of body may regress to smaller size e.g., that occurs in **uterus after pregnancy,** in muscles after long period of inactivity and in mammary glands at the end of lactation. **Lysosomes responsible for this regression**



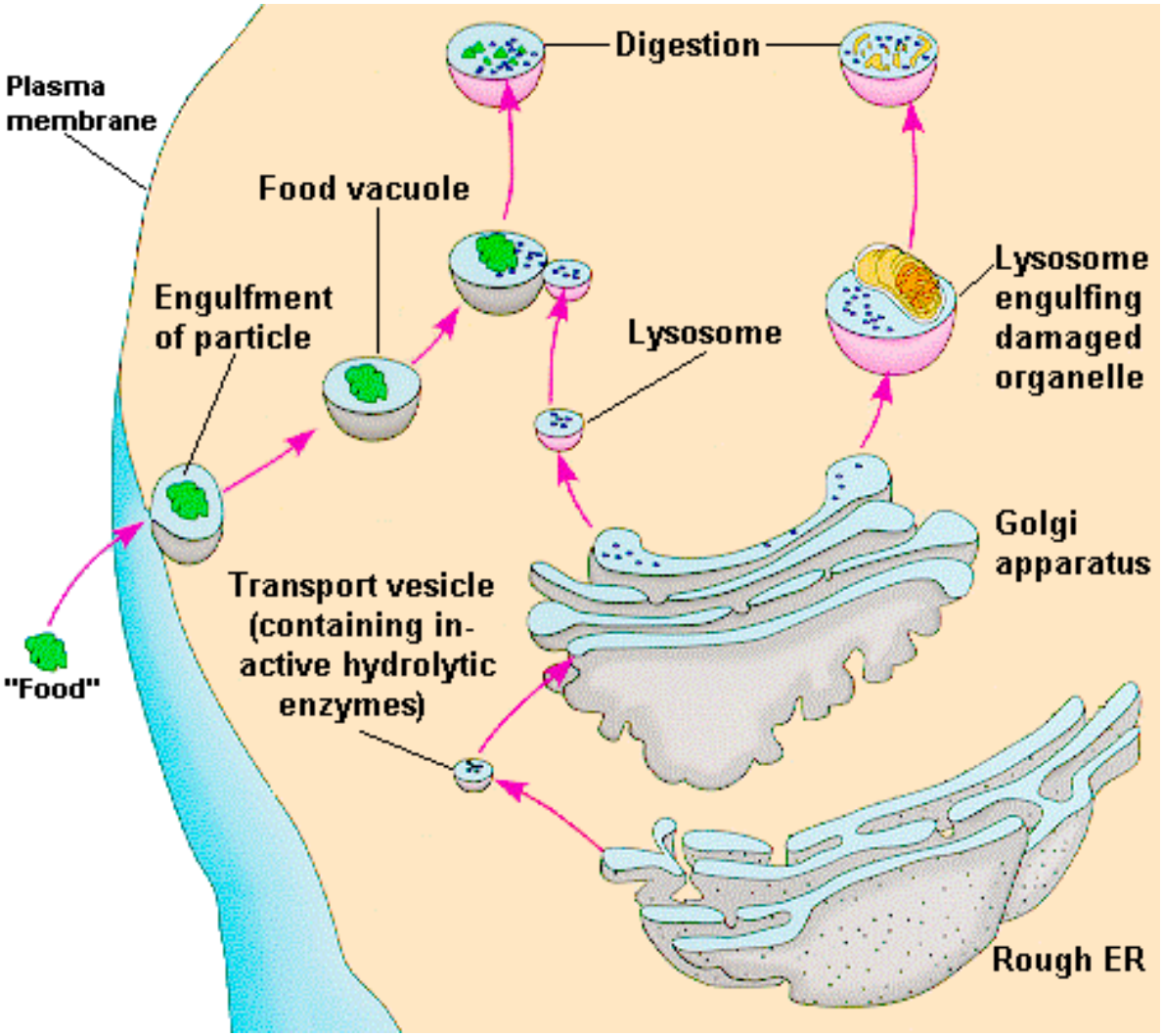
Digestion in Lysosomes

- Lysosomal enzymes mix with contents of vesicle
- now called secondary lysosome. Digestion occurs in the secondary lysosome
- Intracellular material may also be digested in carefully controlled process known as autophagy
- In this case cell forms a membrane around the subcellular components and lysosomal membrane fuses with this membrane and digestion occurs

Core Knowledge

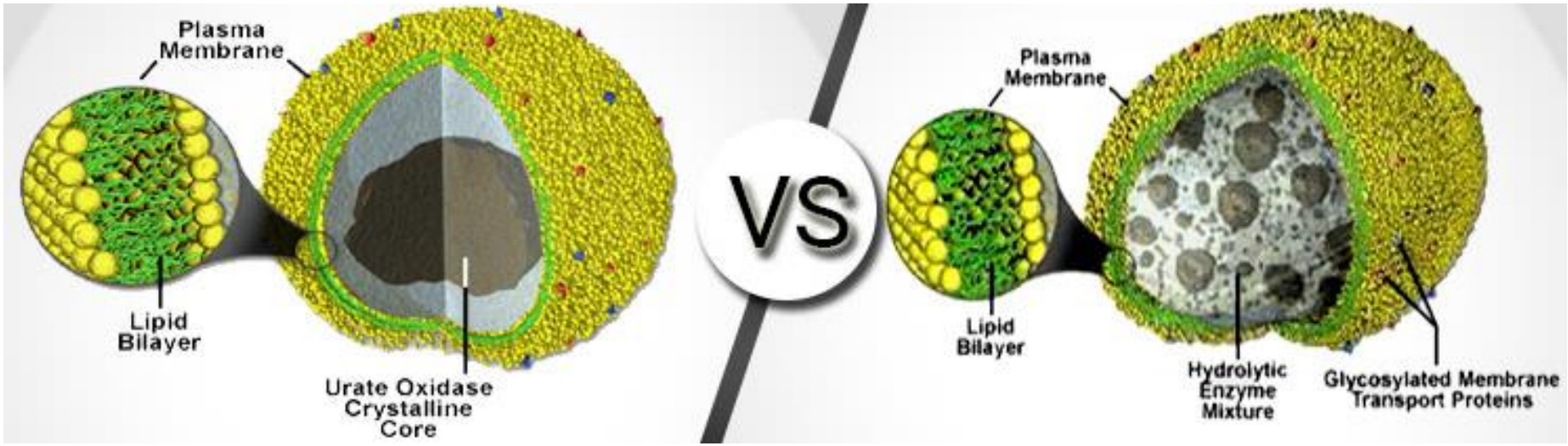
Digestion in Lysosomes

- Another special role of lysosomes is to **remove damaged cell** or its portion from tissues
- If damage is slight, the portion of cell is removed and repaired. In case of severe damage, entire cell is digested by process called **Autolysis**
- Another function is help in **Apoptosis**



Peroxisomes

- These are small bodies present in Eukaryotic cells also called **Micro bodies**
- Approximately 0.5µ in diameter, are **formed by budding off from the SER**
- Present in cells especially of **liver** and **kidneys**
- Lined by a single membrane & **rich in enzymes**



Difference between Lysosomes & Peroxisomes

Lysosomes

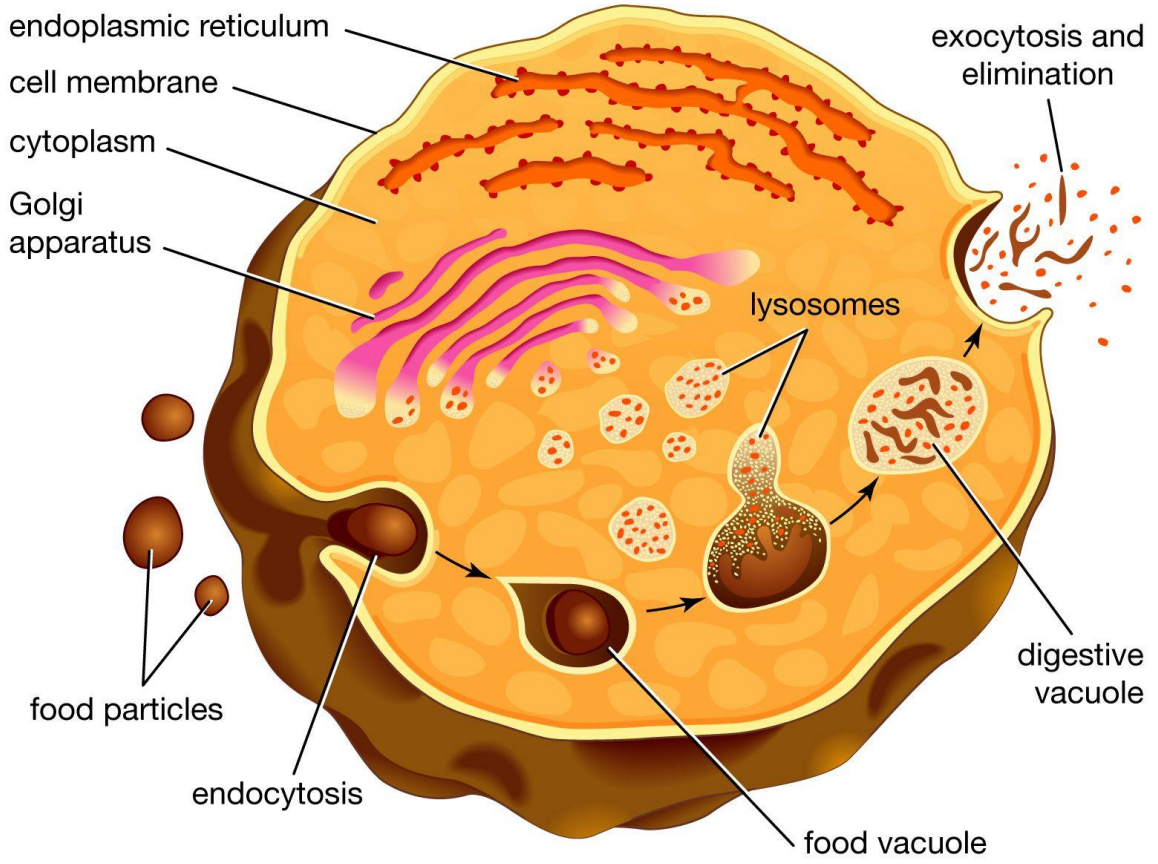
- Membrane bound sacs performing a **digestive** function
- Contains enzymes to digest food, wastes, invading bacteria and breaks down old organelles
- Present in animal cells only
- Golgi apparatus produces lysosomes
- Tay – Sachs disease

Peroxisomes

- Membrane bound sacs performing a digestive function
- Enzymes in peroxisomes are *oxidases* that catalyze redox reactions
- Liver contains many peroxisomes to break down alcohol
- Form by budding off from ER
- Present in animal cells only

Physiology of Lysosomes

- They are regarded as digestive tract since they are involved in **Digestion** of cellular substances i.e. proteins, lipids, carbohydrates and nucleic acids
- They are able to perform this function due to enzymes which belong to the group of **Hydrolases**



Clinical Correlates

Abnormalities of lysosomal functions

- Lysosomal membrane is impermeable both to lysosomal enzymes and to large molecules in cytoplasm that serve as their substrate
- Under normal conditions, the lysosomal membrane protects the cell from digesting itself
- Escape of these enzymes into cytosol will destroy functional macromolecules of cell

Abnormalities of Lysosomal Functions

- The occurrence of several diseases like **arthritis**, muscle diseases, **allergic disorders** etc. has been partly attributed to the release of lysosomal enzymes
- Many hereditary diseases are due to genetic defects in lysosomal enzymes due to which metabolism of glycogen, lipids and proteoglycans is affected

Vertical Integration

Lysosomal Diseases that can present with *Hydrops Fetalis*	Enzyme or Protein Deficiency
Mucopolysaccharidosis (MPS)	
MPS1 (Hurler)	Alpha-L-iduronidase
MPS4 A (Morquio syndrome)	Galactosamine-6- sulfatase
MPS7 (Sly Disease)	β-glucoronidase
Multiple Sulfatase Deficiency	FGE
Oligosaccharidosis (OLGs)	
Galactosialidosis	Cathepsin A
Sialidosis	Neurominidase
Lysosomal Transporter Defects	
Sialic acid storage disease	Sialin (SLC17A5)
Mucolipidosis	
Mucolipidosis type II (I-cell disease)	N-Acetylglucosaminylphosphotrasnferase
Sphingolipidosis	
Gaucher disease type 2	glucocerebrosidase
Niemann-Pick types A and B	Sphingomyelinase
Farber disease	neuramidase
GM1 gangliosidosis	β-galactosidase
Lipid Storage Disease	
Cholesterol Storage Disease and Wolman Disease	Lysosomal acid lipase

Management of Lysosomal storage Diseases

- **Lifestyle:** Supportive care with a focus on improving quality of life. Encourage a balanced diet and physical therapy.
- **Medications:** Enzyme replacement therapy (ERT). Substrate reduction therapy (SRT). Symptomatic treatments, such as pain management, anti-seizure medications.
- **Surveillance:** Regular monitoring of organ function. Annual or bi-annual assessments of disease progression
- **Complications:** Manage organ complications such as splenomegaly, hepatomegaly, and skeletal abnormalities. Consider bone marrow transplant in certain cases .
- **Patient Education:** Inform about genetic basis of the disease, inheritance patterns, and the importance of early diagnosis.

Ethical Considerations

- From an ethical standpoint, the scenario raises considerations regarding **patient autonomy**, **informed consent**, and **confidentiality**
- The physician must ensure that patient fully understands her diagnosis, treatment options, and potential implications
- Discuss the necessity of a healthy lifestyle & treatment plan. This requires clear communication and understanding of risks and benefits.
- Additionally, the physician must respect patient's privacy and confidentiality throughout the diagnostic and treatment process

Role of AI in Management Lysosomal Storage Diseases

- AI can potentially aid in **enhancing diagnostic accuracy and efficiency.**
- AI-powered decision support systems can also help clinicians in **selecting appropriate treatment modalities**
- AI-driven predictive models may help **anticipate the risk of complications of Lysosomal Storage Diseases** in susceptible populations

The Peroxisome: an Update on Mysteries

Link:
https://pmc.ncbi.nlm.nih.gov/articles/PMC10822820/

Journal Name: Histochem Cell Biol. 2024 Jan 20;161(2):99–132.

Title: The peroxisome: an update on mysteries 3.0

Author Name: Rechal Kumar [1], Markus Islinger [2], Harley Worthy [1], Ruth Carmichael [1,✉], Michael Schrader [1]

Abstract

Peroxisomes are highly dynamic, oxidative organelles with key metabolic functions in cellular lipid metabolism, such as the β-oxidation of fatty acids and the synthesis of myelin sheath lipids, as well as the regulation of cellular redox balance. Loss of peroxisomal functions causes severe metabolic disorders in humans. Furthermore, peroxisomes also fulfil protective roles in pathogen and viral defence and immunity, highlighting their wider significance in human health and disease. This has sparked increasing interest in peroxisome biology and their physiological functions. This review presents an update and a continuation of three previous review articles addressing the unsolved mysteries of this remarkable organelle. We continue to highlight recent discoveries, advancements, and trends in peroxisome research, and address novel findings on the metabolic functions of peroxisomes, their biogenesis, protein import, membrane dynamics and division, as well as on peroxisome–organelle membrane contact sites and organelle cooperation. Furthermore, recent insights into peroxisome organisation through super-resolution microscopy are discussed. Finally, we address new roles for peroxisomes in immune and defence mechanisms and in human disorders, and for peroxisomal functions in different cell/tissue types, in particular their contribution to organ-specific pathologies.

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f) Journals and Researches will appear
g) You can find a Journal by clicking on JOURNALS AND DATABASE and enter a keyword to search for your desired journal

Learning Resources

- Textbook of Biochemistry, Lippincott 8th edition, chapter no. 01, 14, 17, 18, 32, page no. 09, 186, 233, 258, 501
- Harper's Illustrated Biochemistry 32nd Edition
- Google scholar
- Google images

THANK YOU