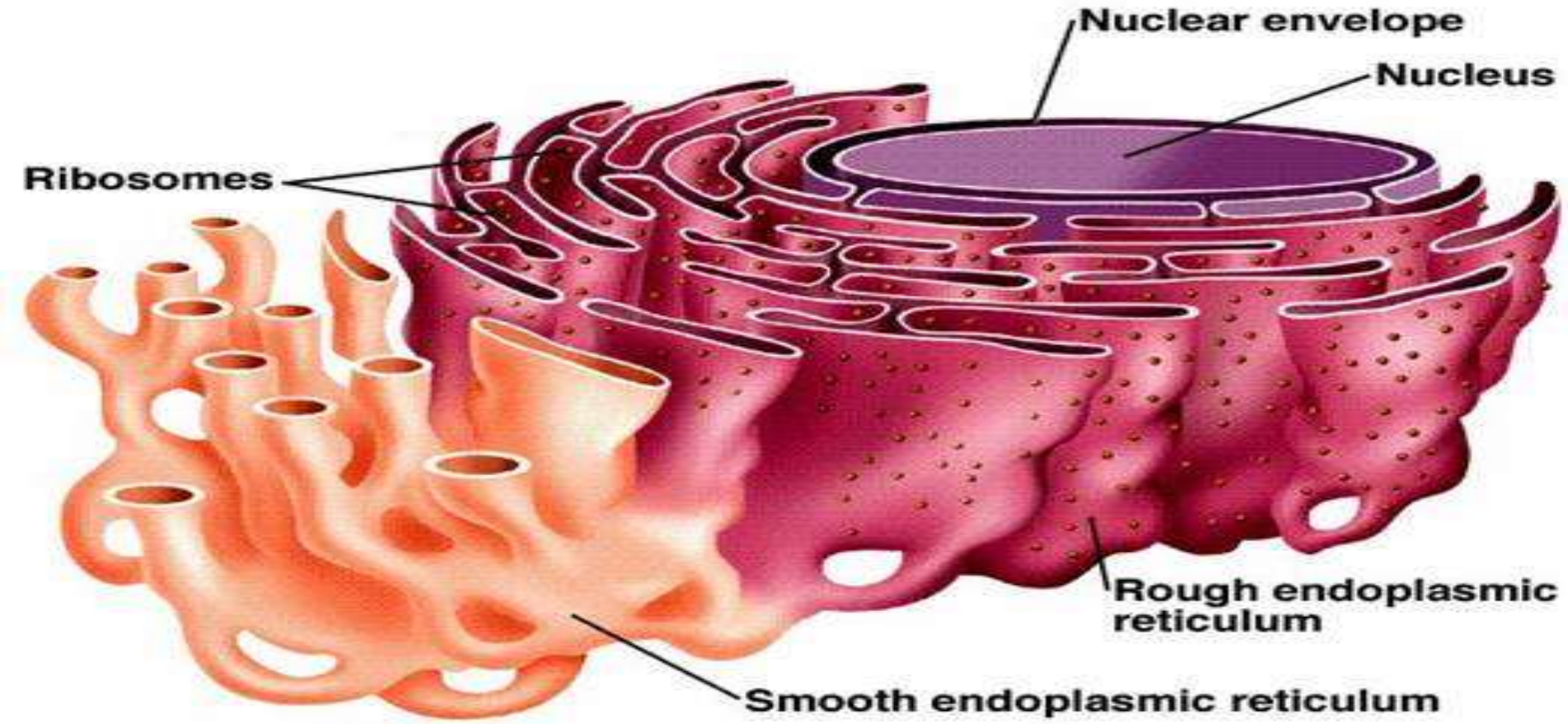
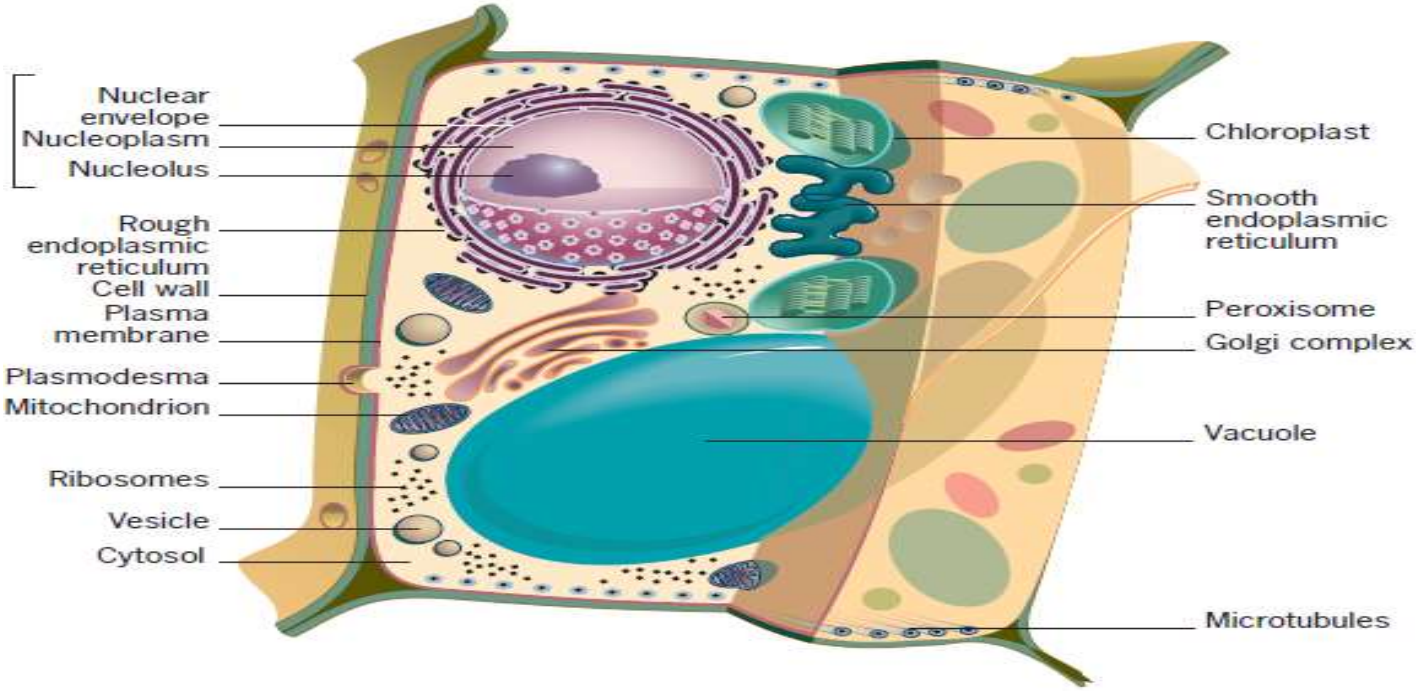
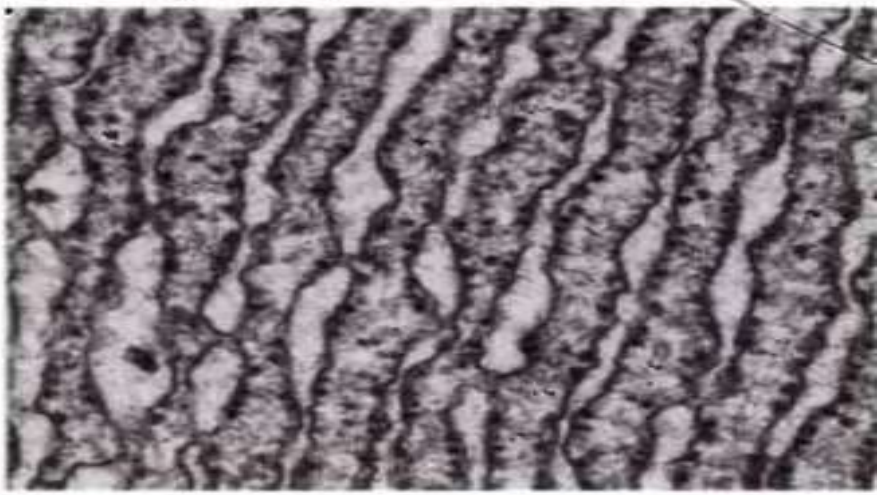
Endoplasmic Reticulum



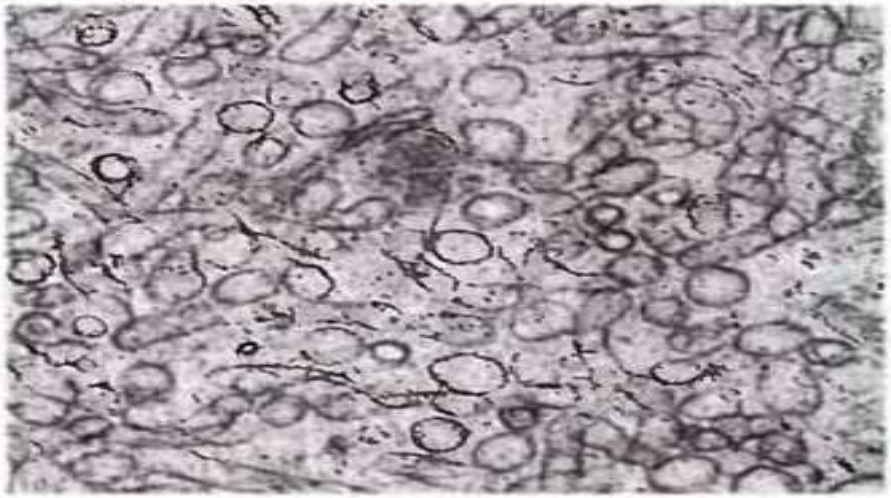
nucleus



(A) Rough endoplasmic reticulum



(B) Smooth endoplasmic reticulum



INTRODUCTION

- Endoplasmic means “within the plasm” and reticulum mean“network”
- The endoplasmic reticulum (**ER**) is a network of flat and vesicular structures which extends throughout the cytoplasm in plant and animal cells.
- These sacs and tubules are all interconnected by a single continuous membrane so that the organelle has only one large, highly convoluted and complexly arranged **lumen** (internal space).
- It takes up aproximately 12% of the total volume of a cell.
- It is connected to the double-layered nuclear envelope.

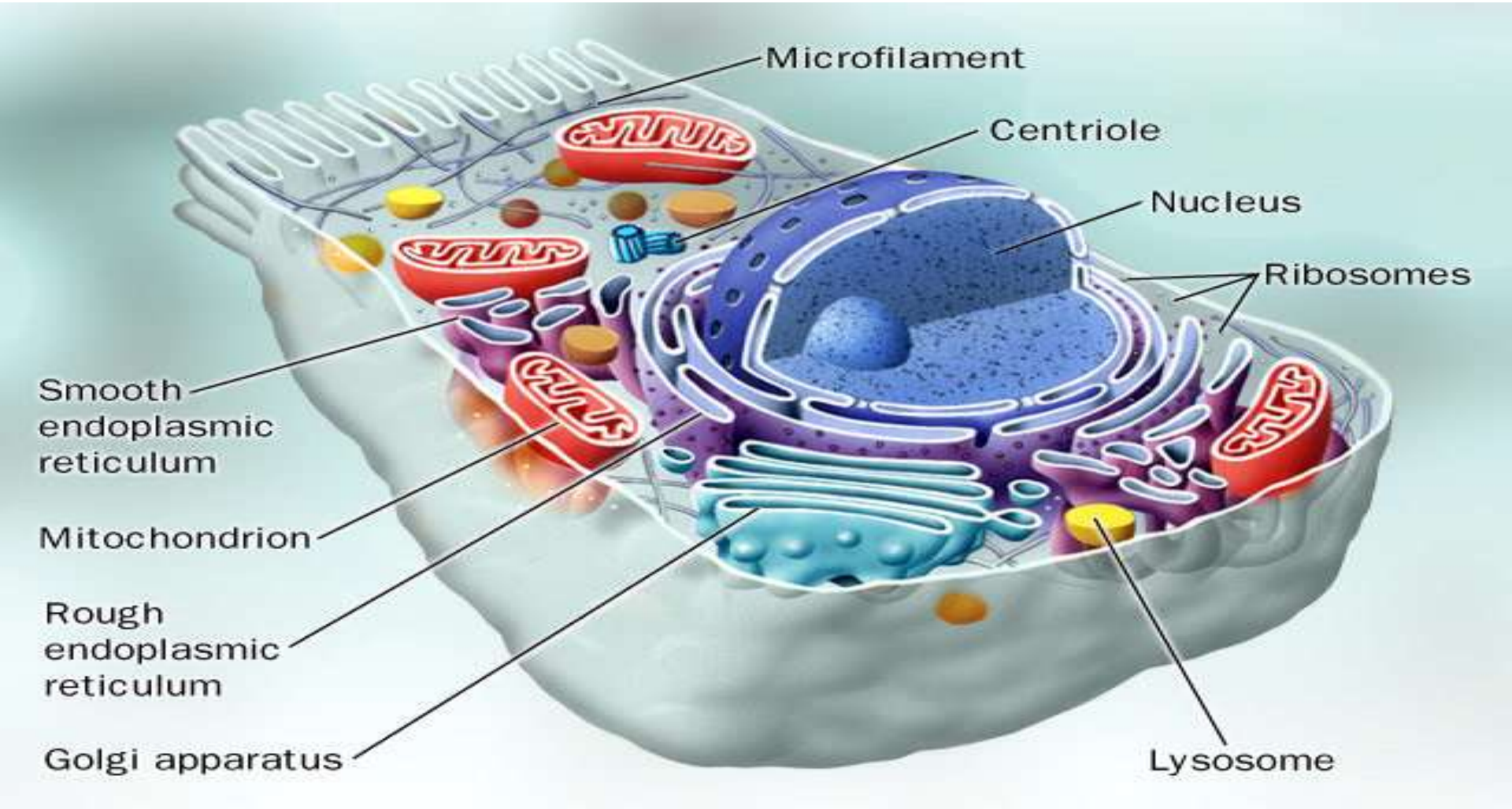
DISCOVERY

Garnier (1897) – first discovered the **Endoplasmic Reticulum** and named it **ergastoplasm,** but its ultrastructure was given by **Porter, Claude, and Fullum** in (1945).

K.R. Porter in (1953).

coined the term endoplasmic reticulum

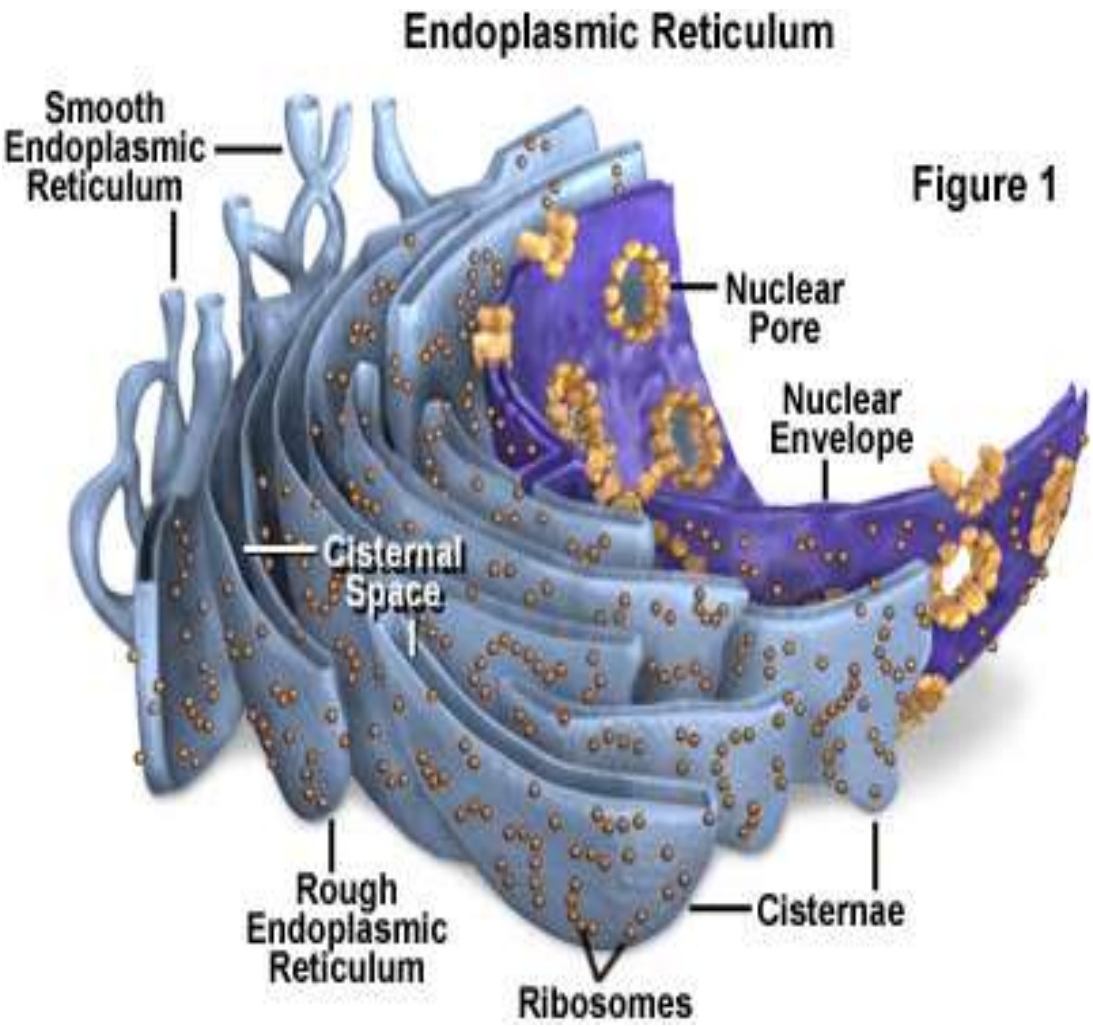
Occurence



A picture showing all the cell organalle including ***Endoplasmic reticulum***

Origin

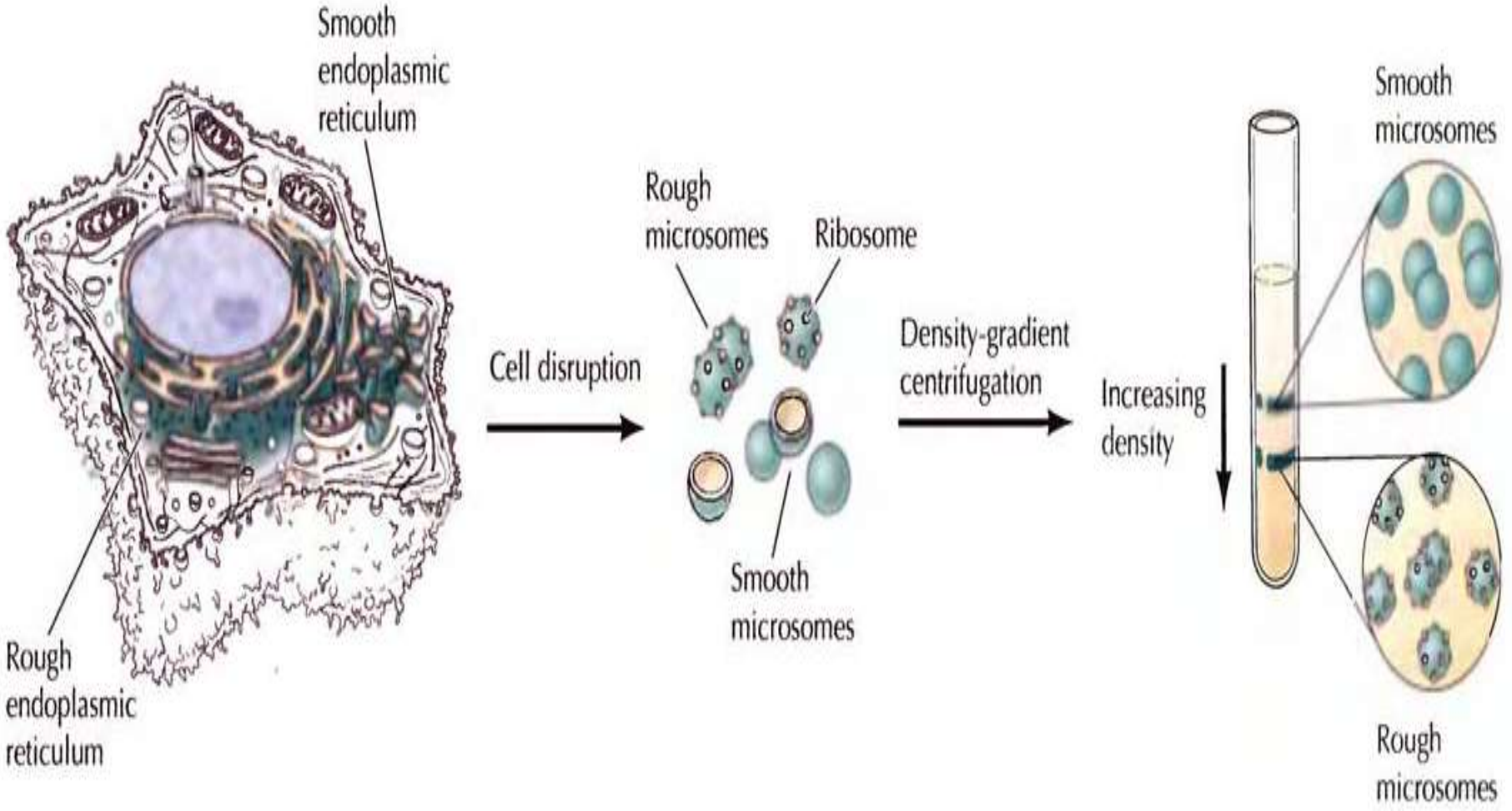
- The most accepted view regarding origin of ER is that RER arises as an invagination of outer nuclear membrane while the SER are formed from RER by loss of ribosomes.
- Intercisternal space of ER is continuous with perinuclear space.
- Fluid present in ER and perinuclear space is of similar nature.



Isolation Of Rough RER

- When the cell are disrupted,ER fragments into small vesicles called microsomes derived from rough ER and lined ribosomes.
- Because ribosomes contains large amount of RNA, rough microsomes are denser than smooth microsomes.
- Which can be isolated by equillibrium density gradient centrifugation.

ISOLATION OF MICROSOMES



STRUCTURE

- The Endoplasmic Reticulum is a part of Endomembranous system and is membrane bound organalle. The membrane of endoplasmic reticulum is 50-60 Å thick.

- E.R. is connected to nuclear pore through outer membrane of nucleus.

- When we look at the ultrastructure of E.R., it is composed of three types of elements.

- **Cisternae** :-These are narrow, flattened and unbranched structures generally present near the nucleus. These lie parallel to each other and may be interconnected .They occur in the cells having active synthetic roles.

- **Tubules** :-Tubules are wider, tubular and irregulary branched elements mainly present near the cell membrane. Each is about 50-100µm diameter.

  These are without ribosomes and are actively involved in glycogen metabolism, lipid and steroid synthesis

- **Vesicles** :- These are spherical or oval bodies scattered in the cytoplasm whose diameter ranges from 25-500 µm. These are also studded with ribosomes and are present mainly in cells that are involved in protein synthesis.

  In spermatocytes vesicles are the only ER structures found

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Similarity and differences with plasma membrane

- Electron microscopic studies revealed that all components of ER are unit membrane ,so are lipo-proteinaceous and trilaminar in structure as plasma membrane. But it differs from plasma membrane as:

1. ER Membrane(50-60Å) is thinner than plasma membrane(75-100Å).
2. ER membrane has less cholesterol.
3. ER membrane has more lipids.

Enzymes of endoplasmic reticulum

ER has following enzymes:

1. NADH-Cytochrome C- reductase.
2. Glucose-6-Phosphatases.
3. Mg^{++}activated ATPase.
4. Nucleotide diphosphaphatases
5. Uridine, Guanosine and Ionosine diphosphatases to hydrolyse UDP,GDP and IDP.
6. Synthetases for synthesis of phospholipids, glycolipids ,plasmalogens, fatty acids, and steroids.

TYPES OF ENDOPLASMIC RETICULUM

- E.R.is of Two types
- Smooth endoplasmic reticulum(S.E.R.)
- Rough endoplasmic reticulum(R.E.R.)
- Smooth ER- which don't have ribosomes on their surface. The have smooth surface.
- Rough ER- which is coated with ribosomes Rough ER is the site of protein synthesis.

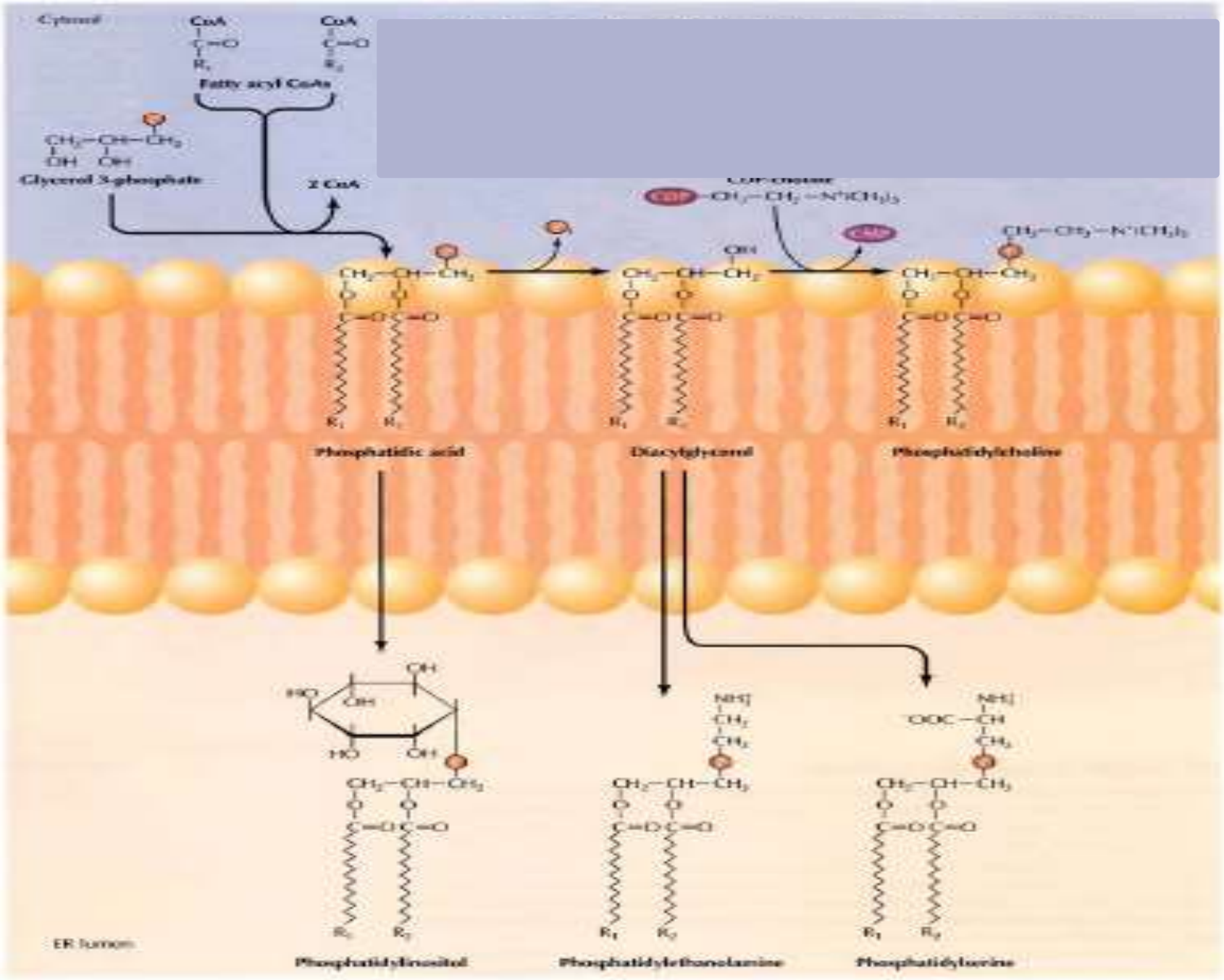
Smooth E.R.

- SER consist of a long network of a folded, tube like structure.
- It is more abundant in mammalian liver cells and gonad cells
- SER is formed from RER when it loses ribosomes

Functions of SER

- **Manufacturing** – SER is involved in lipid synthesis. It is due to distribution of synthatases on the surface of ER. It synthesise steroid hormones.

  SER is found to be well developed in the cells which actively synthesizes steroid hormones e.g. corticoids of adrenal cortex, testosterone in interstitial cells..
- SER is associated with gluconeogenesis in animal cells.


Cytosol
CoA
CoA
Fatty acyl CoAs
Glycerol 3-phosphate
2 CoA
Phosphatidic acid
Diacylglycerol
Phosphatidylcholine
Phosphatidylinositol
Phosphatidylethanolamine
Phosphatidylserine
ER lumen

- **Processing of toxins-**
- SER is helpful in detoxification of certain drugs like phenobarbitol, many carcinogens and 3,4benzpyrene. SER uses enzymes for break down the toxic compounds.
- Detoxification is carried out by a system of oxygen transferring enzymes (oxygenases), including the **cytochrome P-450 family.**
- These enzymes , due to their lack of substrate specificity, being able to oxidize thousands of different hydrophobic compounds and convert them into more hydrophilic, more readily excreted derivatives.

Muscle contraction

- SER helps in Sequestering of calcium ions within the cytoplasm of cells.
- The regulated release of Ca++ from the SER of skeletal and cardiac muscle cells (known as the **sarcoplasmic reticulum** in muscle cells) triggers contraction.

Rough E.R.

- It is composed of membranes that are folded into one another to provide maximum space.
- More abundantly found in hepatocytes.
- Nuclear envelop is formed from the cisternae of RER during telophase of cell division.

Functions of RER-

- **Protein synthesis** :
  RER provides surface to ribosomes and provided two dimensional arrangement and increase the rate of protein synthesis.
- **Transportation:**
  RER is involved in collection and transportation of synthesized proteins and forms transport vesicles which carry the material like proteins to the cisternae of Golgi bodies for their condensation into secretory vesicles.

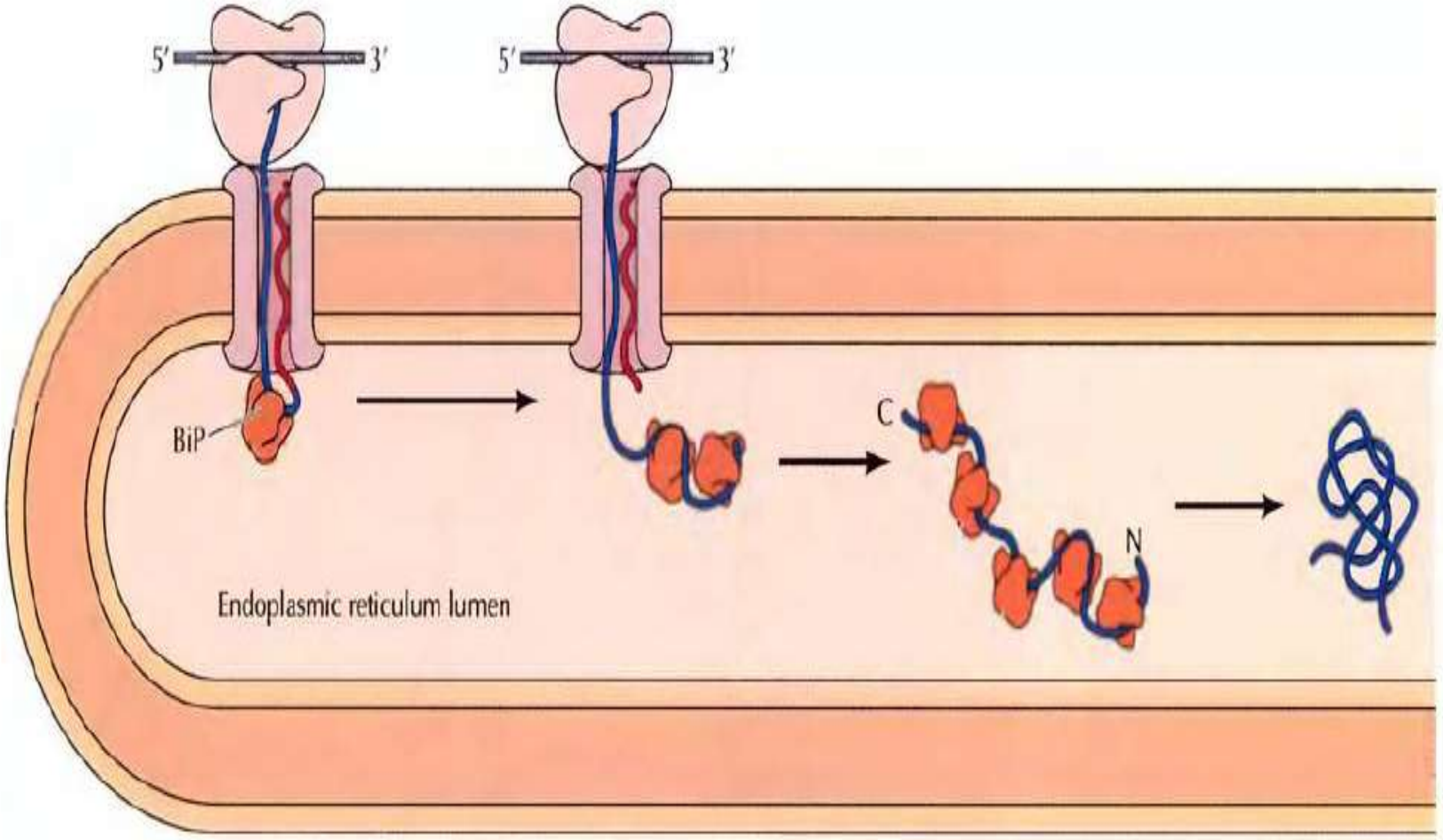
- Glycosylation –

Carbohydrates are added to the nascent poplypeptide by the enzyme **oligosaccharyltransferase**

- **Disulphide bond formation –**

The formation of disulfide bonds is catalyzed by PDI. Disulfide bonds play an important role in maintaining the stability of proteins that are present at the extracellular surface of the plasma membrane or secreted into the extracellular space.

➢ Packaging and folding of proteins:



•Misfolded proteins are not destroyed in the ER, but instead are transported into the cytosol by a process of "**dislocation**."

•It remains unclear whether misfolded proteins are dislocated back into the cytosol through the t**ranslocons** that brought them into the ER or by way of a separate dislocation channel of uncertain identity.

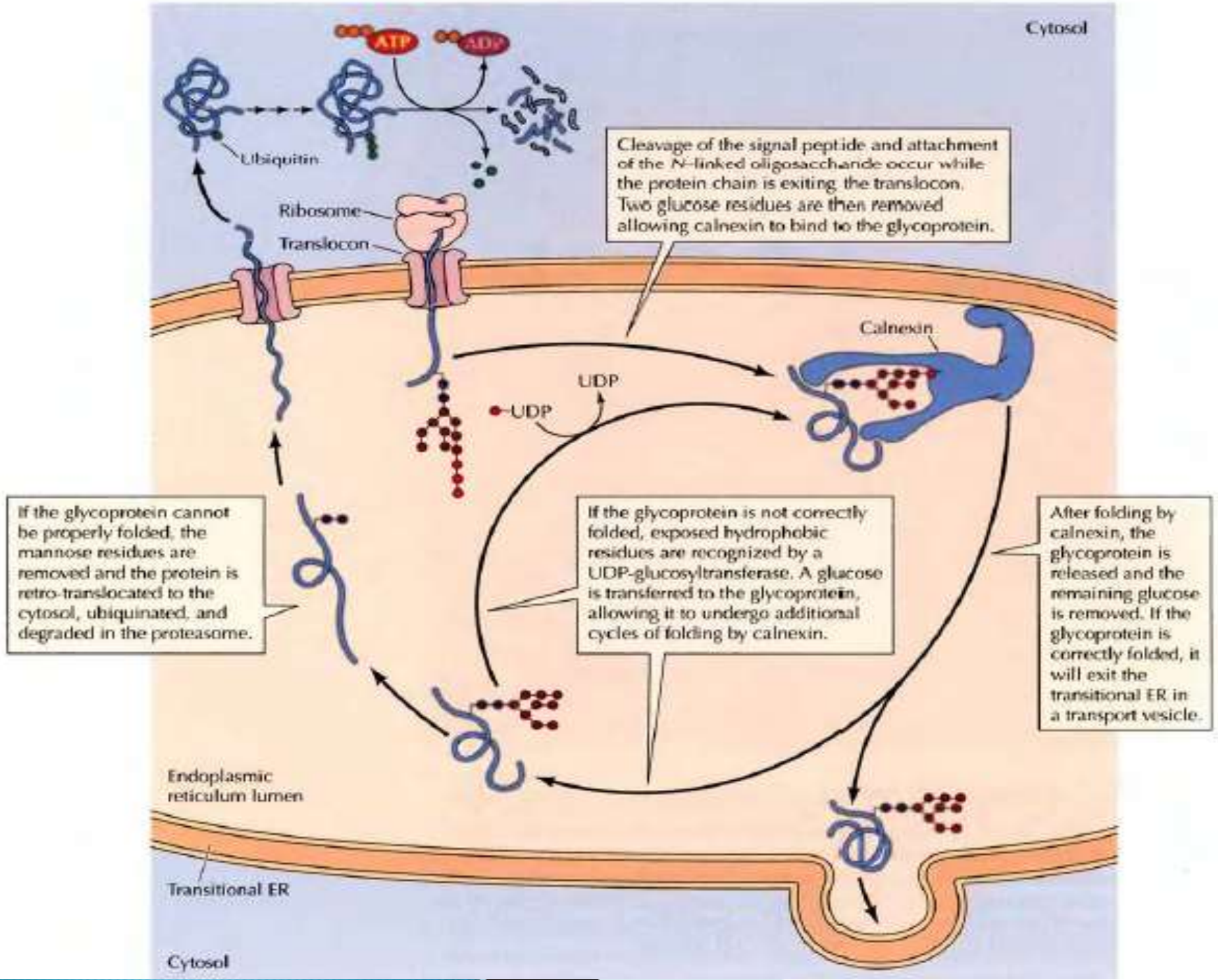
•Once in the cytosol, the oligosaccharide chains are removed, and the misfolded proteins are destroyed in **proteasomes**.

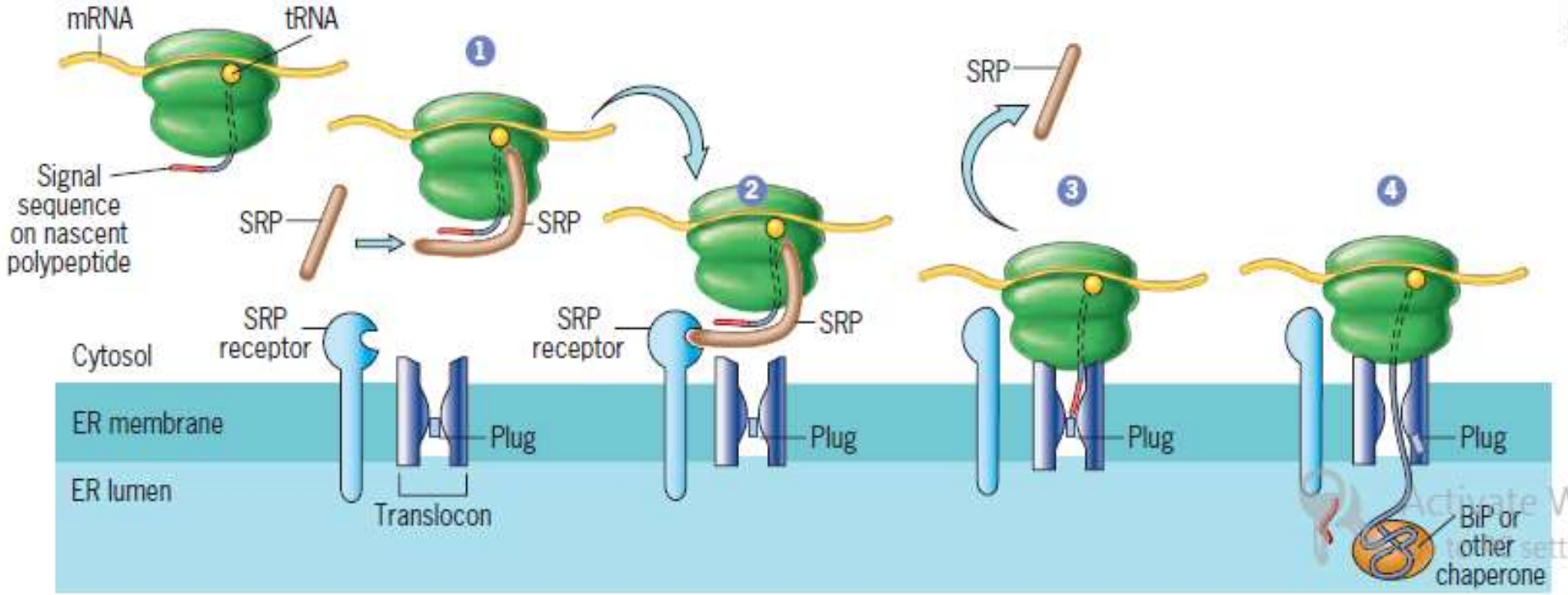
•This process, known as *ER-associated degradation (ERAD),*

•Under certain circumstances, misfolded proteins can be generated in the ER at a rate faster than they can be exported to the cytoplasm.

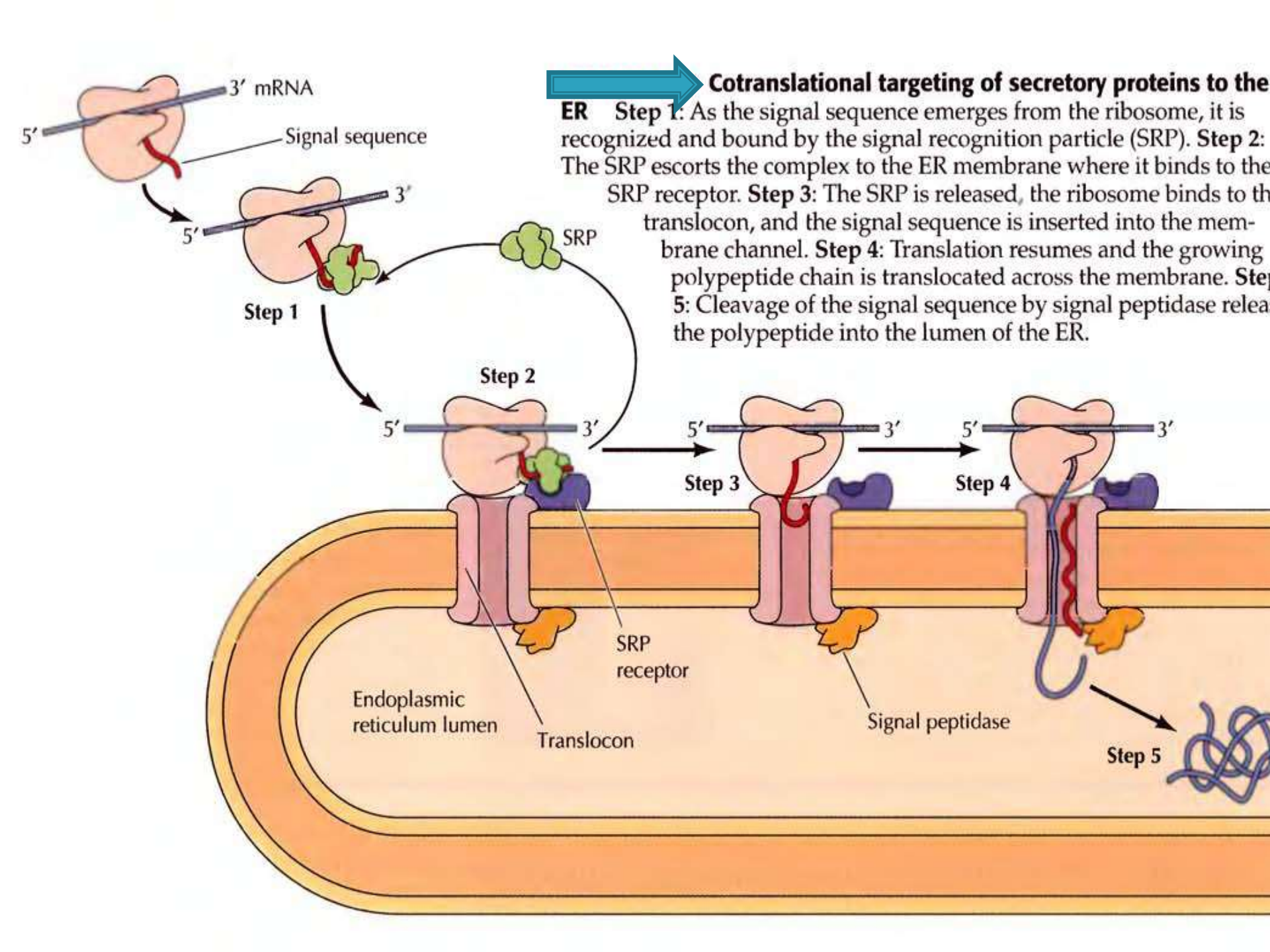
•The accumulation of misfolded proteins, which is potentially lethal to cells, triggers a comprehensive "plan of action" within the cell known as the unfolded protein response (UPR).

•The ER contains protein sensors that monitor the concentration of unfolded or misfolded proteins in the ER lumen.


Cytosol
ATP
ADP
Ubiquitin
Ribosome
Translocon
Cleavage of the signal peptide and attachment of the N-linked oligosaccharide occur while the protein chain is exiting the translocon. Two glucose residues are then removed allowing calnexin to bind to the glycoprotein.
Calnexin
UDP
UDP
If the glycoprotein cannot be properly folded, the mannose residues are removed and the protein is retro-translocated to the cytosol, ubiquinated, and degraded in the proteasome.
If the glycoprotein is not correctly folded, exposed hydrophobic residues are recognized by a UDP-glucosyltransferase. A glucose is transferred to the glycoprotein, allowing it to undergo additional cycles of folding by calnexin.
After folding by calnexin, the glycoprotein is released and the remaining glucose is removed. If the glycoprotein is correctly folded, it will exit the transitional ER in a transport vesicle.
Endoplasmic reticulum lumen
Transitional ER
Cytosol

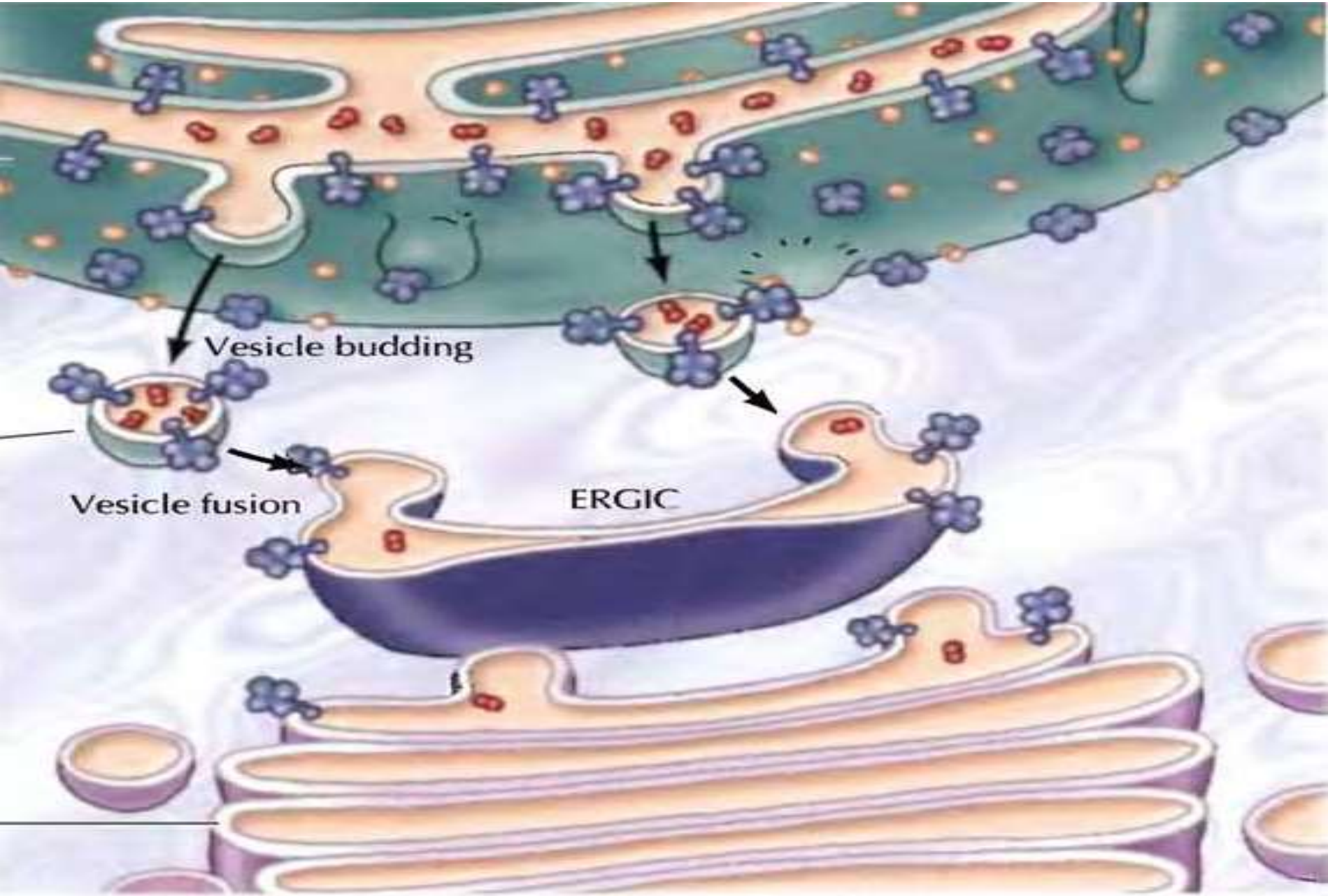


A schematic model of the synthesis of a secretory protein (or a lysosomal enzyme) on a membrane-bound ribosome of the RER.



Cotranslational targeting of secretory proteins to the ER **Step 1**: As the signal sequence emerges from the ribosome, it is recognized and bound by the signal recognition particle (SRP). **Step 2**: The SRP escorts the complex to the ER membrane where it binds to the SRP receptor. **Step 3**: The SRP is released, the ribosome binds to th translocon, and the signal sequence is inserted into the membrane channel. **Step 4**: Translation resumes and the growing polypeptide chain is translocated across the membrane. **Ste 5**: Cleavage of the signal sequence by signal peptidase relea the polypeptide into the lumen of the ER.

Scheme Of Transportation



Interrelation between ER and other membranes.

- Watson(1955) demonstrated a continuity between the outer nuclear membrane and the ER.

- The ER also shows connection with the plasma membrane and golgi complex. It suggest that…….

1. Ectokaryotheca form vesicles by blebbing.
2. These vesicles fuse to form annulated lamellae.
3. Annulated laellae loose their pore complexs, become associated with ribosomes and form RER cisternae.
4. RER produces transition vesicles which fuse to form cisternae of golgi complexes.
5. Golgi complexes form the vesicles which fuse to form the plasmalemma.

conti….

Cont.....

5. Golgi bodies also give rise to secretory vesicles and lysosome by blebbing. Primary lysosome can also arise directly from ER.

6. Now plasmalemma inveginate to form pinocytotic vesicle

7. Pinocytotic vesicles and primary lysosome fuse to form the secondary lysosome.

8. RER loses ribosomes to form SER.

Functions of E.R.

- **Transport of materials-** The ER facilitates transport of materials from one part of the cell to another, thus forming the cell's circulatory system.
- **Formation of Desmotubules-** Tubular ER, extensions, called desmotubules.
- **Support-** The ER acts as an intracellular supporting framework, the cytoskeleton, that also maintains the shape of the cell.
- ER act as passage for transportation of genetic information from nucleus to various cell organelles to control the biosynthesis of proteins, fats and carbohydrates.

Cont...

- **Location of enzymes**- ER membranes contain a variety of enzymes to catalyse synthetic activities. ER has about **30** types of enzymes, mainly **synthetases** which are involved in the biosynthesis of various biomolecules.

- **Storage of materials**- the ER provides space for temporary storage of synthetic products such as glycogen
- .
- ER of muscles cells is called as sarcoplasmic reticulum
- **Contraction** – It help in muscles contraction by regulating ca++ ions concentration in the sarcoplasm.

- **Photoreceptor** –ER of pigmented cells of retina act as a photoreceptor

Cont...

- Helps in formation of primary lysosome with hydrolytic enzymes.
- Rough ER –surface for protein synthesis.
- Smooth ER– Detoxification –converts harmful materials(drugs and poisons) into harmless ones for excretion by the cell.
- Calcium storage
- Formation of organelles– the SER produces Golgi apparatus, and vacuoles.

THANKYOU