CHPATER 4

4 ENDOPLASMIC RETICULUM (ER).

Are elaborate membrane system that divide the cytoplasm of Eukaryotes into multiple components. ER are composed of membranous tubules, vesicles and sacs. This compartmentalization provides a specialized environment that facilitates the various stages in protein biogenesis, modification, sorting, and, ultimately, secretion. The ER is the entry point into the secretory pathway for newly synthesized proteins. Ribosomes dock onto a protein pore in the ER membrane, thereby releasing the nascent polypeptide into the lumen of the ER.

4.1 Types of ER

a) Smooth ER or agranular ER- lacks attached ribosomes.
b) Rough ER or granular ER- contains attached ribosomes.

Rough ER

i) Are arranged in flattened sheets of membrane.
ii) Predominate the cells actively synthesizing protein for export.
iii) Has ribosome attached to it. Ribosomes contains RNA, an acidic molecule exhibiting a strong affinity for basic dyes, this makes RER stain with basic dyes.

Smooth ER

i) Typically consists of interconnected series of convoluted tubules.
ii) SER are associated with cells involved in the metabolism of steroids, hormones, drugs and toxic substances.

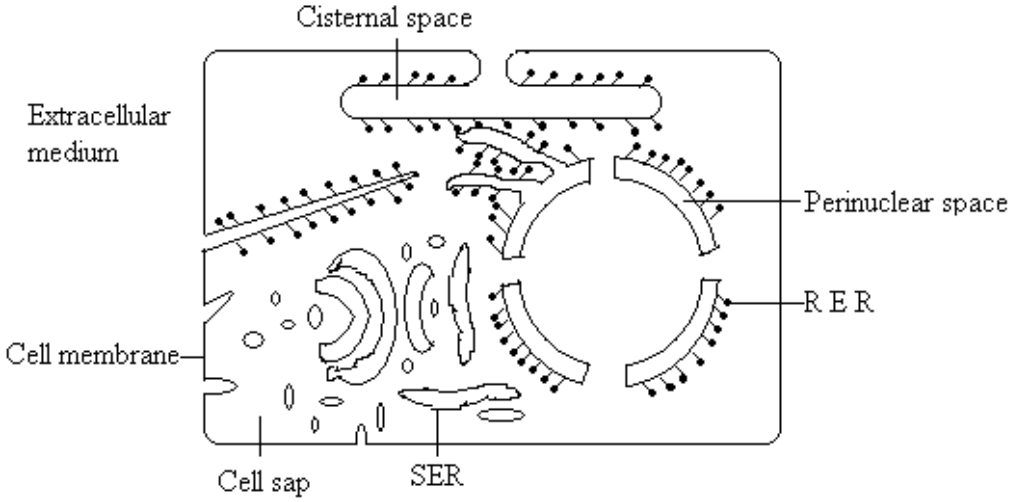


Fig.4.1. Endoplasmic reticulum in relationship to other organelles

By estimation in rat liver cells- the ER accounts for 19% of the total proteins, 48% of the total lipids and 58% of the total RNA of the cell. The ER divides the cytoplasm into two compartments of the cell

i) Cell sap
ii) Cisternal space.

4.2 Cell Sap

i) Contain soluble enzymes involved in intermediary metabolism, transfer of RNAs and other factors required for protein synthesis and free ribosomes.
ii) Ribosomes attached to endoplasmic reticulum are located on the side of the membrane facing the cell sap.

4.3 Cisternal Space

Functionally it is continuous with the internal cavities of Golgi complex, lysosome and peroxisomes, the perinuclear space (between the two nuclear membranes of the nuclear envelope) and the out of the cell. This continuity is maintained by shuttling membrane vesicles that bud off from one membrane system, travel a distance, and then fuse with another membrane.

Advantages of dividing cytoplasm into multiple-bound components

i) Helps to maintain separate environments individually adopted to various activities e.g. ER is semi permeable and capable of carrying active transport. SER is able to transport and maintain Ca^{+}_{2} gradient. This helps in cell secretion, nerve excitation and muscle contraction.
ii) A series of channels are created that provide a route for various substances e.g. newly made protein molecules, Tryglycerides.

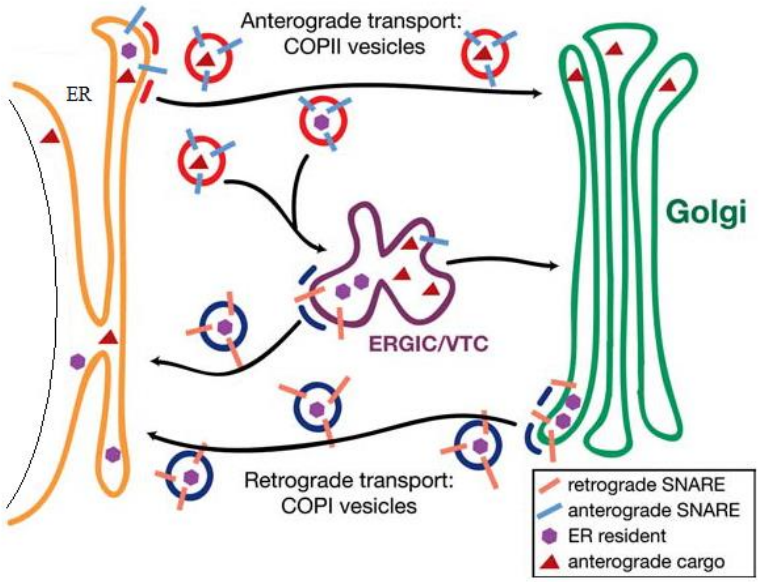


Fig4.2 ER-Golgi transport. Cytosolic Coat protein COPII coat proteins mediate anterograde vesicle formation, selecting anterograde cargo and Soluble *N*-ethylmaleimide-sensitive factor attachment protein receptors (SNAREs). COPII vesicles in plants and yeast fuse directly with the Golgi, but in mammalian cells they

seem to undergo homotypic fusion to generate a pleiomorphic structure known both as the ER-Golgi intermediate compartment (ERGIC) and vesicular tubular clusters (VTC). The ERGIC/VTC is a site for concentrating retrograde cargo into COPI vesicles for delivery back to the ER. The ERGIC/VTC is delivered en bloc to the Golgi in a microtubule-dependent manner. Additional retrograde traffic from the Golgi proper is also mediated by COPI vesicles.

Transport between these organelles occurs in two directions: anterograde (ER-Golgi) transport delivers newly synthesized cargo proteins to the Golgi. Retrograde (Golgi-ER) transport retrieves ER residents and other machinery that constantly cycle between these two compartments

4.4 Functions of ER

ER is associated with the following;

i) The metabolism of carbohydrates and Lipids
ii) Detoxification of drugs and other toxic chemicals.
iii) Synthesis of proteins e.g. membrane and secretory proteins synthesized by ribosomes.
iv) Sorting out of proteins destined to various destinations. This mixture includes proteins en route to the cell surface, Iysosomes, and secretory storage vesicles, as well as proteins that will remain in the ER or the Gogi.
v) Lubricating the process of protein assembly in the ER and, perhaps at the same time, prevent premature export.
vi) The processing of protein molecules. This include correct folding and assembly of secretory proteins which is necessary for their efficient transport. Presumably unfolded proteins tend to bind to other proteins in the ER or form aggregates that are unable to enter transport vesicles. Also binding proteins binds proteins in ER before export. Other ptocessing include addition of oligosaccharide groups to protein processing.
vii) Transport of protein molecules to various utility destinations by a process of vesicle budding and fusion. From ER proteins are exported to Golgi complex.
viii) Efficient targeting of proteins for degradation from the secretory pathway which is essential for homeostasis. This occurs through endoplasmic reticulum (ER)-associated degradation (ERAD). In human ubiquitin protein ligase is used for such function.
ix) Selective import of protein from the cytosol. This is characteristic with nuclear, mitochondrial, or chloroplast proteins.
x) ER is to provide a milieu that facilitates protein folding. Chaperones that massage a newly synthesized protein into its correct conformation, sometimes through the catalysis of disulfide bond formation. Post-translational modification of nascent chains first occurs in the ER, including addition of N-linked glycan chains and hydroxylation of proline residues.

Example of carbohydrates metabolism is the localization of the glucose-6-phosphatase shown below;

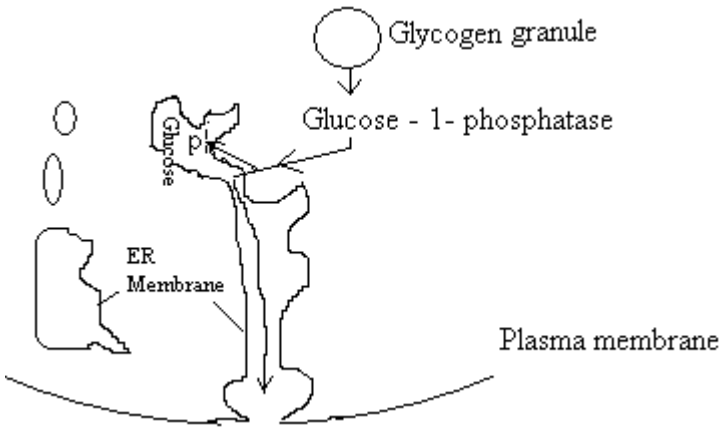
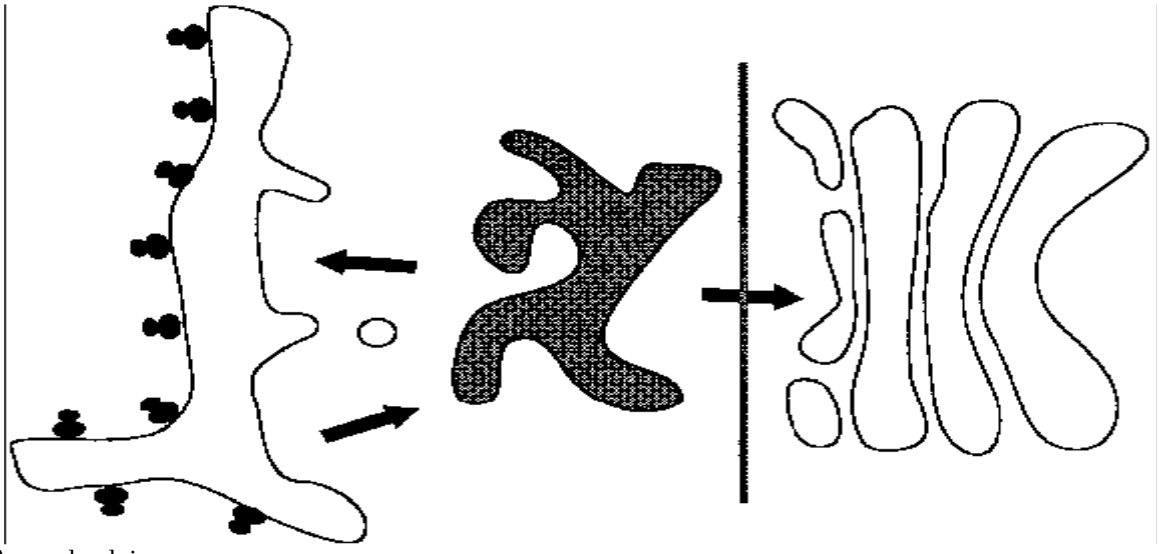


Fig. 4.5 Relationship between ER and Golgi Apparatus

Sorted materials for export is translocated to Golgi complex through vesicles. Below is example of how ER residential materials are sorted out from secretion materials.



Aer and golgi

ER oligosaccharyl transferase glucosidase I & II ER mannosidase	Salvage compartment phospho transferase	cis-GOLGI N-acetylglucosaminidase mannosidase I phosphotransferase

Fig. 4.6 Sorting of material between

This figure depicts the transitional region of the ER, the salvage compartment (shaded) and the Golgi stack, and the proposed location of various marker enzymes is indicated. The phosphotransferase and N-acetylglucosaminidase act on lysosomal enzymes to generate the mannose-6-phosphate marker. This shows that phosphotransferase activity may be present in the cis-Golgi as well as in the salvage compartment.