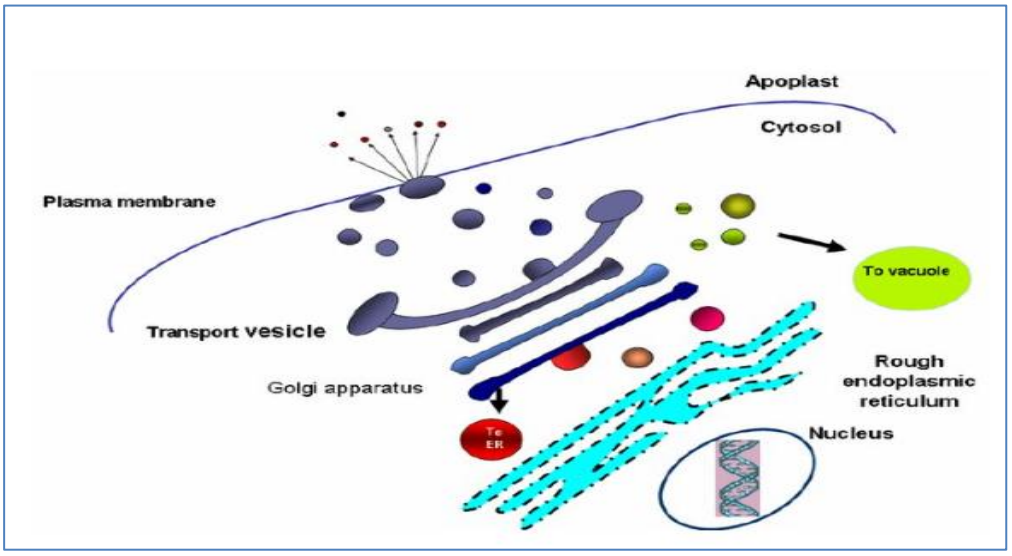
Tutorial N6: The ENDOMEMBRANE SYSTEM

Introduction

Observation of fixed cells under an electron microscope allowed Porter (1945) to describe, within the cytoplasm, a whole set of highly polymorphic cavities under the name of **the endoplasmic reticulum**. Alongside the disordered set of reticulum cavities, there are cavities, whose arrangement is much more regular, which correspond to an organelle that has been known for a long time: the **Golgi apparatus**. These two organelles participate in "Cell Sorting", i.e. in the production of proteins and their addressing to the cell's own, and also dedicated to exocyte, membrane proteins and those intended for enveloped organelles.
The study of the secretion pathway in eukaryotes was initiated by the pioneering work of Georges Palade and his collaborators on mammalian cells in the 1970s. In addition to this work, various studies carried out in yeast have provided many keys to understanding this mechanism, by providing an easily manipulated single-celled eukaryotic model.



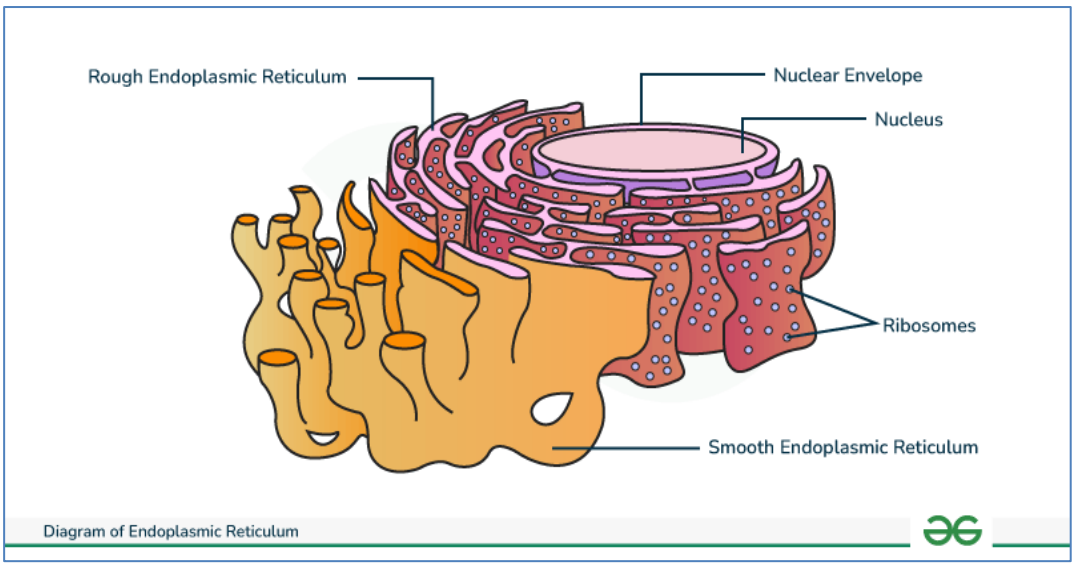
The secretion of proteins through the tricellular.

II.1.The endoplasmic reticulum

II.1.1.Morphology and structure

The endoplasmic reticulum is in the form of a system of **finely branched** canaliculi or flattened **laminae** 500 A° thick, some regions of which are dilated, or **globular vesicles** more or less voluminous (500 to 800 A°) or **convoluted** tubeswhich extend throughout the cytoplasm from the nuclear membrane to the plasma membrane. The cavities are each limited by a membrane made up of two sheets.
The outer membrane of the canaliculi bears an alignment of granules 150 A° in diameter, called **ribosomes**, which makes it possible to distinguish, depending on whether or not there are ribosomes at the edge, the rough endoplasmic reticulum **(RER or REG)** and the smooth endoplasmic reticulum **(REL)**

- **The R.E.G:** is associated with ribosomes; under the microscope, these ribosomes form small "balls" on the surface of the endoplasmic reticulum, which has earned it its name rough. It participates in protein synthesis.
- **The R.E.L.:** There are no ribosomes here. It participates in the synthesis of membrane lipids. May serve as a storage of calcium (skeletal striated muscle cells). Participates in the detoxification functions of xenobiotics (liver cells).



Structure of the endoplasmic reticulum

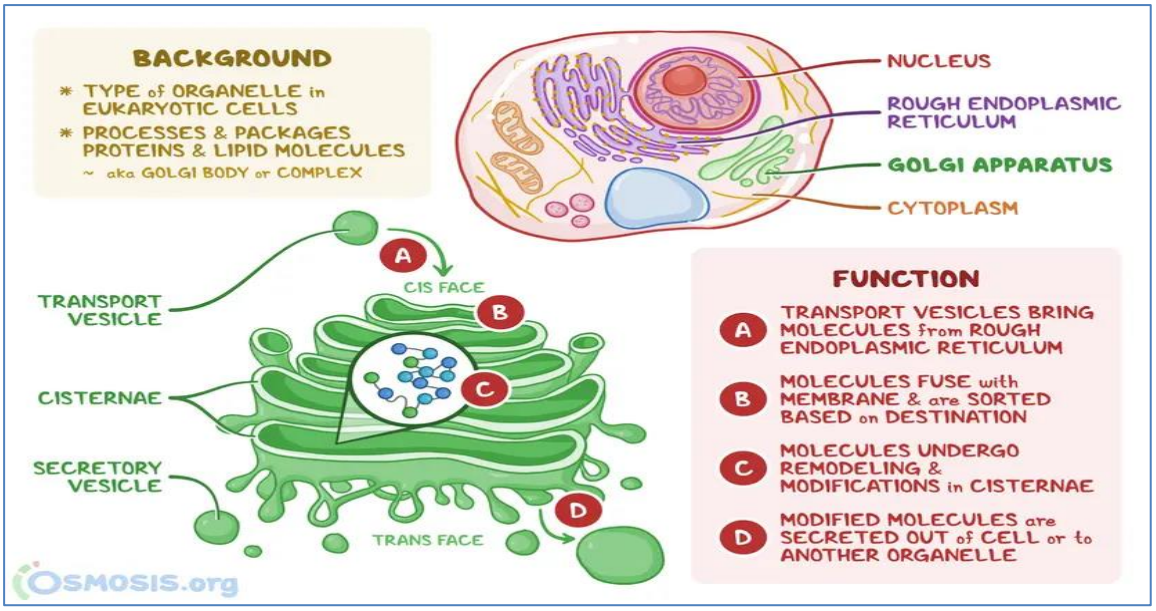
II.2.The Golgi apparatus

II.2.1.Organization and ultrastructure

In the M.E.T., piles of saccules and small vesicles. Each stack of 4 to 8 saccules is a **dictyosome** (on average 20 dictyosomes per cell). This organelle is grouped together in a particular place in the cell. It is divided into 3 zones:

1. A close friend of R.E.: the "***cis-golgi" that receives the budded vesicles of the R.E.***
2. A second part: the "golgi-median".
3. A third part: the "trans-golgi" which emits exocytosis vesicles, or intended for other organelles.

In continuity with a network of canaliculi called the Trans Golgi Network or TGN (Trans Golgi Network). The intermediate compartment between REG and the Golgi apparatus is called the "Endoplasmic Reticulum-Golgi Intermediate Compartment" or **ERGIC.**



Structure of the Golgi apparatus

II.2.2.Mechanisms of communication between the reticulum and the Golgian compartments

The transport of macromolecules between two compartments is based on a bidirectional flow of vesicles for both the exocytosis (biosynthesis-secretion) and endocytosis pathways. Vesicular communication between two compartments requires three successive steps:

- The formation of a bud at the membrane of a donor compartment
- The formation of a vesicle by pinching the bud. This step isolates a fraction of the donor compartment as well as the membrane components.
- The docking (lashing) of the vesicle to the acceptor compartment with which it merges.

II.2.3. Dictyosome-associated vesicles

Vesicles of variable size accompany the Golgian saccules:

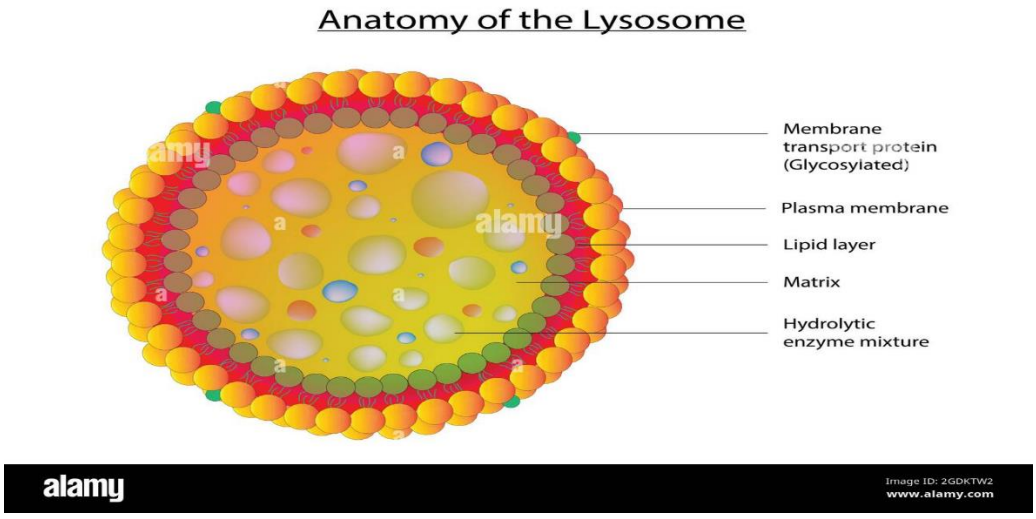
- **Transitional vesicles** : the transitional vesicles are located between the ERGIC and the cis golgians, they are covered with coatomers.
- **Transport vesicles** : the transport vesicles are located between the saccules, they are also covered with coatomers.
- **Secretory vesicles** : Secretory vesicles bud from the TGN and contain the final product. They are covered with:

- **Coatomer**: during a constitutive exocytosis pathway. Example: extracellular matrix components, peripheral plasma membrane proteins.
- **Clathrin**: during a regulated exocytosis pathway, they form secretory grains of dense content. Example: insulin, acid hydrolase vesicles.
- **Caveolin**: during a renewal pathway of membrane microdomains.

II.3.Lysosomes

II.3.1.Definition

The lysosome was first described and named in 1955 by Christian de Duve. They are membrane-bound organelles that contain a matrix rich in hydrolytic enzymes (acid hydrolases) involved in intracellular digestion. For their activity to be optimal, these hydrolases must be activated by proteolytic cleavage and they require an acidic environment that the lysosomes provide them by maintaining a pH of about 4.5-5.0 in their lumen. Lysosomes exist in all eukaryotic cells except red blood cells: they also exist in protozoa or protophytes. The diversity of lysosome shape, size and number are variable and depend on the functions of the cell.



Microscopic structure of lysosomes

II.3.2. Types of lysosomes :

At present the distinction relates to the source of the digested material.05

routes are thus considered:

- Endocytosis products, contained in **endosomes**, fuse with the primary lysosomes loaded with hydrolases, to form **endolysosomes.**
- In phagocytic cells, **phagosomes** (vesicles containing waste or bacteria) are transformed into **phagolysosomes** by association with a primary lysosome.
- Non-functional cell organelles surround themselves with a membrane from the endoplasmic reticulum. This forms an **autophagosome**, which, by fusion with a primary lysosome, would result in the formation of an **autophagolysosome.** Autophagolysosomes provide the mechanism of cellular autophagy.
- Another type of cellular autophagy allows the formation of cytophagosomes, membranes of the endoplasmic reticulum encircling a whole part of the cytoplasm thus forming **cytophagosomes**, which, by fusion with a primary lysosome, would lead to the formation of **cytophagolysosomes**. This phenomenon is very common in species with complete metamorphosis. An example of the transformation of the tadpole into a frog, in fact the lysosomal activity is very important in the tadpole whose tail disappears in the adult state.
- There is also another particular form of autophagy which results in the lysis of secretory products in **crinolysosomes.** Crinophagy is observed in secretory cells, endocrine or exocrine. When the body's needs are met, the secretory grains are no longer excreted, but accumulate in the cell. They are destroyed by lysosomes. For example, at the end of the breastfeeding period, the secretory grains of prolactin cells (the hormone responsible for milk secretion) are destroyed by crinophagy.

II.3.3.Importance of hydrolases

Lysosomes contain digestive enzymes (acid hydrolases) to digest macromolecules. To function properly, digestive enzymes require the acidic environment of the lysosome. For this reason, if acid hydrolases were to leak to the cytosol, their potential danger to the cell would be reduced, as they would not be at their optimum pH. All these enzymes are produced by the endoplasmic reticulum, and transported and processed by the Golgi apparatus. Each acid hydrolase is then targeted to a lysosome. Some important enzymes in lysosomes are:

1. **Lipases,** which break down lipids into fatty acids.
2. **Carbohydrases,** which break down carbohydrates (sugars).
3. **Proteases**, which degrade proteins into peptides, which are then broken down by peptidase into tripeptides, dipeptides, and then amino acids.
4. **Nucleases**, which break down nucleic acids into nucleosides

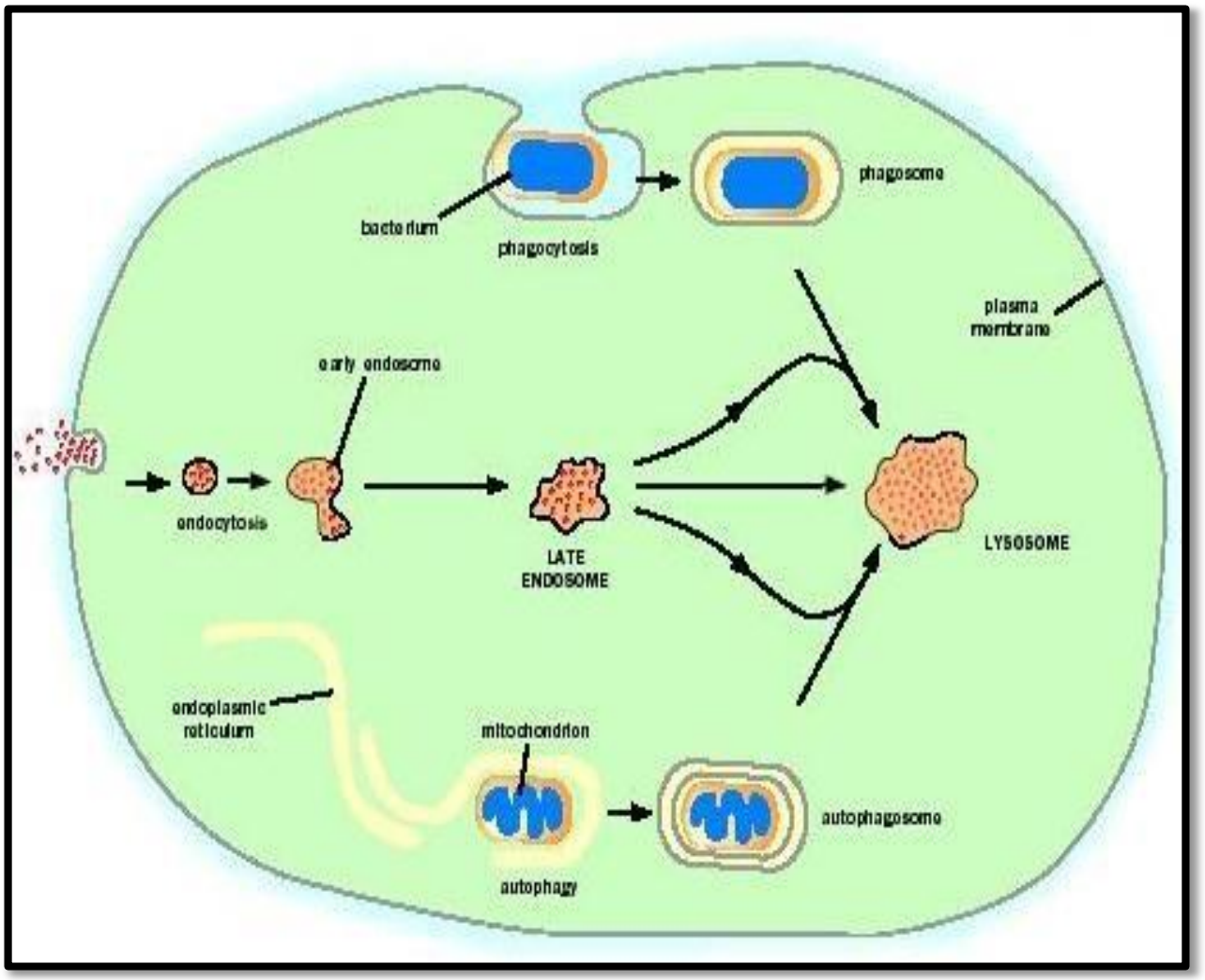
II.3.4.The different types of digestions

II.3.4.1.Heterophagy

Corresponds to the digestion of exogenous substances that enter the cell either by endocytosis or by phagocytosis. The endocytosis vesicles fuse with the endosomes, which in turn fuse with the primary lysosomes to form the mature lysosomes.

II.3.4.2.Autophagy

It is an expansion of the trans-Golgian network that surrounds the material to be digested. It then fuses with lysosomes, forming **auto-phagolysosomes**. Autophagy plays a big role in the renewal of cellular components



The different types of lysosome digestion