Chapter 7
The Golgi Apparatus, Lysosomes & Peroxisomes

7.1. The Golgi Apparatus

The Golgi apparatus is a cell structure mainly devoted to processing the proteins synthesized in the **endoplasmic reticulum** (**ER**). Some of these will eventually end up as **integral membrane proteins** embedded in the plasma membrane. Other proteins moving through the Golgi apparatus will end up in lysosomes or be secreted by **exocytosis** (e.g., digestive enzymes). The major processing activity is **glycosylation**: the adding of sugar molecules to form **glycoproteins**. In some cells, e.g., mucus-secreting cells in epithelia, the amount of carbohydrate so far exceeds that of the protein that the product is called a **mucopolysaccharide** (also known as a **proteoglycan**). In plant cells, the Golgi apparatus secretes the **cell plate** and **cell wall**. Small **peptides**, e.g., some **hormones** and **neurotransmitters**, are too small to be synthesized directly by ribosomes. Instead, the ribosomes on the ER synthesize a large precursor protein that is later cut up into small peptide fragments as it traverses the Golgi apparatus. Example: **pro-opiomelanocortin** (**POMC**) — a polypeptide of 265 amino acids from which is cut **ACTH** , alpha and beta **MSH**, **beta-endorphin** and others. The Golgi consists of a stack of membrane-bounded **cisternae** located between the endoplasmic reticulum and the cell surface.

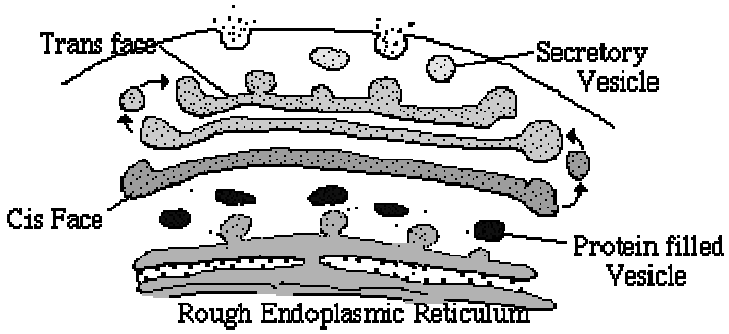

Fig.7.1. Golgi Apparatus

Many different enzymes (proteins) are present in the Golgi apparatus to perform its various synthetic activities. So there must be mechanisms to sort out the processed proteins and send them on to their destinations while reclaiming processing proteins (e.g., glycosylases) for reuse. All the details are far from worked out, but these are some of the features for which there is considerable experimental evidence.

(a) The Outbound Path

Transition vesicles pinch off from the surface of the endoplasmic reticulum carrying integral membrane proteins, soluble proteins awaiting processing and processing enzymes. Pinching off requires that the vesicle be coated with **COPII** (**Coat Protein II**). The transition vesicles move toward the **cis Golgi** on microtubules. As they do so, their COPII coat is removed and they may fuse together forming larger vesicles. These fuse

with the cis Golgi apparatus. Sugars are added to proteins in small packets so many glycoproteins have to undergo a large number of sequential steps of **glycosylation**, each requiring its own enzymes. These steps take place as **shuttle vesicles** carry the proteins from **cis** to **medial** to the **trans Golgi** compartments. At the outer face of the trans Golgi apparatus, vesicles pinch off and carry their completed products to their various destinations.

(b) The Inbound Path

The movement of **cisternal** contents through the stack means that essential processing enzymes are also moving away from their proper site of action. Using a variety of signals, the Golgi apparatus separates the products from the processing enzymes that made them and returns the enzymes back to the endoplasmic reticulum. This transport is also done by pinching off vesicles, but the inbound vesicles are coated with **COPI** (**coat protein I**)

(c) How a Vesicle Recognizes its Correct Target

This involves pairs of **complementary** integral membrane proteins

- **v-SNAREs** = "vesicle SNAREs" — on the vesicle surface;
- **t-SNAREs** = "target SNAREs" — on the surface of the target membrane.

v-SNAREs and t-SNAREs bind specifically to each other thanks to the complementary structure of their surface **domains**. Binding is followed by fusion of the two membranes.

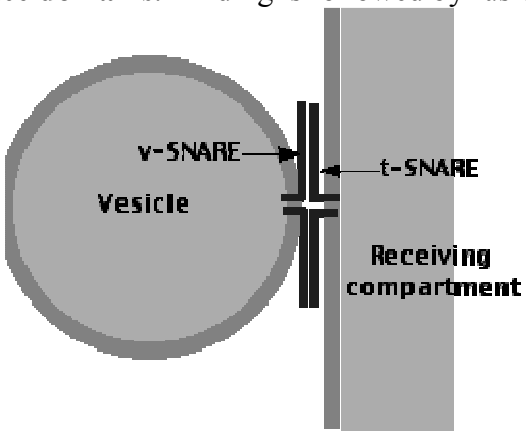

Fig.7.2. Vesicle Recognition of its target

(d) Another Mechanism of Golgi Apparatus Traffic

There is evidence (in yeast) that in addition to the pinching off and fusing of shuttle vesicles (and perhaps more important), the cisternae of the Golgi actually migrate themselves; that is, the cis Golgi gradually migrates up the stack becoming a medial and finally a trans Golgi (depicted in the top figure with red arrows).

(f) The Golgi Apparatus is not a Static Cell Organelle

The Golgi breaks up and disappears at the onset of mitosis. By telophase of mitosis, the Golgi apparatus reappears. How it is recreated is still uncertain.

7.2. Lysosomes

Lysosomes are roughly spherical bodies bounded by a single membrane. They are manufactured by the Golgi apparatus. They contain over 3 dozen different kinds of hydrolytic enzymes including **proteases, lipases, nucleases** and **polysaccharidases.** The

pH within the lysosome is about pH 5, substantially less than that of the cytosol (~pH 7.2). All the enzymes in the lysosome work best at an acid pH. This reduces the risk of their digesting their own cell if they should escape from the lysosome.

At one time, it was thought that lysosomes were responsible for killing cells scheduled to be removed from a tissue; for example, the resorption of its tail as the tadpole metamorphoses into a frog. This is incorrect. These examples of programmed cell death (PCD) or **apoptosis** take place by an entirely different mechanism. Materials within the cell scheduled for digestion are first deposited within lysosomes. These may be other organelles, such as mitochondria, that have ceased functioning properly and have been engulfed in **autophagosomes**, food molecules or, in some cases, food particles taken into the cell by **endocytosis,** foreign particles like bacteria that are engulfed by **neutrophils,** and antigens that are taken up by "professional" **antigen-presenting cells** like **dendritic cells** (by phagocytosis) and B cells (by binding to their antigen receptors (BCRs) followed by **receptor-mediated endocytosis**.

(a) Lysosomal Storage Diseases

Lysosomal storage diseases are caused by the accumulation of macromolecules (proteins, polysaccharides, lipids) in the lysosomes because of a genetic failure to manufacture an enzyme needed for their breakdown. Neurons of the central nervous system are particularly susceptible to damage. Most of these diseases are caused by the inheritance of two defective alleles of the gene encoding **one** of the hydrolytic enzymes. Examples:

1. **Tay-Sachs disease** and **Gaucher's disease** — both caused by a failure to produce an enzyme needed to break down **sphingolipids** (fatty acid derivatives found in all cell membranes).
2. **Mucopolysaccharidosis I** (MPS-I). Caused by a failure to synthesize an enzyme (α-L-iduronidase) needed to break down proteoglycans like **heparan sulphat**e. This enzyme (containing 628 amino acids) is manufactured by recombinant DNA technology.

However, one lysosomal storage disease, **I-cell disease** ("inclusion-cell disease"), is caused by a failure to "tag" (by phosphorylation) **all** the hydrolytic enzymes that are supposed to be transported from the **Golgi apparatus** to the lysosomes. Lacking the mannose 6-phosphate (M6P) tag, they are secreted from the cell instead. The result: all the macromolecules incorporated in lysosomes remain undegraded forming "inclusion bodies" in the cell.

(b) Secretory Lysosomes

In some cells, lysosomes have a secretory function — releasing their contents by exocytosis. **Cytotoxic T cells** (CTL) secrete **perforin** from lysosomes. **Mast cells** secrete some of their many mediators of **inflammation** from modified lysosomes. Melanocytes secrete **melanin** from modified lysosomes. The exocytosis of lysosomes provides the additional membrane needed to quickly **seal wounds** in the plasma membrane.

7.3. Peroxisomes

Peroxisomes are also called **microbodies**. Peroxisomes are about the size of lysosomes (0.5–1.5 μm) and like them are bound by a single membrane. They also resemble lysosomes in being filled with enzymes.

However, peroxisomes bud off from the **endoplasmic reticulum**, not the Golgi apparatus (that is the source of lysosomes). The enzymes and other proteins destined for peroxisomes are synthesized in the cytosol. Each contains a **P**eroxisomal **T**argeting **S**ignal (**PTS**) that binds to a receptor molecule that takes the protein into the peroxisome and then returns for another load. Two peroxisomal targeting signals have been identified:

1. a 9-amino acid sequence at the N-terminal of the protein;
2. a tripeptide at the C-terminal.

Each has its own receptor to take it to the peroxisome. Some of the functions of the peroxisomes in the human liver include:

1. Breakdown (by oxidation) of excess **fatty acids**.
2. Breakdown of hydrogen peroxide (H_2O_2), a potentially dangerous product of fatty-acid oxidation. It is catalyzed by the enzyme **catalase**.
3. Participates in the synthesis of **cholesterol**. One of the enzymes involved, **HMG-CoA reductase**, is the target of the popular cholesterol-lowering "statins".
4. Participates in the synthesis of **bile acids**.
5. Participates in the synthesis of the lipids used to make **myelin**.
6. Breakdown of excess **purines** (AMP, GMP) to **uric acid**.

Peroxisomes are also present in **plant** cells where they participate is such functions as

1. symbiotic nitrogen fixation
2. photorespiration

A variety of rare inherited disorders of peroxisome function occur in humans. Most involve mutant versions of one or another of the enzymes found within peroxisomes. Example: **X-linked adrenoleukodystrophy** (**X-ALD**). This disorder results from a failure to metabolize fatty acids properly. One result is deterioration of the **myelin sheaths** of neurons. The disorder occurs in young boys because the gene is **X-linked**