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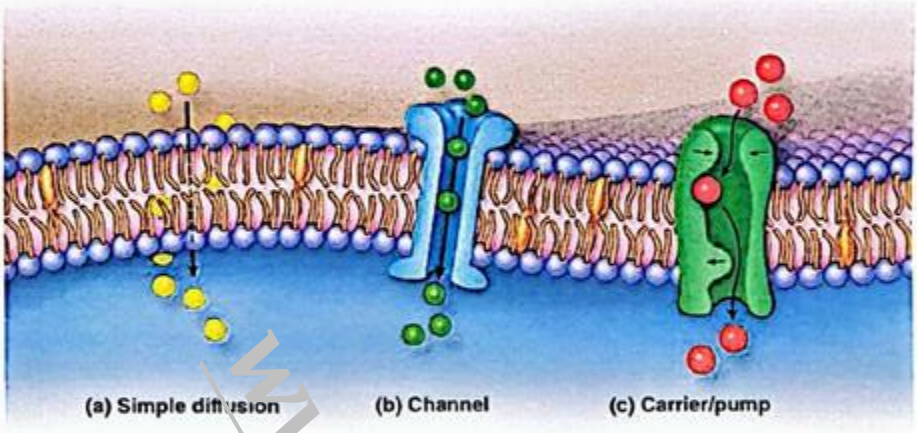
FIGURE 2–5 Major mechanisms by which molecules cross membranes.



Lipophilic and some small, uncharged molecules can cross membranes by simple diffusion (**a**).

Most ions cross membranes in multipass proteins called channels (**b**) whose structures include transmembrane ion-specific pores.

Many other larger, water-soluble molecules require binding to sites on selective carrier proteins (**c**), which then change their conformations and release the molecule to the other side of the membrane.

Diffusion, channels and most carrier proteins translocate substances across membranes using only kinetic energy. In contrast, **pumps** are carrier proteins for active transport of ions or other solutes and require energy derived from ATP.

Exocytosis of macromolecules made by cells occurs via either of two pathways:

- **Constitutive secretion** is used for products that are released from cells continuously, as soon as synthesis is complete, such as collagen subunits for the ECM.
- **Regulated secretion** occurs in response to signals coming to the cells, such as the release of digestive enzymes from pancreatic cells in response to specific stimuli. Regulated exocytosis of stored products from epithelial cells usually occurs specifically at the apical domains of cells, constituting a major mechanism of glandular secretion (see Chapter 4).

Portions of the cell membrane become part of the endocytotic vesicles or vacuoles during endocytosis; during exocytosis, membrane is returned to the cell surface. This process of membrane movement and recycling is called **membrane trafficking** (see Figure 2–7a). Trafficking of membrane components occurs continuously in most cells and is not only crucial for maintaining the cell but also for physiologically important processes such as reducing blood lipid levels.

In many cells, subpopulations of vacuoles and tubules within the endosomal compartment accumulate small vesicles *within* their lumens by further invaginations of their limiting membranes, becoming **multivesicular bodies**. While multivesicular bodies may merge with lysosomes for selective degradation of their content, this organelle may also fuse with the plasma membrane and release the intraluminal vesicles outside the cell. The small (50-150 nm diameter) vesicles released are called **exosomes**, some of which can fuse with other cells transferring their contents and membranes in one form of cell-to-cell communication.

Signal Reception & Transduction

Cells in a multicellular organism communicate with one another to regulate tissue and organ development, to control their growth and division, and to coordinate their functions. Many adjacent cells form communicating **gap junctions** that couple the cells and allow exchange of ions and small molecules (see Chapter 4).

Cells also use about 25 families of **receptors** to detect and respond to numerous extracellular molecules and physical stimuli. Each cell type in the body contains a distinctive set of cell surface and cytoplasmic receptor proteins that enable it to respond to a complementary set of signaling molecules in a specific, programmed way. Cells bearing receptors for a specific ligand are referred to as **target cells** for that molecule. The routes of signal molecules from source to target provide one way to categorize the signaling processes:

- In **endocrine signaling**, the signal molecules (here called **hormones**) are carried in the blood from their sources to target cells throughout the body.
- In **paracrine signaling**, the chemical ligand diffuses in extracellular fluid but is rapidly metabolized so that its effect is only local on target cells near its source.
- In **synaptic signaling**, a special kind of paracrine interaction, neurotransmitters act on adjacent cells through special contact areas called **synapses** (see Chapter 9).

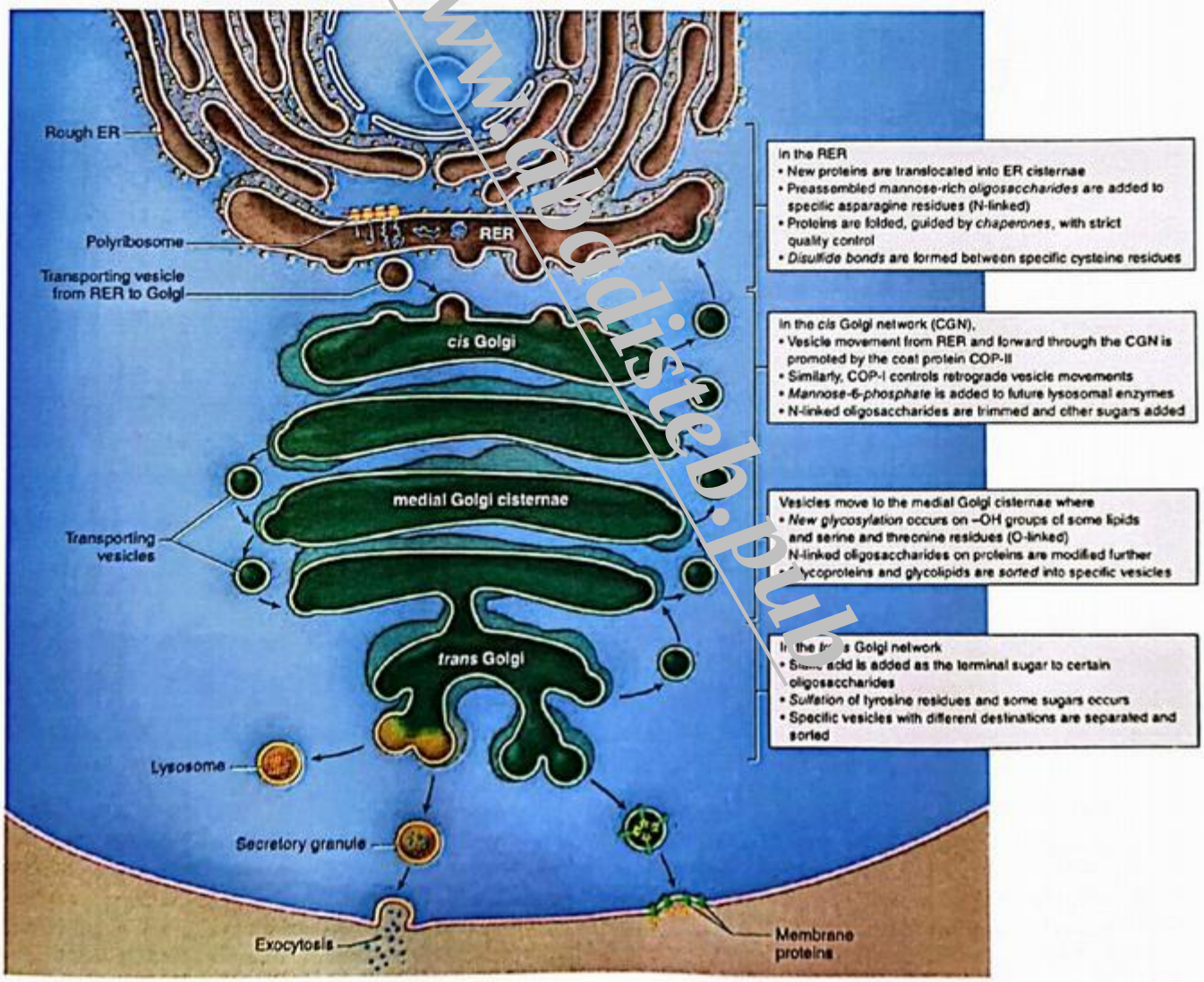
for directed vesicle fusion include various Rab proteins and other enzymes, receptors and specific binding proteins, and fusion-promoting proteins that organize and shape membranes. Depending on the activity of these proteins, vesicles are directed toward different Golgi regions and give rise to lysosomes or secretory vesicles for exocytosis.

As indicated in Figure 2–14, Golgi saccules at sequential locations contain different enzymes at different *cis*, *medial*, and *trans* levels. Enzymes of the Golgi apparatus are important for glycosylation, sulfation, phosphorylation, and limited proteolysis of proteins. Along with these activities, the Golgi apparatus initiates packaging, concentration, and storage of secretory products. Protein movements through the Golgi and the control of protein processing are subjects of active research.

Secretory Granules

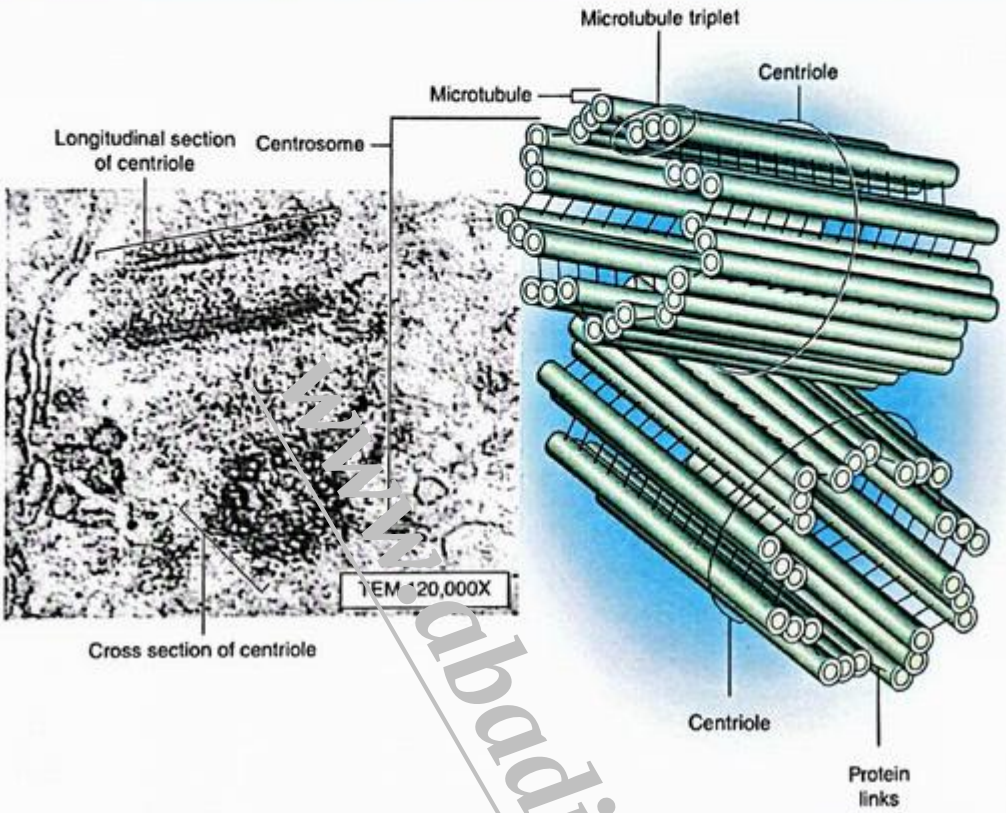
Originating as condensing vesicles in the Golgi apparatus, **secretory granules** are found in cells that store a product until its release by exocytosis is signaled by a metabolic, hormonal, or neural message (regulated secretion). The granules are surrounded by the membrane and contain a concentrated form of the secretory product (Figure 2–15). The contents of some secretory granules may be up to 200 times more concentrated than those in the cisternae of the RER.

FIGURE 2–14 Summary of functions within the Golgi apparatus.



The main molecular processes are listed at the right, with the major compartments where they occur. In the *trans* Golgi network, the proteins and glycoproteins combine with specific receptors that guide them to the next stages toward their destinations.

FIGURE 2–24 Centrosome.



The **centrosome** is the microtubule-organizing center for the mitotic spindle and consists of paired centrioles. The TEM reveals that the two centrioles in a centrosome exist at right angles to each other in a dense matrix of free tubulin subunits and other proteins. Each centriole consists of **nine microtubular triplets**. In a poorly understood process, the centrosome duplicates itself and the pair is divided equally during a cell's interphase, each half having a duplicated centriole pair. At the onset of mitosis, the two daughter centrosomes move to opposite sides of the nucleus and become the two poles of the mitotic spindle of microtubules attaching to chromosomes.

(Micrograph used with permission from Dr Gwen V. Childs, University of Arkansas for Medical Sciences, Department of Neurobiology and Developmental Sciences)

within networks of F-actin increases cytoplasmic viscosity, while severing (and capping) the filaments tends to decrease viscosity. The lengths and other physical properties of actin filaments are controlled by various other types of actin-binding proteins, including those indicated in Figure 2–26.

Just as the molecular motors kinesin and dynein move structures along microtubules, various **myosin motors** use ATP to transport cargo along F-actin. Movement is usually toward the barbed (+) ends of actin filaments; myosin VI is the only known myosin that moves in the other direction. Interactions between F-actin and myosins form the basis for various cell movements:

- Transport of organelles, vesicles, and granules in the process of *cytoplasmic streaming*
- Contractile rings of microfilaments with myosin II constricting to produce two cells by *cytokinesis* during mitosis
- Membrane-associated molecules of myosin I whose movements along microfilaments produce the cell surface changes during *endocytosis*

Stabilized arrays of actin filaments integrated with arrays of thicker (16 nm) myosin filaments permit very forceful contractions in specialized cells such as those of muscle (see Chapter 10).

Intermediate Filaments

The third class of cytoskeletal components includes filaments intermediate in size between the other two, with a diameter averaging 10 nm (Table 2–4). Unlike microtubules and actin filaments, these **intermediate filaments** are stable, confer increased mechanical stability to cell structure, and are made up of different protein subunits in different cell types. More than a dozen proteins, ranging in size from 40 to 230 kDa, serve as subunits of various intermediate filaments and can