Lecture 9

Internal structure of Nucleus

- Nucleoplam
- Nucleolus
- Chromosomes

Nucleoplasm

The space between the nuclear envelope and nucleolus is filled by transparent, semisolid granular and slightly acidophilic ground substance or matrix known as **nucleoplasm or karyolymph**

Chromatin thread and nucleolus remain suspended in it.

It contains mainly the nucleoproteins but also contains nucleic acids, proteins enzymes and minerals

Chromatin

The extent of chromatin condensation varies during the life cycle of the cell

In interphase (nondividing) cells, most of the chromatin called **euchromatin which** is relatively decondensed form and distributed throughout the nucleus

During this period of the cell cycle, genes are transcribed and the DNA is replicated in preparation for cell division

In contrast to **euchromatin** about 10% of interphase chromatin called **heterochromatin** is in a very highly condensed state that resembles the chromatin of cells undergoing mitosis

• Heterochromatin is **transcriptionally inactive** and contains highly repeated DNA sequences, such as those present at centromeres and telomeres

Types of heterochromatin

- Constitutive heterochromatin - More stable, Permanent factor of a particular cell type
- Facultative heterochromatin – Reversible, Not a permanent factor

Nucleolus

It is the site of rRNA transcription and processing, and of ribosome assembly

• The **nucleolus is a ribosome production factory**, designed to fulfill the need for large-scale production of rRNAs and assembly of the ribosomal subunits

• Recent evidence suggests that nucleoli also have a more general role in RNA modification and that several types of RNA move in and out of the nucleolus at specific stages during their processing

Endoplasmic reticulum

Generally, the largest membrane in a eukaryotic cell encloses the **endoplasmic reticulum (ER)**—an extensive network of closed, flattened membrane-bounded sacs called **cisternae**

The endoplasmic reticulum has a number of functions in the cell but is particularly important in the **synthesis of lipids, membrane proteins, and secreted proteins.**

The ***smooth endoplasmic reticulum*** is smooth because it lacks ribosomes.

In contrast, the cytosolic face of the ***rough endoplasmic reticulum*** is studded with ribosomes.

The Smooth Endoplasmic Reticulum

The **synthesis of fatty acids and phospholipid**s takes place in the smooth ER.

Although many cells have very little smooth ER, this organelle is abundant in **hepatocytes.**

Enzymes in the smooth ER of the liver also modify or detoxify hydrophobic chemicals such as pesticides and carcinogens by chemically converting them into more water-soluble, conjugated products that can be excreted from the body.

High doses of such compounds result in a large proliferation of the smooth ER in liver cells.

The Rough Endoplasmic Reticulum

Ribosomes bound to the rough ER synthesize certain membrane and organelle proteins and virtually all proteins to be secreted from the cell.

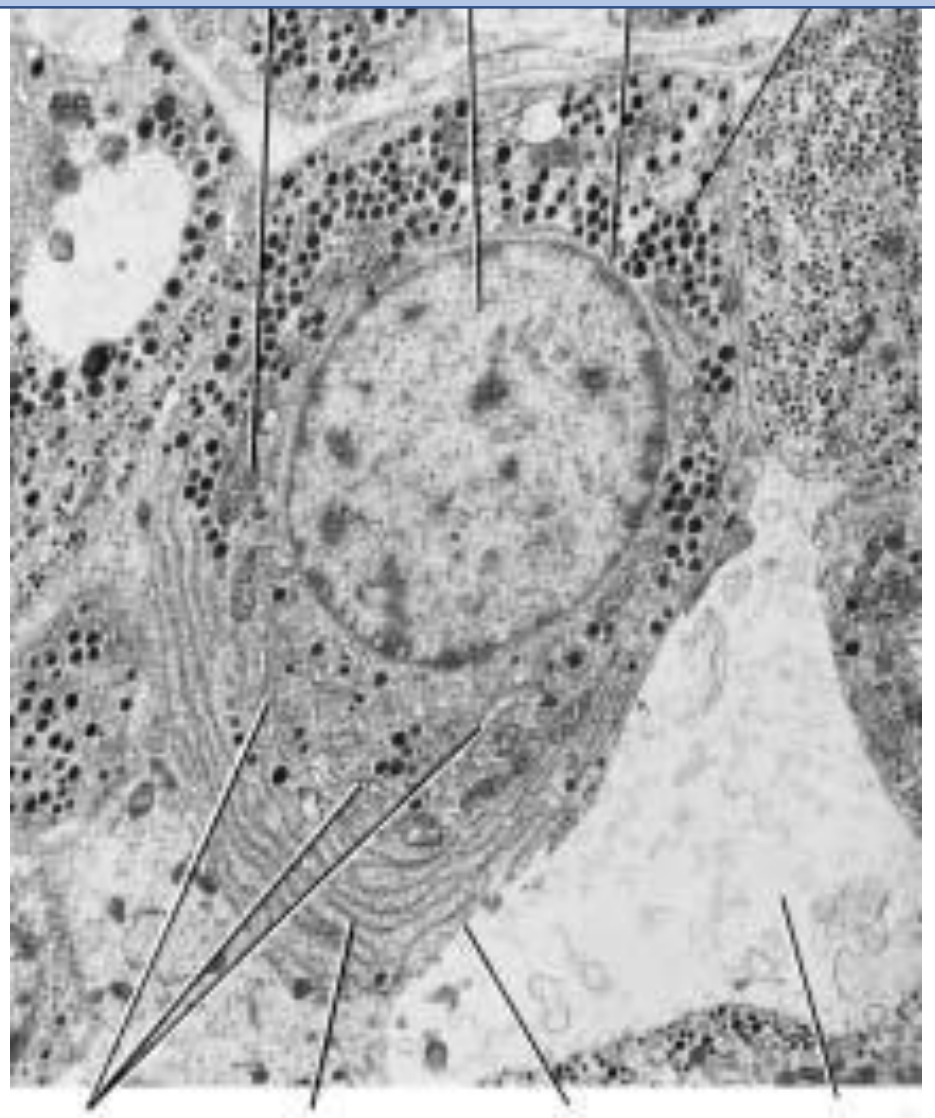
A ribosome that fabricates such a protein is bound to the rough ER by the nascent polypeptide chain of the protein.

As the growing polypeptide emerges from the ribosome, it passes through the rough ER membrane, with the help of specific proteins in the membrane.

Newly made membrane proteins remain associated with the rough ER membrane, and proteins to be secreted accumulate in the lumen of the organelle.

Characteristic features of cells specialized to secrete large amounts of particular proteins

One end of the cell is filled with abundant rough ER and Golgi sacs, where polypeptide hormones are synthesized and packaged.
At the opposite end of the cell are numerous secretory vesicles, which contain recently made hormones eventually to be secreted



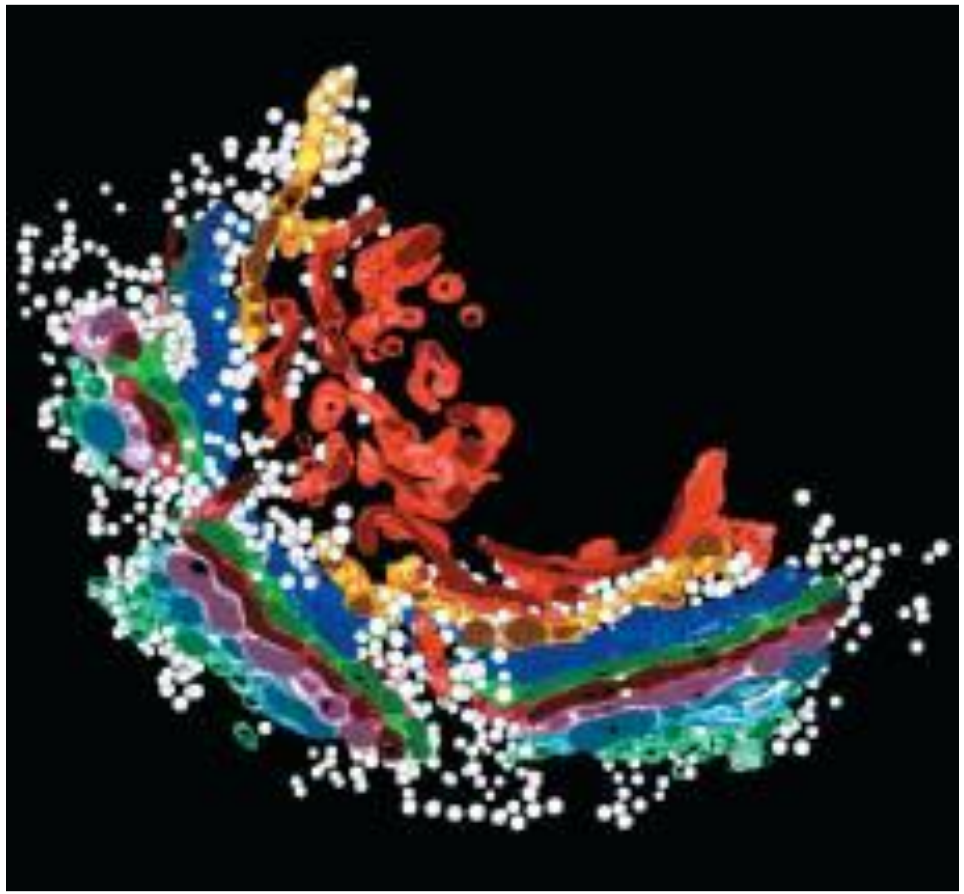
Electron micrograph of a thin section of a hormone-secreting cell from the rat pituitary.

Golgi complex

Several minutes after proteins are synthesized in the rough ER, most of them leave the organelle within small membrane bounded transport vesicles.

These vesicles, which bud from regions of the rough ER not coated with ribosomes, carry the proteins to another membrane-limited organelle, the **Golgi complex**

Three-dimensional reconstructions from serial sections of a Golgi complex reveal this organelle to be a **series of flattened vesicles or sacs (cisternae),** surrounded by a number of more or less spherical membrane-limited vesicles



The stack of Golgi cisternae has three defined regions—**the *cis,* the *medial,* and the *trans.***

Transport vesicles from the rough ER fuse with the *cis* region of the Golgi complex, where they deposit their protein contents.

These proteins then progress from the *cis* to the *medial* to the *trans* region.

Within each region are **different enzymes that modify proteins** to be secreted and membrane proteins differently, depending on their structures and their final destinations.

After proteins to be secreted and membrane proteins are modified in the Golgi complex, they are transported out of the complex by a second set of vesicles, which seem to bud from the trans side of the Golgi complex.

Some vesicles carry membrane proteins destined for the plasma membrane or soluble proteins to be released from the cell surface

Typical mammalian cell contains up to 10,000 different kinds of proteins; a yeast cell, about 5000.

The vast majority of these proteins are synthesized by cytosolic ribosomes, and many remain within the cytosol.

However, as many as half the different kinds of proteins produced in a typical cell are delivered to a particular cell membrane, an aqueous compartment other than the cytosol, or to the cell surface for secretion.

For example, many hormone receptor proteins and transporter proteins must be delivered to the plasma membrane, some water-soluble enzymes such as RNA and DNA polymerases must be targeted to the nucleus, and components of the extracellular matrix as well as polypeptide signaling molecules must be directed to the cell surface for secretion from the cell.

These and all the other proteins produced by a cell must reach their correct locations for the cell to function properly.

The delivery of newly synthesized proteins to their proper cellular destinations, usually referred to as ***protein targeting* or *protein sorting,*** encompasses two very different kinds of processes.

The first general process involves targeting of a protein to the membrane of an intracellular organelle and can occur either during or soon after synthesis of the protein by translation at the ribosome.

For membrane proteins, targeting leads to insertion of the protein into the lipid bilayer of the membrane, whereas for water-soluble proteins, targeting leads to translocation of the entire protein across the membrane into the aqueous interior of the organelle.

Proteins are sorted to the endoplasmic reticulum (ER), mitochondria, Chloroplasts, peroxisomes, and the nucleus by this general process

How a given protein could be targeted to only one specific membrane?

How relatively large protein molecules could be translocated across a membrane without disrupting the bilayer?

The information to target a protein to a particular organelle destination is encoded within the amino acid sequence of the protein itself, usually within sequences of 20–50 amino acids, known generically as **signal sequences,** or *uptake-targeting sequences*

Each organelle carries a set of **receptor proteins** that bind only to specific kinds of signal sequences, thus assuring that the information encoded in a signal sequence governs the specificity of targeting.

Once a protein containing a signal sequence has interacted with the corresponding receptor, the protein chain is transferred to some kind of ***translocation channel*** that allows the protein to pass through the membrane bilayer.

The unidirectional transfer of a protein into an organelle, without sliding back out into the cytoplasm, is usually achieved by coupling translocation to an energetically favorable process such as hydrolysis of ATP.

Some proteins are subsequently sorted further to reach a sub-compartment within the target organelle; such sorting depends on yet other signal sequences and other receptor proteins.

Finally, **signal sequences often are removed from the mature protein** by specific proteases once translocation across the membrane is completed.

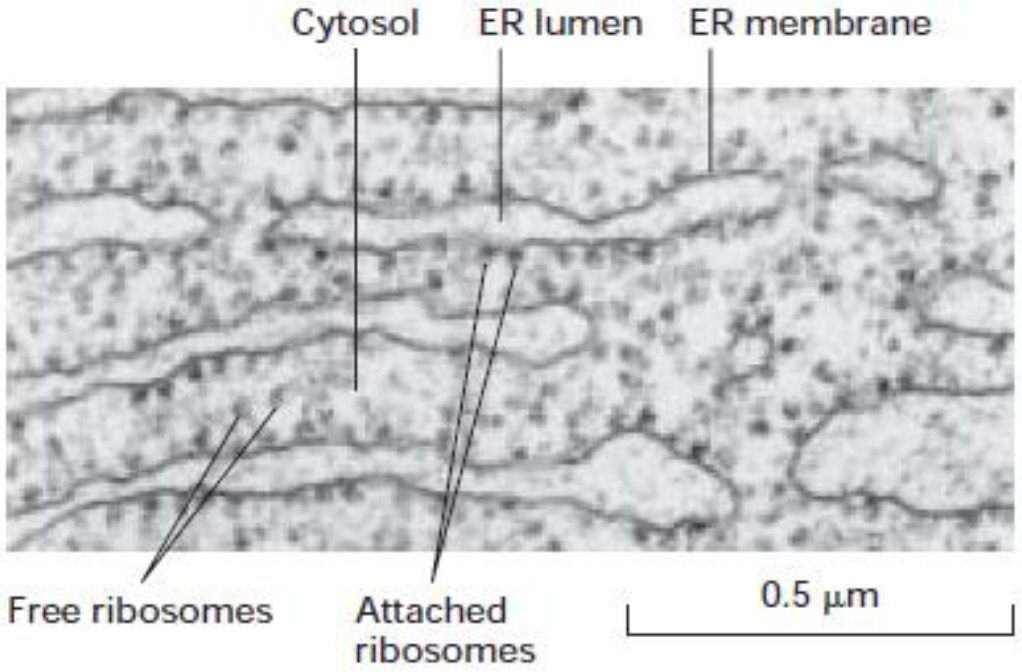
- What is the nature of the *signal sequence,* and what distinguishes it from other types of signal sequences?
- What is the *receptor* for the signal sequence?
- What is the structure of the *translocation channel* that allows transfer of proteins across the membrane bilayer? In particular, is the channel so narrow that proteins can pass through only in an unfolded state, or will it accommodate folded protein domains?
- What is the source of *energy?*

A Hydrophobic N-Terminal Signal Sequence Targets Nascent Secretory Proteins to the ER

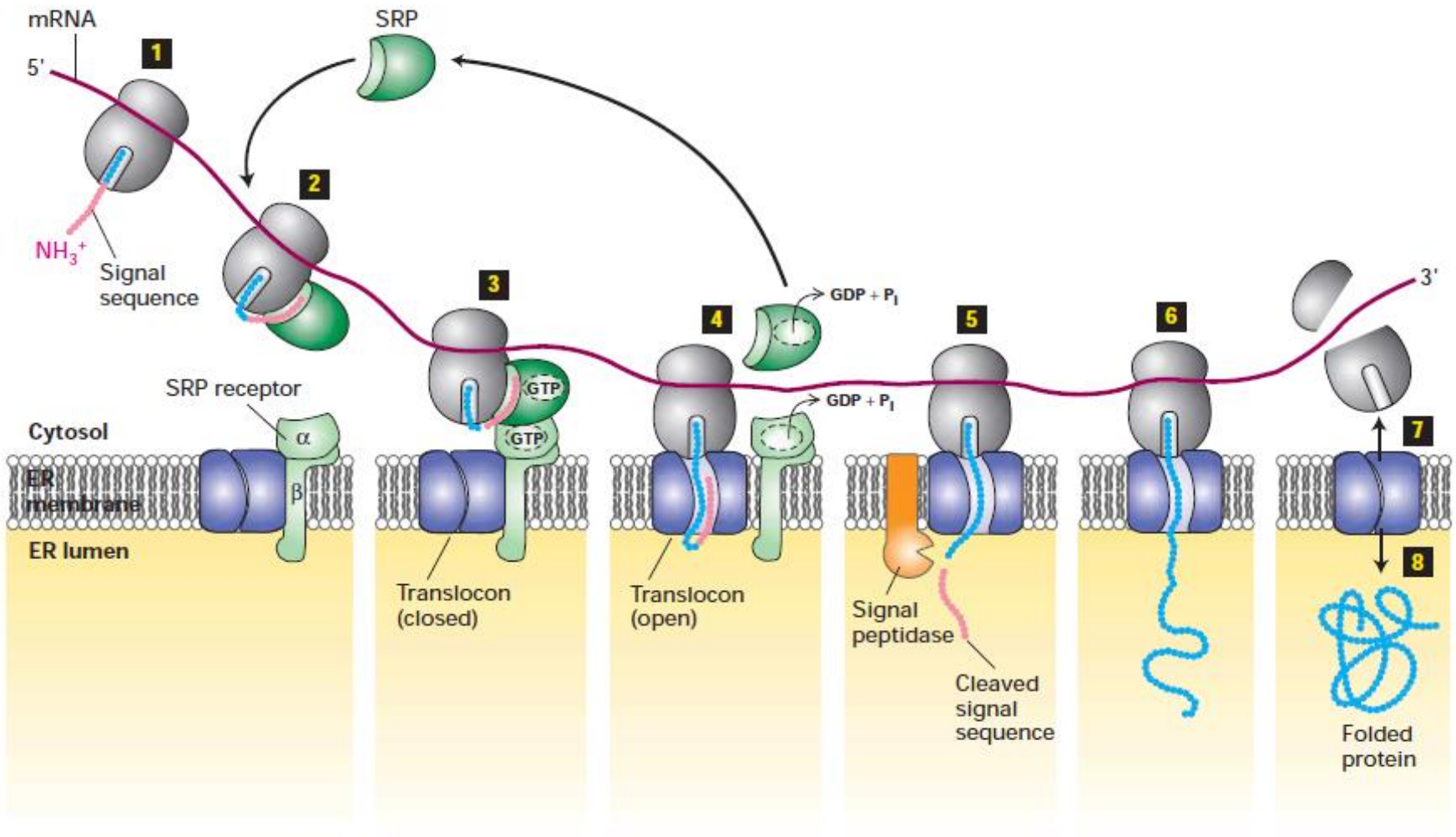
An ER signal sequence typically is located at the N-terminus of the protein, the first part of the protein to be synthesized.

The signal sequences of different secretory proteins contain one or more positively charged amino acids adjacent to a continuous stretch of 6–12 hydrophobic residues (the core), but otherwise they have little in common.

For most secretory proteins, the signal sequence is cleaved from the protein while it is still growing on the ribosome; thus, signal sequences are usually not present in the “mature” proteins found in cells.



Co-translational translocation



Post-translational translocation

- Common in which organism/organisms
- SRP needed?
- SRP recognition sequence needed?
- Energy form?
- Specific translocon?
- Any other differences?