NUCLEUS

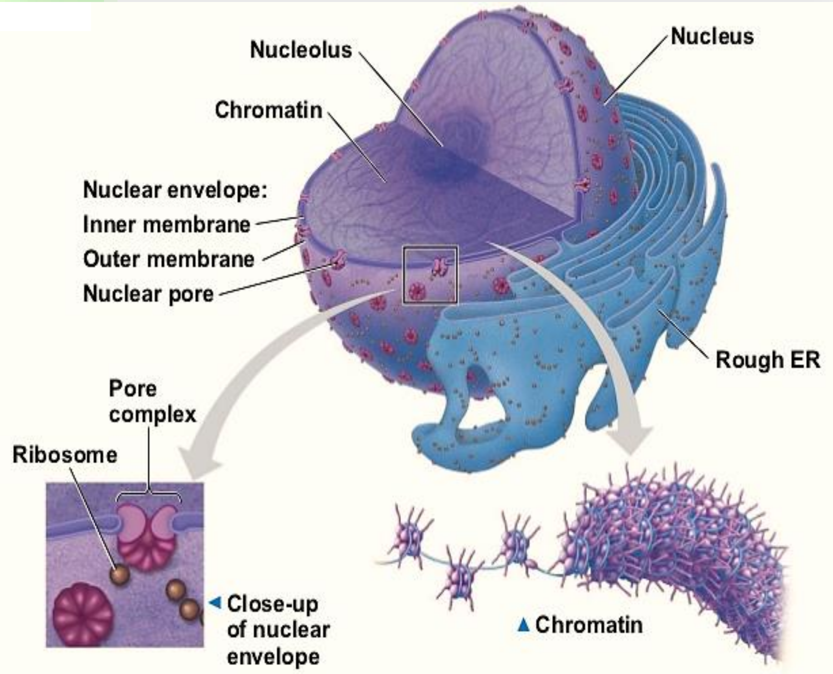
Lec. 5 | NUCLEUS (Pt.4)

THE HEREDITARY ORGANELLE

Introduction to The NUCLEUS

General structure of **Nucleus**:

i. It is the largest organelle seen clearly when the cell is not dividing.
ii. It stains deeply, is mostly spherical, WBC have lobed nuclei.
iii. It is mostly one in each cell (uninucleate, some cells have many nuclei; (multinucleate).
iv. Double layered nuclear membrane enclosing nucleoplasm which contains chromatin network and a nucleolus.



Functions

- Maintains the cell in a working order.
- Co-ordinates the activities of organelles.
- Takes care of repair work.
- Participates directly in cell division to produce genetically identical daughter cells, this division is called mitosis.
- Participates in production of gametes through another type of cell division called meiosis.

The part of a nucleus are given here:

Nuclear membrane

- Double layered membrane is interrupted by large number of pores.
- Membrane is made up of lipids and proteins (like plasma membrane) and has ribosomes attached on the outer membrane which make the outer membrane rough.

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- The pores allow the transport of large molecules in and out of nucleus, and the membranes keep the hereditary material in contact with the rest of the cell.

Chromatin

- Within the nuclear membrane there is jelly like substance (karyolymph or nucleoplasm) rich in proteins.
- In the karyolymph, fibrillar structures form a network called *chromatin fibrils*, which gets condensed to form distinct bodies called **Chromosomes** during cell division.

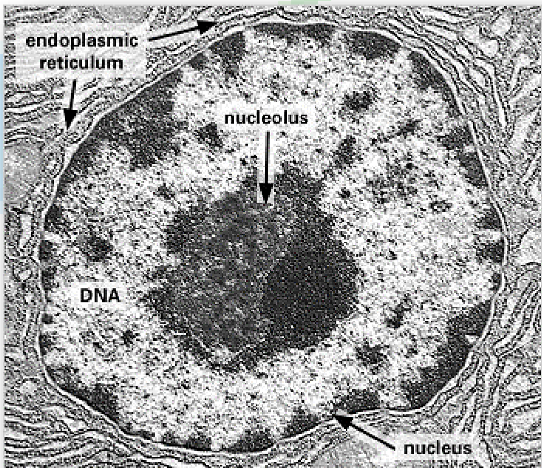
On staining the chromosomes, two regions can be identified in the chromatin material Heterochromatin (dark) and Euchromatin (light). **Heterochromatin** has less DNA and genetically less active than **Euchromatin** which has more DNA and genetically more active.

- Number of chromosomes is fixed in an organism. During cell division chromosomes divide in a manner that the daughter cells receive identical amounts of hereditary matter.

Nucleolus

- Membrane less, spheroidal bodies present in all eukaryotic cells except in sperms and in some algae.
- Their number varies from one to few, they stain uniformly and deeply.
- It has DNA, RNA and proteins.
- Store house for RNA and proteins; it disappears during cell division and reappears in daughter cells.
- Regulates the synthetic activity of the nucleus.
- Thus nucleus and cytoplasm are interdependent, and this process is equal to nucleocytoplasmic interaction.

The nucleus



The nucleus is the information center of the cell and is surrounded by a nuclear membrane in all eukaryotic organisms. It is separated from the cytoplasm by the **nuclear envelope**, and it houses the double-stranded, spiral-shaped deoxyribonucleic acid (**DNA**) molecules, which contain the genetic information necessary for the cell to retain its unique character as it grows and divides. The presence of a nucleus distinguishes the eukaryotic cells of multicellular organisms from the **prokaryotic**, one-celled organisms such as bacteria. In

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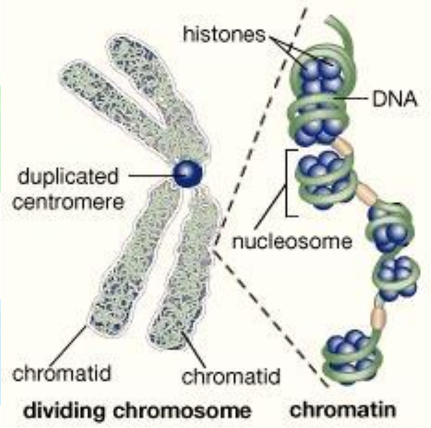
contrast to the higher organisms, prokaryotes do not have nuclei, so their DNA is maintained in the same compartment as their other cellular components. The primary function of the nucleus is the expression of selected subsets of the genetic information encoded in the DNA double helix. Each subset of a DNA chain, called a **gene**, codes for the construction of a specific protein out of a chain of amino acids. Information in DNA is not decoded directly into proteins, however. First it is transcribed, or copied, into a range of **messenger ribonucleic acid** (**mRNA**) molecules, each of which encodes the information for one protein (or more than one protein in bacteria). The mRNA molecules are then transported through the nuclear envelope into the cytoplasm, where they are translated, serving as templates for the synthesis of specific proteins.

The nucleus must not only synthesize the mRNA for many thousands of proteins, but it must also regulate the amounts synthesized and supplied to the cytoplasm. Furthermore, the amounts of each type of mRNA supplied to the cytoplasm must be regulated differently in each type of cell. In addition to mRNA, the nucleus synthesizes and exports other classes of **RNA** involved in the mechanisms of protein synthesis.

Structural organization of the nucleus



The nucleus of the average human cell is only 6 micrometers (6×10^{-6} meter) in diameter, yet it contains about 1.8 meters of DNA. This is distributed among 46 **Chromosomes**, each consisting of a single DNA molecule about 40 mm (1.5 inches) long. The extraordinary packaging problem this poses can be envisaged by a scale model enlarged a million times. On this scale a DNA molecule would be a thin string 2 mm thick, and the average chromosome would contain 40 km (25 miles) of DNA. With a diameter of only 6 meters, the nucleus would contain 1,800 km (1,118 miles) of DNA.

These contents must be organized in such a way that they can be copied into RNA accurately and selectively. DNA is not simply crammed or wound into the nucleus like a ball of string; rather, it is organized, by molecular interaction with specific nuclear proteins, into a precisely packaged structure. This combination of DNA with proteins creates a dense, compact fiber called **Chromatin**. An extreme example of the ordered folding and compaction that chromatin can undergo is seen during **Cell Division**, when the chromatin of each chromosome condenses and is divided between two daughter cells.

Nucleosomes: the subunits of chromatin

The compaction of DNA is achieved by winding it around a series of small proteins called histones. Histones are composed of positively charged amino acids that bind tightly to

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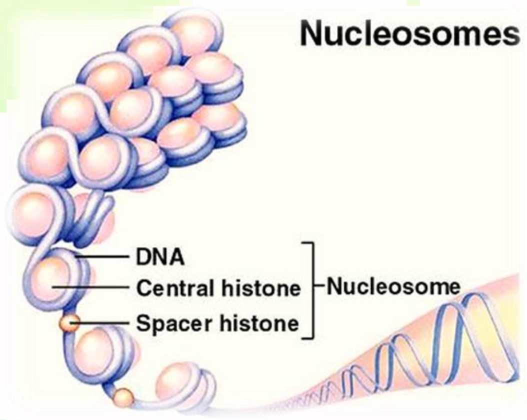
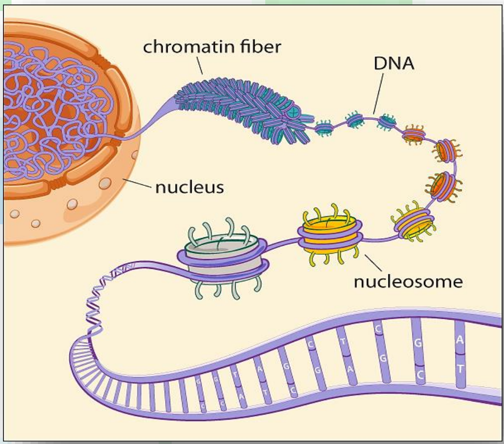
and neutralize the negative charges of DNA. There are five classes of **Histone**. Four of them, called H2A, H2B, H3, and H4, contribute two molecules each to form an octamer, an eight-part core around which two turns of DNA are wrapped. The resulting beadlike structure is called the **Nucleosome**. The DNA enters and leaves a series of nucleosomes, linking them like beads along a string in lengths that vary between species of organism or even between different types of cell within a species. A string of nucleosomes is then coiled into a solenoid configuration by the fifth histone, called **H1**. One molecule of H1 binds to the site at which DNA enters and leaves each nucleosome, and a chain of H1 molecules coils the string of nucleosomes into the solenoid structure of the chromatin fiber.



Nucleosomes not only neutralize the charges of DNA, but they have other consequences. First, they are an efficient means of packaging. DNA becomes compacted by a factor of six when wound into nucleosomes and by a factor of about 40 when the nucleosomes are coiled into a solenoid chromatin fibre. The winding into nucleosomes also allows some inactive DNA to be folded away in inaccessible conformations, a process that contributes to the selectivity of gene expression.

Organization of chromatin fiber

Several studies indicate that chromatin is organized into a series of large radial loops anchored to specific scaffold proteins. Each loop consists of a chain of nucleosomes and may be related to units of genetic organization. This radial arrangement of chromatin loops compacts DNA about a thousand fold. Further compaction is achieved by a coiling of the entire looped chromatin fiber into a dense structure called a chromatid, two of which form the chromosome. During cell division, this coiling produces a 10,000-fold compaction of DNA.



Chromatin classification

i. Heterochromatin

This is **condensed chromatin** and is therefore **Genetically Inactive**; that is, transcription is not occurring. Heterochromatin is seen associated with the nuclear envelope (**peripheral chromatin**), with the nucleolus (**nucleolar associated chromatin**), and

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scattered throughout the nucleus (**chromatin granules**). There are two types of heterochromatin:

- Constitutive heterochromatin, which is permanently inactive (e.g., centromere region of chromosome).
- Facultative heterochromatin, which may have been active in the past and may be so again in the future. It represents inactivated genes. The amount of facultative heterochromatin depends on the cell type and stage of development.

ii. Euchromatin

This is **extended chromatin** and is therefore **Genetically Active**; that is, transcription is occurring. At the EM level, Euchromatin appears as electron lucent regions interspersed among clumps of electron dense heterochromatin.

Chromatin function

During **transcription**, the genetic information encoded in the base sequence of DNA is copied onto a molecule of **messenger RNA** or ribonucleic acid. RNA differs from DNA in two fundamental ways. First, it contains **ribose** instead of 2-deoxyribose and, second, it contains **uracil** in place of thymine.

Using one strand of DNA as a template, a single molecule of mRNA is constructed by complimentary base pairing, incorporating uracil in place of thymine. The **precursor mRNA** molecule thus formed contains transcripts not only for sequences of DNA that contain genetic instructions (**exons**), but also for sequences of irrelevant DNA interposed in between (**introns**). Before the genetic instructions encoded in the mRNA can be translated, however, the irrelevant sequences must be excised and the exon-coded regions spliced back together. This is called **RNA processing** and it also occurs in the nucleus.

Into the cytoplasm. Once in the cytoplasm, the information encoded in the mRNA molecule is **translated** into a polypeptide chain. As you recall from our discussion of the 3 cytoplasm, this requires the participation of two other forms of RNA: **transfer RNA** and **ribosomal RNA**. Each molecule of tRNA contains a specific attachment site for one of twenty amino acids, as well as a base triplet called an **anticodon** that matches a specific **codon** on the mRNA molecule.

As the molecule of mRNA passes between the large and small subunits of a ribosome, molecules of tRNA insert amino acids into a polypeptide chain in a specific order that is determined by the base sequence of the mRNA. After each amino acid is inserted into the growing end of the polypeptide chain, the ribosome shifts to the next codon sequence and another tRNA carrying an amino acid moves into place.

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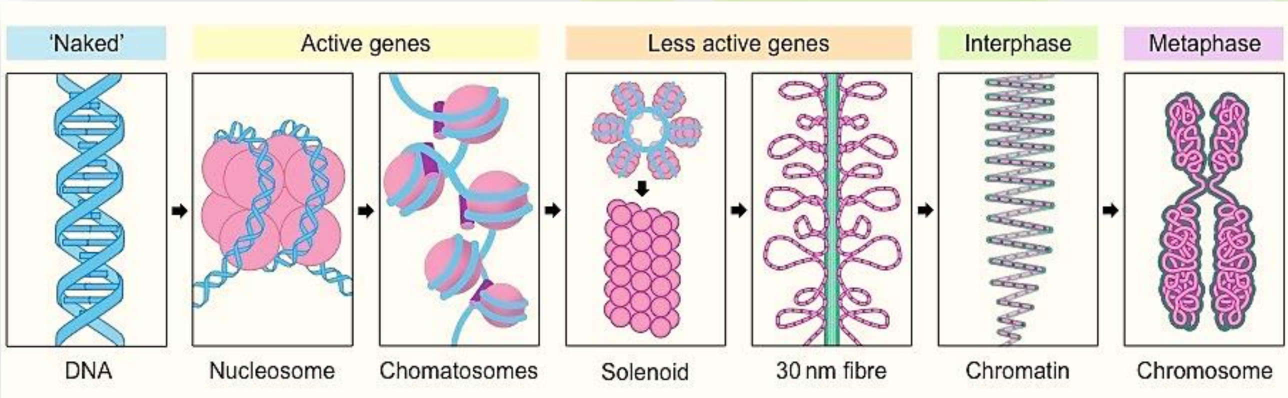

The nuclear envelope

The nuclear envelope is a double membrane composed of an outer and an inner phospholipid bilayer. The thin space between the two layers connects with the lumen of the rough endoplasmic reticulum (RER), and the outer layer is an extension of the outer face of the RER. The inner surface of the nuclear envelope has a protein lining called the nuclear lamina, which binds to chromatin and other contents of the nucleus. The entire envelope is perforated by numerous nuclear pores. These transport routes are fully permeable to small molecules up to the size of the smallest proteins, but they form a selective barrier against movement of larger molecules. Each pore is surrounded by an elaborate protein structure called the nuclear pore complex, which selects molecules for entrance into the nucleus. Entering the nucleus through the pores are the nucleotide building blocks of DNA and RNA, as well as adenosine triphosphate, which provides the energy for synthesizing genetic material. Histones and other large proteins must also pass through the pores. These molecules have special amino acid sequences on their surface that signal admittance by the nuclear pore complexes. The complexes also regulate the export from the nucleus of RNA and subunits of ribosomes. DNA in prokaryotes is also organized in loops and is bound to small proteins resembling histones, but these structures are not enclosed by a nuclear membrane.

The Nucleolus

Ribosomal RNA is a structural component of ribosomes and is synthesized in the nucleolus. The nucleolus is a separate entity within the nucleus consisting largely of rRNA and protein. It is intensely **basophilic** but **Feulgen-negative**. Moreover, treatment with RNAase abolishes most of the staining, suggesting that it is due primarily to the presence of rRNA. The nucleolus is very prominent in cells that are active in protein synthesis. Often, two or more nucleoli are present in the same nucleus. Ribosomal RNA

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is transcribed from multiple copies of **nucleolar genes**. These genes are located along the **nucleolar organizing regions** of five different chromosomes (13, 14, 15, 21, and 22). During active transcription, each nucleolar gene has the appearance of a "lamp brush" as viewed in the EM. Each stand of the "brush" represents a molecule of precursor rRNA at various stages of completion. The completed molecules of precursor rRNA are then cleaved into two smaller pieces, which will be incorporated into the large (60s) and small (40s) ribosomal subunits. The mature rRNA quickly associates with basic protein that enters the nucleus from the cytoplasm and forms ribonucleoprotein particles. These subunits leave the nucleus through the pores and are assembled into ribosomes in the cytoplasm. At the ultrastructural level, the nucleolus displays a characteristic organization:

- **Fibrillar centers**, which represent the nucleolar organizing regions of the chromosomes carrying the nucleolar genes. These centers are surrounded by the
- **Pars fibrosa**, which represents the newly transcribed precursor molecules of rRNA. Outside the pars fibrosa is the
- **Pars granulosa**, which represents the ribonucleoprotein particles after the rRNA has complexed with protein.

The Nuclear Matrix

The nuclear matrix is analogous to the cytoplasmic matrix we discussed earlier. It consists of a protein skeletal framework surrounded by a fluid **nucleoplasm**. The nuclear matrix supports and organizes the nucleus. It is also involved in the regulation of DNA replication and transcription. The main component of the nuclear matrix is the **fibrous lamina**, which is seen attached to the inner surface of the nuclear envelope. It is composed of **lamins** (a type of intermediate filament) and associated proteins. Extending from the fibrous lamina into the interior of the nucleus is a fibro granular network that supports the chromatin and nucleolus.

Nuclear indicators of cell death

Alterations in nuclear morphology are often the best indicators of cell death. There are three types:

- ✓ **Pyknosis**: the nucleus shrinks to a dark-staining homogeneous mass.
- ✓ **Karyorrhexis**: the nucleus fragments.
- ✓ **Karyolysis**: the nucleus dissolves away.