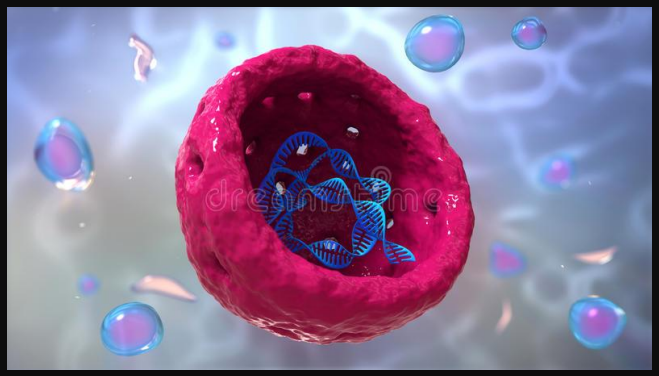

Nucleus

Abstract
Nucleus, nuclear envelope, , nuclear pore complex, nucleolus chromatin: euchromatin and hetrochromatin and packaging (nucleosome)

By –

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Introduction

The nucleus (pl. *nuclei*;from Latin *nucleus* or *nuculeus*,meaning *kernel* or *seed*)is a membrane-bound organelle found in eukaryotic cells. Eukaryotes usually have a single nucleus, but a few cell types, such as mammalian red blood cells, have no nuclei, and a few others including osteoclasts have many.

The cell nucleus contains all of the cell's genome, except for a small fraction of mitochondrial DNA, organized as multiple long linear DNA molecules in a complex with a large variety of proteins, such as histones, to form chromosomes. The genes within these chromosomes are structured in such a way to promote cell function. The nucleus maintains the integrity of genes and controls the activities of the cell by regulating gene expression—the nucleus is, therefore, the control center of the cell.

HISTORY

The nucleus was the first organelle to be discovered. What is most likely the oldest preserved drawing dates back to the early microscopist Antonie van Leeuwenhoek (1632–1723). He observed a "lumen", the nucleus, in the red blood cells of salmon. Unlike mammalian red blood cells, those of other vertebrates still contain nuclei.

The nucleus was also described by Franz Bauer in 1804 and in more detail in 1831 by Scottish botanist Robert Brown in a talk at the Linnea Society of London

STRUCTURE

The nucleus is the largest organelle in animal cells. In mammalian cells, the average diameter of the nucleus is approximately 6 micrometres (μm), which occupies about 10% of the total cell volume. The contents of the nucleus are held in the nucleoplasmsimilar to the cytoplasm in the rest of the cell. The fluid component of this is termed the nucleosol, similar to the cytosol in the cytoplasm.

In most types of granulocyte, a white blood cell, the nucleus is lobated and can be bi-lobed, tri-lobed or multi-lobed.

The nuclear envelope, The nucleus consists of two cellular membranes, an inner and an outer membrane, arranged parallel to one another and separated by 10 to 50 nm. The nuclear envelope completely encloses the nucleus and separates the cell's genetic material from the surrounding cytoplasm, serving as a barrier to prevent macromolecules from diffusing freely between the nucleoplasm and the cytoplasm. The outer nuclear membrane is continuous with the membrane of the rough endoplasmic reticulum (RER), and is similarly studded

with ribosomes. The space between the membranes is called the perinuclear space and is continuous with the RER lumen.

Nuclear pores, which provide aqueous channels through the envelope, are composed of multiple proteins, collectively referred to as nucleoporins. The pores are about 125 million daltons in molecular weight and consist of around 50 (in yeast) to several hundred proteins (in vertebrates). The pores are 100 nm in total diameter; however, the gap through which molecules freely diffuse is only about 9 nm wide, due to the presence of regulatory systems within the center of the pore. This size selectively allows the passage of small water-soluble molecules while preventing larger molecules, such as nucleic acids and larger proteins, from inappropriately entering or exiting the nucleus. These large molecules must be actively transported into the nucleus instead.

The nucleus of a typical mammalian cell will have about 3000 to 4000 pores throughout its envelope, each of which contains an eightfold-symmetric ring-shaped structure at a position where the inner and outer membranes fuse. Attached to the ring is a structure called the *nuclear basket* that extends into the nucleoplasm, and a series of filamentous extensions that reach into the cytoplasm. Both structures serve to mediate binding to nuclear transport proteins.

Most proteins, ribosomal subunits, and some DNAs are transported through the pore complexes in a process mediated by a family of transport factors known as karyopherins. Those karyopherins that mediate movement into the nucleus are also called importins, whereas those that mediate movement out of the nucleus are called exportins. Most karyopherins interact directly with their cargo, although some use adaptor proteins.

Steroid hormones such as cortisol and aldosterone, as well as other small lipid-soluble molecules involved in intercellular signaling, can diffuse through the cell membrane and into the cytoplasm, where they bind nuclear receptor proteins that are trafficked into the nucleus. There they serve as transcription factors when bound to their ligand; in the absence of a ligand, many such receptors function as histone deacetylases that repress gene expression.

Nuclear lamina

In animal cells, two networks of intermediate filaments provide the nucleus with mechanical support: The nuclear lamina forms an organized meshwork on the internal face of the envelope, while less organized support is provided on the cytosolic face of the envelope. Both systems provide structural support for the nuclear envelope and anchoring sites for chromosomes and nuclear pores.

The nuclear lamina is composed mostly of lamin proteins. Like all proteins, lamins are synthesized in the cytoplasm and later transported to the nucleus interior, where they are assembled before being incorporated into the existing network of nuclear lamina. Lamins found on the cytosolic face of the membrane, such as emerin and nesprin, bind to the cytoskeleton to provide structural support. Lamins are also found inside the nucleoplasm where they form another regular structure, known as the **nucleoplasmic veil**, that is visible using fluorescence microscopy. The actual function of the veil is not clear, although it is excluded from the nucleolus and is present during interphase. Lamin structures that make up the veil, such as LEM3, bind chromatin and disrupting their structure inhibits transcription of protein-coding genes.

Like the components of other intermediate filaments, the lamin monomer contains an alpha-helical domain used by two monomers to coil around each other, forming a dimer structure called a coiled coil. Two of these dimer structures then join side by side, in an antiparallel arrangement, to form a tetramer called a *protofilament*. Eight of these protofilaments form a lateral arrangement that is twisted to form a ropelike *filament*. These filaments can be assembled or disassembled in a dynamic manner, meaning that changes in the length of the filament depend on the competing rates of filament addition and removal.

Mutations in lamin genes leading to defects in filament assembly cause a group of rare genetic disorders known as *laminopathies*. The most notable laminopathy is the family of diseases known as progeria, which causes the appearance of premature aging in its sufferers. The exact mechanism by which the associated biochemical changes give rise to the aged phenotype is not well understood.

The nucleolus is the largest of the discrete densely stained, membraneles structures known as nuclear bodies found in the nucleus. It forms around tandem repeats of rDNA, DNA coding for ribosomal RNA (rRNA).

These regions are called nucleolar organizer regions (NOR). The main roles of the nucleolus are to synthesize rRNA and assemble ribosomes.

The structural cohesion of the nucleolus depends on its activity, as ribosomal assembly in the nucleolus results in the transient association of nucleolar components, facilitating further ribosomal assembly, and hence further association. This model is supported by observations that inactivation of rDNA results in intermingling of nucleolar structures.

In the first step of ribosome assembly, a protein called RNA polymerase I transcribes rDNA, which forms a large pre-rRNA precursor.

This is cleaved into the subunits 5.8S, 18S, and 28S rRNA. The transcription, post-transcriptional processing, and assembly of rRNA occurs in the nucleolus, aided by small nucleolar RNA (snoRNA) molecules, some of which are derived from spliced introns from messenger RNAs encoding genes related to ribosomal function.

The assembled ribosomal subunits are the largest structures passed through the nuclear pores.

When observed under the electron microscope, the nucleolus can be seen to consist of three distinguishable regions: the innermost *fibrillar centers* (FCs), surrounded by the *dense fibrillar component* (DFC) (that contains fibrillarin and nucleolin), which in turn is bordered by the *granular component* (GC) (that contains the protein nucleophosmin).

Transcription of the rDNA occurs either in the FC or at the FC-DFC boundary, and, therefore, when rDNA transcription in the cell is increased, more FCs are detected. Most of the cleavage and modification of rRNAs occurs in the DFC, while the latter steps involving protein assembly onto the ribosomal subunits occur in the GC.

Chromosomes

The cell nucleus contains the majority of the cell's genetic material in the form of multiple linear DNA molecules organized into structures called chromosomes. Each human cell contains roughly two meters of DNA. During most of the cell cycle these are organized in a

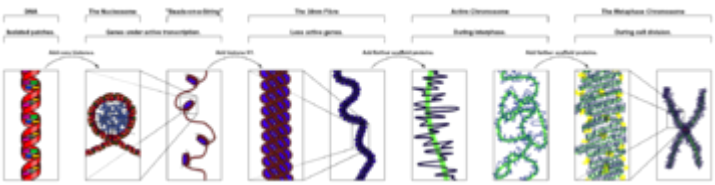
DNA-protein complex known as chromatin, and during cell division the chromatin can be seen to form the well-defined chromosomes familiar from a karyotype. A small fraction of the cell's genes are located instead in the mitochondria.

There are two types of chromatin.

Euchromatin is the less compact DNA form, and contains genes that are frequently expressed by the cell.

The other type, heterochromatin, is the more compact form, and contains DNA that is infrequently transcribed.

Chromatin



DNA-protein complex known as chromatin,.

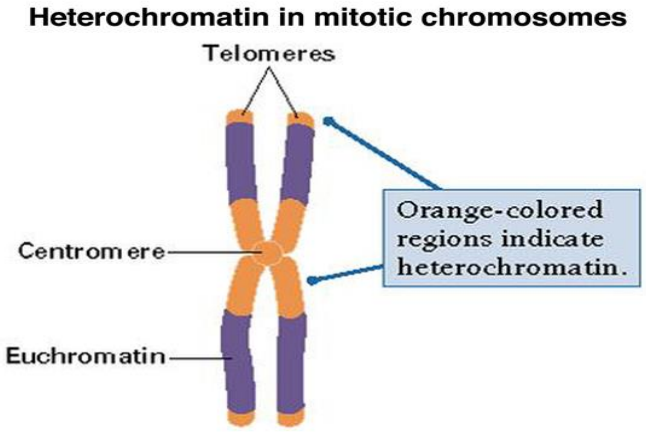
Chromatin is a complex of DNA and protein found in eukaryotic cells. Chromatin is a macromolecular complex of a DNA macromolecule and protein macromolecules (and RNA). The proteins package and arrange the DNA and control its functions within the cell nucleus.

The *DNA* + *histone* = *chromatin* definition: The DNA double helix in the cell nucleus is packaged by special proteins termed histones. The formed protein/DNA complex is called chromatin. The basic structural unit of chromatin is the nucleosome

Its primary function is packaging long DNA molecules into more compact, denser structures. This prevents the strands from becoming tangled and also plays important roles in reinforcing the DNA during cell division, preventing DNA damage, and regulating gene expression and DNA replication.

During mitosis and meiosis, chromatin facilitates proper segregation of the chromosomes in anaphase; the characteristic shapes of chromosomes visible during this stage are the result of DNA being coiled into highly condensed chromatin.

The primary protein components of chromatin are histones, which bind to DNA and function as "anchors" around which the strands are wound. In general, there are three levels of chromatin organization:



1. DNA wraps around histone proteins, forming nucleosomes and the so-called "beads on a string" structure (euchromatin).
2. Multiple histones wrap into a 30-nanometer fibre consisting of nucleosome arrays in their most compact form (heterochromatin).
3. Higher-level DNA supercoiling of the 30-nm fiber produces the metaphase chromosome (during mitosis and meiosis).

Many organisms, however, do not follow this organization scheme. For example, spermatozoa and avian red blood cells have more tightly packed chromatin than most eukaryotic cells, and trypanosomatid protozoa do not condense their chromatin into visible chromosomes at all. Prokaryotic cells have entirely different structures for organizing their DNA (the prokaryotic chromosome equivalent is called a genophore and is localized within the nucleoid region).

The overall structure of the chromatin network further depends on the stage of the cell cycle. During interphase, the chromatin is structurally loose to allow access to RNA and DNA polymerases that transcribe and replicate the DNA.

The local structure of chromatin during interphase depends on the specific genes present in the DNA.

Regions of DNA containing genes which are actively transcribed ("turned on") are less tightly compacted and closely associated with RNA polymerases in a structure known as euchromatin, while regions containing inactive genes ("turned off") are generally more condensed and associated with structural proteins in heterochromatin.

Epigenetic modification of the structural proteins in chromatin
via methylation and acetylationalso alters local chromatin structure and therefore gene expression.

The structure of chromatin networks is currently poorly understood and remains an active area of research in molecular biology.

Chromatin undergoes various structural changes during a cell cycle. Histone proteins are the basic packer and arranger of chromatin and can be modified by various post-translational modifications to alter chromatin packing (Histone modification). Most of the modifications occur on the histone tail. The consequences in terms of chromatin accessibility and compaction depend both on the amino-acid that is modified and the type of modification.

Nucleosomes and beads-on-a-string

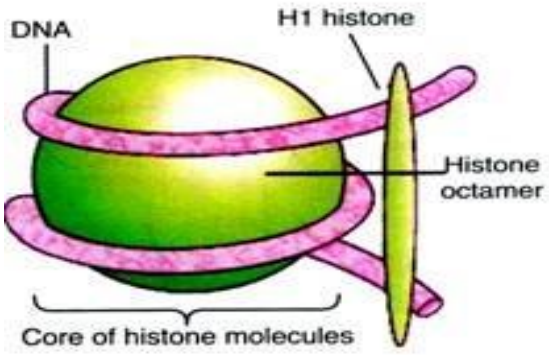


Image 4.4. Nucleosome

A **nucleosome** is the basic structural unit of DNA packaging in eukaryotes. The structure of a nucleosome consists of a segment of DNA wound around eight histone proteins and resembles thread wrapped around a spool. The **nucleosome** is the fundamental subunit of chromatin. Each **nucleosome** is composed of a little less than two turns of DNA wrapped around a set of eight proteins called histones, which are known as a histone octamer.
Each histone octamer is composed of two copies each of the histone proteins H2A, H2B, H3, and H4

The basic repeat element of chromatin is the nucleosome, interconnected by sections of linker DNA, a far shorter arrangement than pure DNA in solution.

In addition to the core histones, there is the linker histone, H1, which contacts the exit/entry of the DNA strand on the nucleosome.

The nucleosome core particle, together with histone H1, is known as a chromatosome.

Nucleosomes, with about 20 to 60 base pairs of linker DNA, can form, under non-physiological conditions, an approximately 10 nm "beads-on-a-string" fibre.

The nucleosomes bind DNA non-specifically, as required by their function in general DNA packaging.

There are, however, large DNA sequence preferences that govern nucleosome positioning.

This is due primarily to the varying physical properties of different DNA sequences: For instance, adenine and thymine are more favorably compressed into the inner minor grooves.

This means nucleosomes can bind preferentially at one position approximately every 10 base pairs (the helical repeat of DNA)- where the DNA is rotated to maximise the number of A and T bases that will lie in the inner minor groove.