The Nucleus, DNA and Chromatin Structure

Size of the human genom:

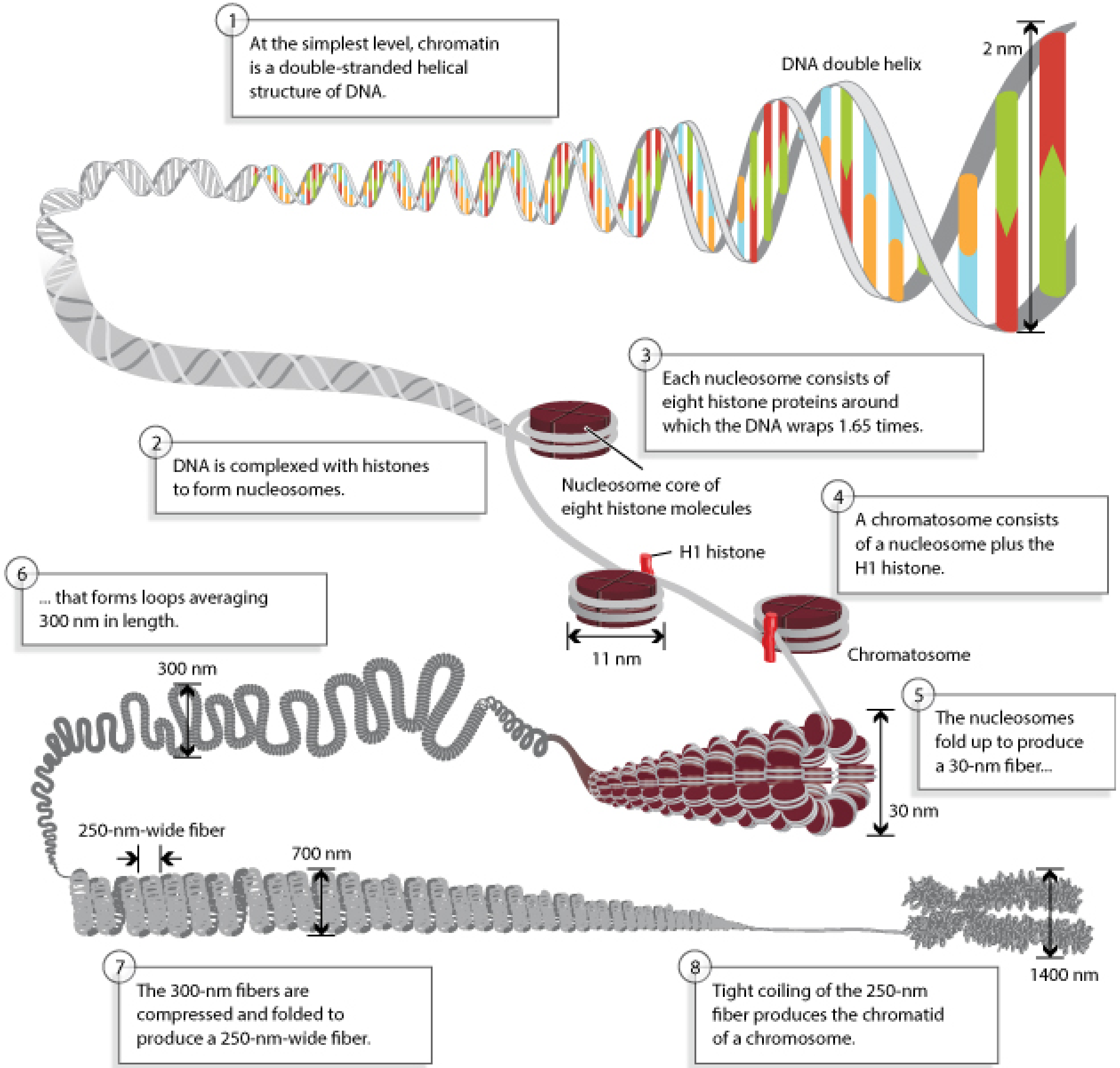
The diploid human genome contains approximately 6 billion base pairs of DNA packaged into 23 chromosome pairs.

Each diploid cell therefore contains about 2 meters of DNA, putting together the DNA of all of our cells we have enough DNA to go from here to the Sun and back more than 300 times.

In condensed form, the DNA winds itself around proteins called histones forming a complex called chromatin.

Chromosomes are composed of DNA tightly-wound around histones.

DNA is packaged with the help of histones, positively-charged proteins. They strongly adhere to negatively-charged DNA and form complexes called nucleosomes. Each nuclesome is composed of a DNA and 8 histone proteins. Nucleosomes fold up to form a 30-nm chromatin fiber. These fibers are compressed and folded to produce a 250 nm-wide fiber, which is tightly coiled into the chromatid of a chromosome.



Chromatin not only serves as a way to condense DNA within the cellular nucleus, but also as a way to control how that DNA is used.

In eukaryotes, genes are not expressed unless they can be accessed by RNA polimerase and transcription factor proteins.

The tight coiling of the chromatin structure limits the access of these substances to eukaryotic DNA. For gene expression the cell's chromatin must "open". This process is called chromatin remodeling.

A nucleosome core particle consists of eight histone proteins (two each of H2A, H2B, H3 and H4) and 146 base pairs of DNA. The original (canonical) histones, however, can be replaced by histone variants or modified by specific enzymes, thereby making the surrounding DNA more or less accessible to the transcriptional machinery.

Histone modification:

Histone modification can open chromatin, thus permitting selective binding of transcription factors that, in turn, recruit RNA polymerase II.

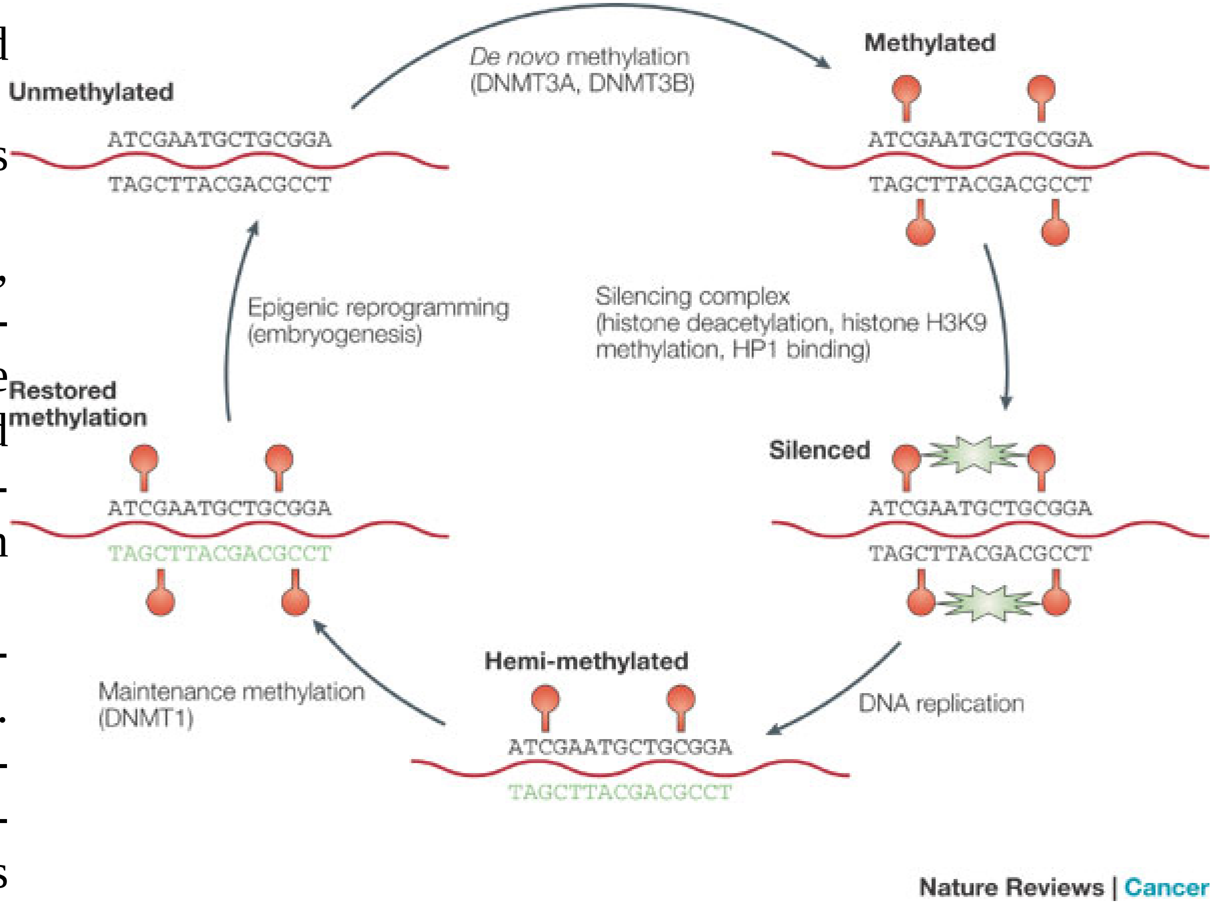
Varying levels and types of histone modifications have been shown to correlate with levels of chromatin activation.

Acetylation of histone H3 and methylation at lysine residue K4 appeared to coincide with each other, and aso with transcriptional activation in chicken embryos.

Methylation at lysine residue K9 marked inactive chromatin.

DNA methylation gene silencing

Transcription is also controlled by the methylation of the DNA strand itself.



In early embryogenesis, DNA is devoid of methylation (top left).
Post implantation, methylation begins (red circles).
When methylation affects CpG islands, methyl-binding proteins trigger a silencing cascade (green stars), histone H3K9 is sequentially deaceylated and then methylated, allowing heterochromatin protein1 (HP1) to bind; resulting in closed chromatin (bottom right).
After DNA replication, newly synthesized DNA (in green) is unmethylated. DNMT1 rapidly scans DNA and deposits methyl groups on newly synthesized DNA, opposite methyl groups present on the old DNA strand resulting the faithful replication of methylation patterns (bottom left) and the maintenance of silencing. Adult patterns of methylation are erased by epigenetic reprogramming in early embryogenesis (top left).

Summary

Chromatin and the DNA sequences it contains are constantly undergoing modifications, thereby periodically exposing different regions of DNA to transcription factors and RNA polymerases.

The cumulative effects of these changes are various states of transcriptional control and the ability of eukaryotic cells to turn genes on and off as needed.

This complexity provides eukaryotes with a means of making the most of a relatively small number of genes.

The Cell Nucleus

It is a highly specialized organelle that serves as the information processing and administrative center of the cell.

It stores the cell's hereditary material, or DNA,

It coordinates the cell's activities: growth, intermediary metabolism, protein synthesis, and reproduction (cell division).

Generally there is only one nucleus per eukaryotic cell;

exceptions: lens cell, red blood cells with no nucleus, paramecyum with 2 nuclei, Siphonales group of algae multinucleated cells.

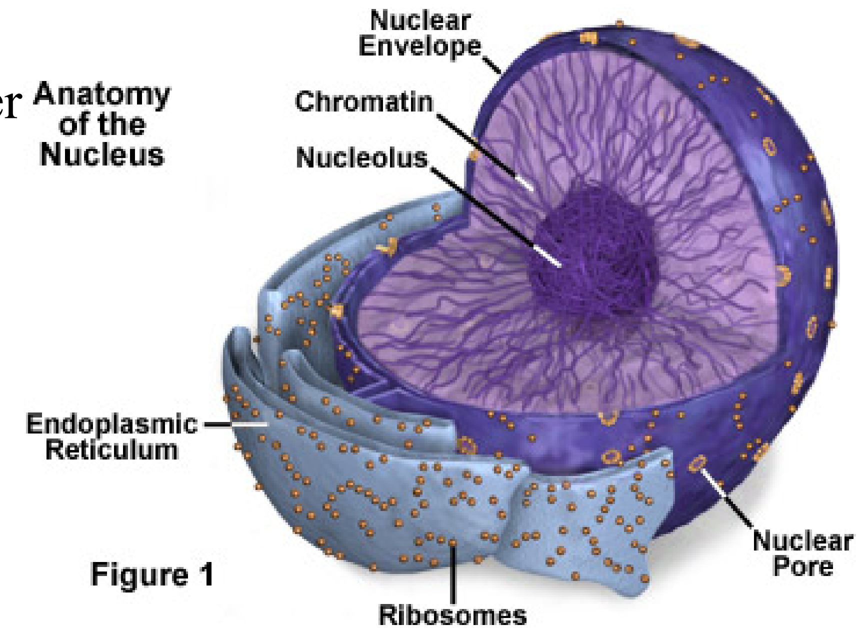


Figure 1

Nuclear envelope:

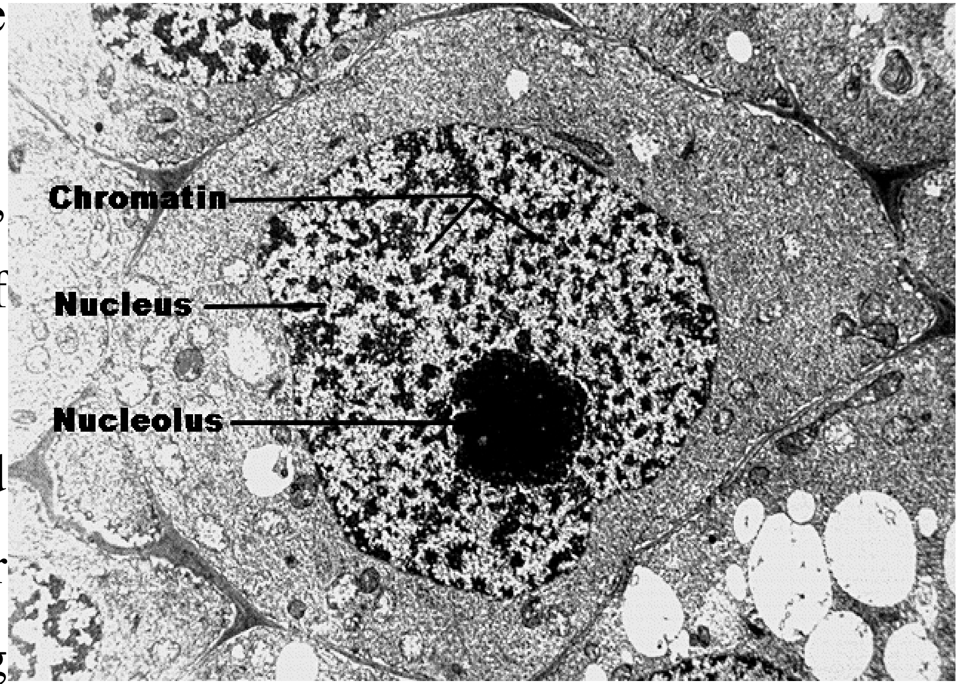
A double-layered membrane, separates the contents of the nucleus from the cellular cytoplasm. It is attached to the rough endoplasmic reticulum, where protein synthesis occurs. The space between the layers is called the perinuclear space and appears to connect with the rough endoplasmic reticulum.

The envelope is perforated with tiny holes called nuclear pores. These pores regulate the passage of molecules between the nucleus and cytoplasm, permitting some to pass through the membrane, but not others. The inner surface has a protein lining called the nuclear lamina, which binds to chromatin and other nuclear components. During mitosis, or cell division, the nuclear envelope disintegrates, but reforms as the two cells complete their formation and the chromatin begins to unravel and disperse.

Inside, within the nucleoplasm, most of the nuclear material consists of chromatin, the less condensed form of the cell's DNA.

Nucleolus:

It is a membrane-less organelle within the nucleus that manufactures ribosomes.



A nucleus may contain up to four nucleoli, but within each species the number of nucleoli is fixed.

After a cell divides, a nucleolus is formed when chromosomes are brought together into nucleolar organizing regions. During cell division, the nucleolus disappears.

Some studies suggest that the nucleolus may be involved with cellular aging and, therefore, may affect the senescence of an organism.