Lecture: 3 Molecular Biology Dr.Sarween

What is chromatin?

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.

Where is the chromatin?

Chromatin is a mass of genetic material composed of DNA and **proteins** that condenses to form chromosomes during **eukaryotic** cell division. Chromatin is located in the **nucleus** of our cells.

The function of chromatin

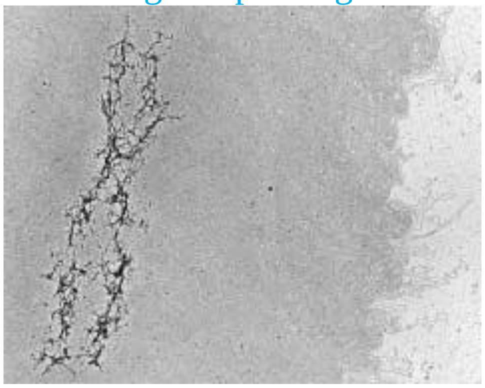
The function of chromatin is to efficiently package DNA into a small volume to fit into the nucleus of a cell and protect the DNA structure and sequence. Packaging DNA into chromatin allows for mitosis and meiosis, prevents chromosome breakage and controls gene expression and DNA replication.

Chromatin Structure

Eukaryotic DNA is closely associated with proteins, creating *chromatin.* The two basic types of chromatin are: **euchromatin,** which undergoes the normal process of condensation and decondensation in the cell cycle, and **heterochromatin,** which remains in a highly condensed state throughout the cell cycle, even during interphase. Euchromatin constitutes the majority of the chromosomal material, whereas heterochromatin is found at the centromeres and telomeres of all chromosomes.

The most abundant proteins in chromatin are the *histones*, which are relatively small, positively charged proteins of five major types: H1, H2A, H2B, H3, and H4. All histones have a high percentage of arginine and lysine, positively charged amino acids that give them a net positive charge. The positive charges attract the negative charges on the phosphates of DNA and holds the DNA in contact with the histones.

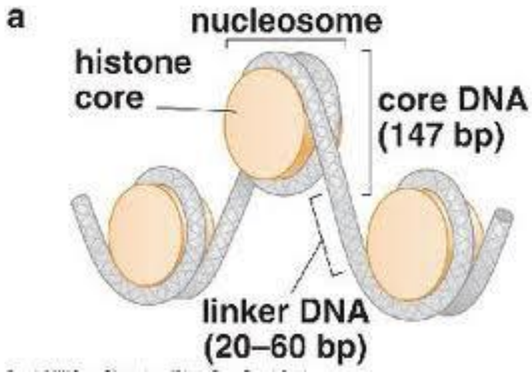
A heterogeneous assortment of **nonhistone chromosomal proteins** make up about half of the protein mass of the chromosome. Chromosomal scaffold proteins are revealed when chromatin is treated with a concentrated salt solution, which removes histones and most other chromosomal proteins, leaving a chromosomal protein “skeleton” to which the DNA is attached. These scaffold proteins may play a role in the folding and packing of the chromosome.



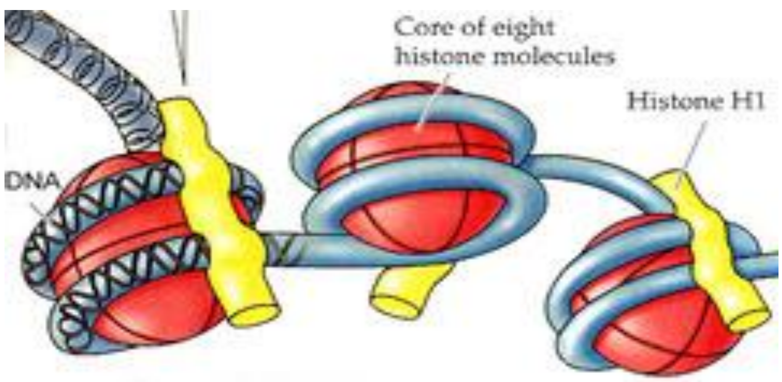
Other types of nonhistone chromosomal proteins play a role in genetic processes. They are components of the replication machinery (DNA polymerases, helicases, primases) and proteins that carry out and regulate transcription (RNA polymerases, transcription factors). **High-mobility-group proteins** are small, highly charged proteins that vary in amount and composition, depending on tissue type and stage of the cell cycle. Several of these proteins may play an important role in altering the packing of chromatin during transcription.

The nucleosome

When chromatin is isolated from the nucleus of a cell and viewed with an electron microscope, it frequently looks like beads on a string If a small amount of nuclease is added to this structure, the enzyme cleaves the string between the beads, leaving individual beads attached to about 200 bp of DNA.If more nuclease is added, the enzyme chews up all of the DNA between the beads and leaves a core of proteins attached to a fragment of DNA.
The repeating core of protein and DNA produced by digestion with nuclease enzymes is the simplest level of chromatin structure, the **nucleosome**. The nucleosome is a core particle consisting of DNA wrapped about two times around an octamer of eight histone proteins (two copies each of H2A, H2B, H3, and H4), much like thread wound around a spool. The DNA in direct contact with the histone octamer is between 145 and 147 bp in length, coils around the histones .



The fifth type of histone, H1, is not a part of the core particle but plays an important role in the nucleosome structure.Regardless of its position, H1 helps to lock the DNA into place, acting as a clamp around the nucleosome octamer.
Together, the core particle and its associated H1 histone are called the **chromatosome,** the next level of chromatin organization. The H1 protein is attached to between 20 and 22 bp of DNA, and the nucleosome encompasses an additional 145 to 147 bp of DNA; so about 167 bp of DNA are held within the chromatosome. Chromatosomes are located at regular intervals along the DNA molecule and are separated from one another by **linker DNA,** which varies in size among cell types—most cells have from about 30 bp to 40 bp of linker DNA. Nonhistone chromosomal proteins may be associated with this linker DNA, and a few also appear to bind directly to the core particle.



Higher-order chromatin structure

In chromosomes, adjacent nucleosomes are not separated by space equal to the length of the linker DNA; rather, nucleosomes fold on themselves to form a dense, tightly packed structure. This structure is revealed when nuclei are gently broken open and their contents are examined with the use of an electron microscope; much of the chromatin that spills out appears as a fiber with a diameter of about 30 nm. The next-higher level of chromatin structure is a series of loops of 30-nm fibers, each anchored at its base by proteins in the nuclear scaffold. On average,each loop encompasses some 20,000 to 100,000 bp of DNA and is about 300 nm in length, but the individual loops vary considerably. The 300-nm fibers are packed and folded to produce a 250-nm-wide fiber. Tight helical coiling of the 250-nm fiber, in turn, produces the structure that appears in metaphase: an individual chromatid approximately 700 nm in width.