Zoo-342 Molecular biology
Lecture 3

The eukaryotic chromosome and chromatin organization

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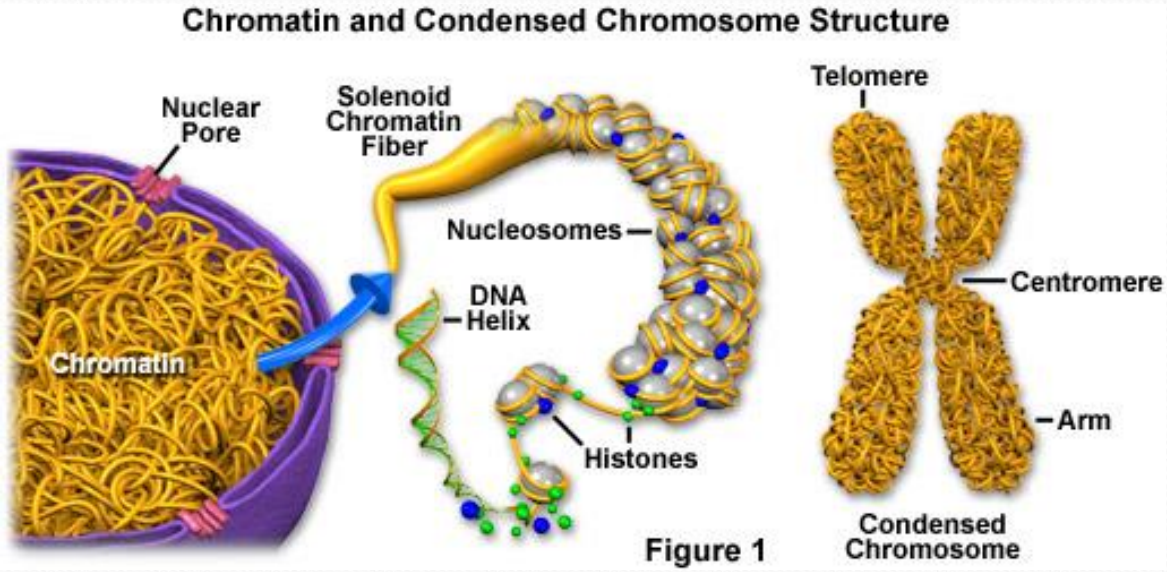

The eukaryotic chromosome:

- The eukaryotic chromosome is composed of both **double-stranded DNA** and **proteins**. The combination of DNA and protein is called **chromatin**.
- Two types of chromatins are formed:

1) Euchromatin: loosely packaged (less condensed), can be transcribed.

2) Heterochromatin: tightly packaged (highly condensed), not transcribed.

Chromatin organization:

- The total extended length of DNA in a single human cell would be nearly 2 m long if stretched from end to end.
- The problem is how to package this DNA inside the nucleus, which is only 2-4 µm (10^{-6} m) in diameter. Therefore, the primary function of chromatin is to package DNA into a smaller volume to fit in the cell.
- The basic structural unit of chromatin is the **nucleosome**.
- Nucleosomes consist of DNA wrapped around the protein core, which is composed of histone protein.
- The nucleosomes can be observed by placing interphase nuclei in a **hypotonic**, which releases the higher order packaging of the chromosomes.
- The major proteins of chromatin are the histones, basic amino acid (arginine and lysine) that facilitate binding to the negatively charged DNA molecule.

- There are five major types of histones called H1, H2A, H2B, H3 and H4 (Table 1).
- The structure of nucleosomes have been studied by treating chromatin with **DNase**, large amount of DNA are degraded, leaving only small particles composed of **DNA and proteins**.
- The DNA in these small DNA-protein complexes consists of fragments of about 210 bp (Figure 1). This DNA is protected from DNase digestion **due to its tight association with the proteins.**
- **Treatment** of the 210-bp DNA-protein complex with **micrococcal nuclease** removes additional DNA. At this point, **the protected DNA is 165 bp** in length.
- Harsh micrococcal nuclease treatment of these smaller DNA-protein complex releases of the basic **H1 histone** protein, and the DNA is digested down to a final size of approximately **145 bp** (Figure 1).
- The protein part of the core consisted of two molecules of each of four different histones: H2A, H2B, H3 and H4.

Class	Amino Acids	Number of Amino Acids	Percentage of Basic Amino Acids
H1	Very lysine-rich	213	30
H2A	Lysine-, arginine-rich	129	23
H2B	Moderately lysine-rich	125	24
H3	Arginine-rich	135	24
H4	Arginine-, glycine-rich	102	27

Table 1: Types and composition of histones

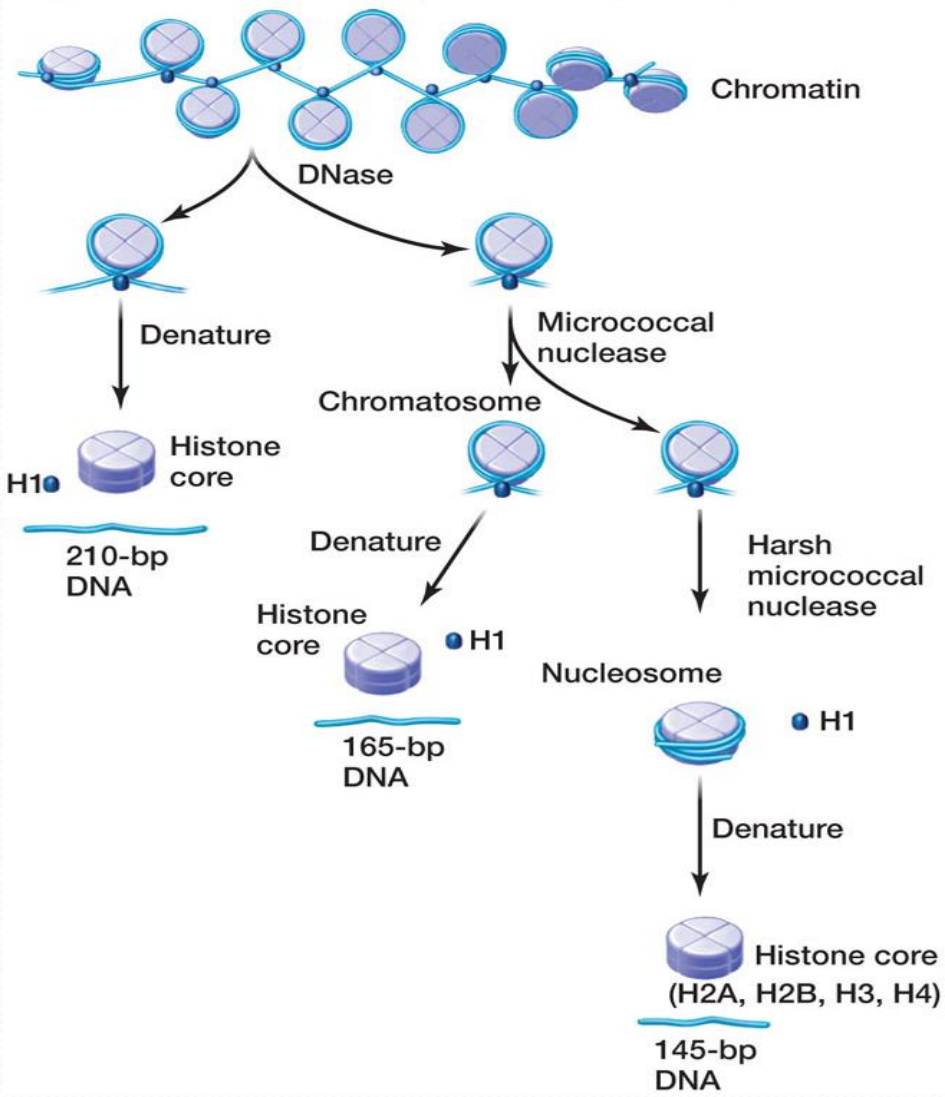

Figure 1: Studying the structure and composition of chromatin

- These data allow us to build a model for the organization of the nucleosome. Approximately 145 bp of genomic DNA is associated with the octamer of four histone proteins (8 proteins).
- The DNA located between the nucleosomes, which amounts to approximately 55-75 bp depending on the species, is termed the **linker DNA** (Figure 2).
- The **H1 histone** interacts with the nucleosome and some of the linker DNA as it enters and exits the nucleosome, which implies that it may serve to cross-link nucleosomes.
- The term **chromatosome** is defined as the core nucleosome plus the **H1** protein, a unit that includes approximately 165 bp of DNA.

- The binding of the histone core by the DNA is a major factor in controlling gene expression.
- The histones and nucleosome can be altered to regulate transcription in two major ways.

1) Some histone proteins can be modified in particular, **phosphate groups**, **methyl groups**, and **acetyl groups** added and removed from specific amino acids in the H3 and H4 histone proteins. These modifications can lead to enhanced or repressed transcription.
2) Histone cores can be removed from the DNA or moved to a different location on the DNA.

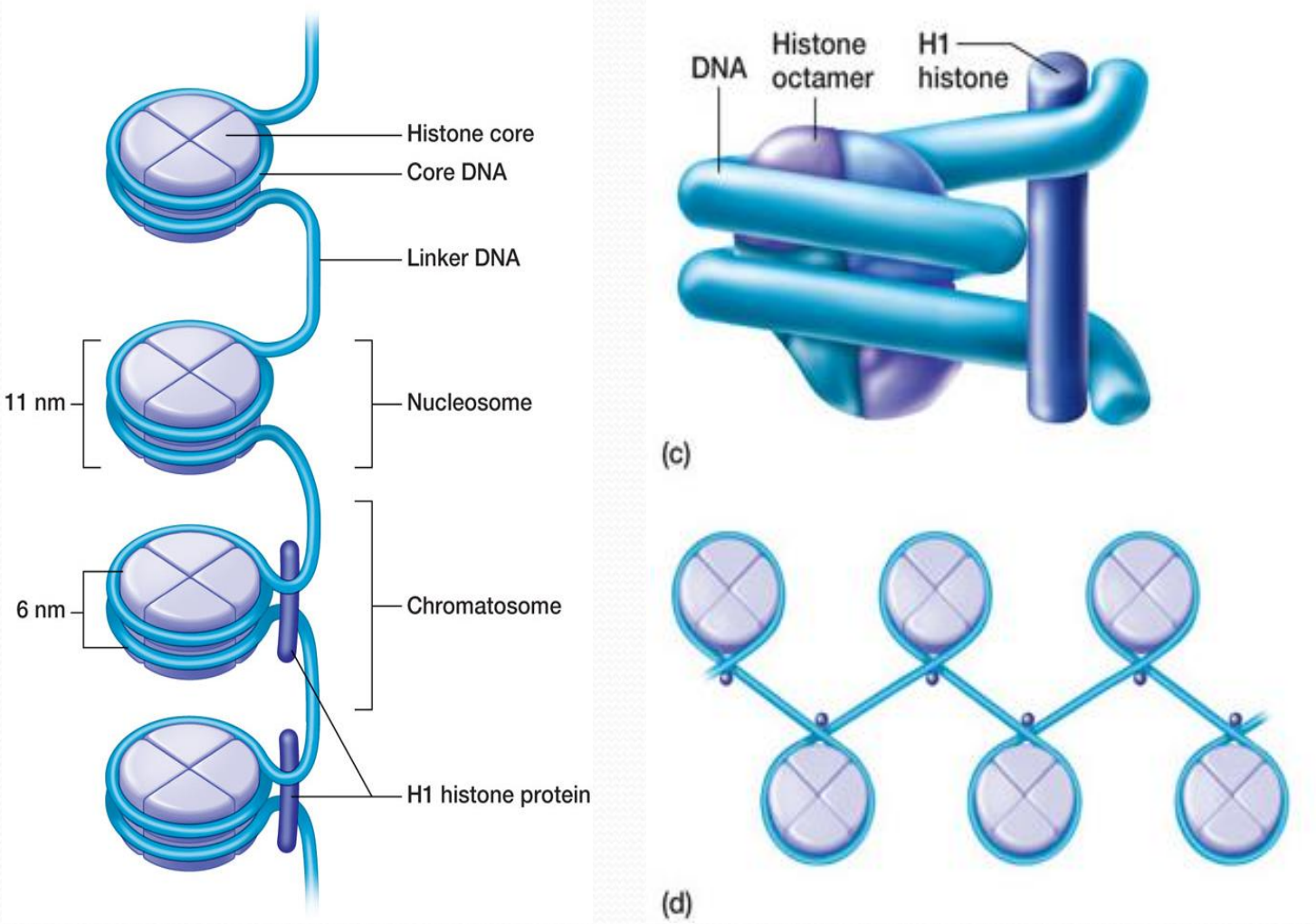

Figure 2: The eukaryotic chromosome is associated with histone proteins to forms nucleosome.