

Chromatin: The long fine thread like filamentous structures of DNA-histone proteins complexes present in the nucleoplasm are known as chromatin fibres. During cell division, these fibres become thick, short thread like structures known as chromosomes.

## MOLECULAR ORGANIZATION OF CHROMATIN

→ Histone -  $H_1, H_2A, H_2B, H_3, H_4$

→ Lysine and Arginine

→ Histone octamer + 146bp = Nucleosome

→ Linker DNA

→ 30nm fibre (Solenoid fibre)

→ Nuclease enzyme breaks DNA.

\* Less condensed form of chromosomes is chromatin.

\* Condensed form of chromosomes

During interphase of dividing cells and  $G_0$  of non-dividing cells, DNA exists as a nucleoprotein complex called chromatin. Chromatin during M phase, is converted into a more condensed form termed as chromosomes. Each chromosome consists of a single, linearly long linear DNA molecule associated with proteins that fold and pack the fine DNA thread into a more compact structure.

The proteins that bind the DNA to form eukaryotic chromosomes are traditionally divided into two general classes: - 1. The histones 2. Non-histone chromosomal proteins. Histones are basic proteins and classified into two categories - Replication Dependent and Replication Independent histones.  $H_1, H_2A, H_2B, H_3, H_4$  are common replication dependent histones.

Histones are responsible for the first and most basic level of chromosome organization, the nucleosome. The nucleosome contains a histone octamer that consists of two copies <sup>each</sup> of  $H_2A, H_2B, H_3, H_4$ . These are known as the core histones, which are rich in lysine and arginine (two amino acids with

basic side chains), and their positive charges can effectively neutralize the negatively charged DNA backbone. These eight proteins form a barrel shaped core octamer with the DNA wound around the outside. Nucleosomes provide the first level of DNA packing and gives beads-on-a-string structure. Treatment with micrococcal nuclease initially cleaves the DNA between nucleosomes and produces mononucleosomes. On further digestion Mononucleosomes typically have approximately 220 nbp DNA. On further digestion, the length of DNA has been reduced to approximately 165 nbp and finally to the length of the DNA of the core particle, 147 nbp. Each nucleosome is separated by 50-70 bp of linker DNA giving the repeat length of 190-200 nbp.  $H_1$ , termed linker histone is associated with linker DNA and may lie at the point where DNA enters and leaves the nucleosome.

30nm fibre: The second level of organisation is the coiling of the series of nucleosomes into a helical array to constitute the fibre of diameter approximately 30nm. It has approximately 6 nucleosomes for every turn. The exact way in which nucleosomes associate to form the 30nm fibre is not known, but several models have been proposed, the most popular being the Solenoid structure. The 30nm and 11nm fibres can be reversibly converted by changing the ionic strength. This suggests that the linear array of nucleosomes in the 11nm fibres is coiled into the 30nm structure at higher ionic strength and in the presence of  $H_1$ .

Metaphase Chromosomes: The 30nm fibre is probably the major type of chromatin in the nucleus during interphase. When the nucleus divides, the DNA adopts a more compact form of packaging, resulting in the highly condensed metaphase chromosomes. The DNA in a metaphase chromosome is compacted to about  $1/50,000$  of its stretched out length. Loops of the

30 nm chromatin fibre, containing 20-100 kb. of DNA per loop are attached to a central scaffold. This consists of non-histone acidic proteins namely topoisomerase I. Besides histones and topoisomerase, structural

Maintenance of Chromosome (SMC) proteins: maintained the condensed chromosome structure. Eukaryotes have two major SMC proteins — Cohesins and Condensins.