# The Human Chromosome

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Chromosomes are thread like structures, which are located in the cell nucleus. The word chromosome is derived from Greek, chroma (= color) and soma (= body). They are quite literally the vehicles which facilitate reproduction and maintenance of species.

- Most of our knowledge of chromosome structure has been gained using light microscopy. Special stains selectively taken by DNA have enabled each individual chromosome to be identified .These are best seen during cell division when the chromosomes are maximally contracted and the constituent genes can no longer be transcribed.
- Each chromosome contains a single molecule of DNA organized into several orders of packaging to construct a metaphase chromosome, DNA in chromosomes is associated with DNA binding proteins .The DNA protein complex is called chromatin. Proteins in DNA may mediate gene transcription or DNA replication or be the structural proteins that organize the DNA.
- Histones are the structural proteins of chromatin and are the most abundant proteins in the nucleus
- The nucleosome which is the fundamental protein packaging unit consists of tightly bound package of eight histones with a DNA helix wound twice around the surface.
- Each nucleosome core binds 146 basepairs of DNA helix and the cores are linked together by about 60 bases into a bead like structure.
- The width of the nucleosome package is 11 nanometers compared to 2nmfor DNA double helix.
- Nucleosomes are packed tightly together with the aid of histone H1 to form a 30nm wide fiber which is the basic chromatin unit seen in interphase nuclei when using electron microscopy ,the 30nm fiber is further packed into a system of looped domains.

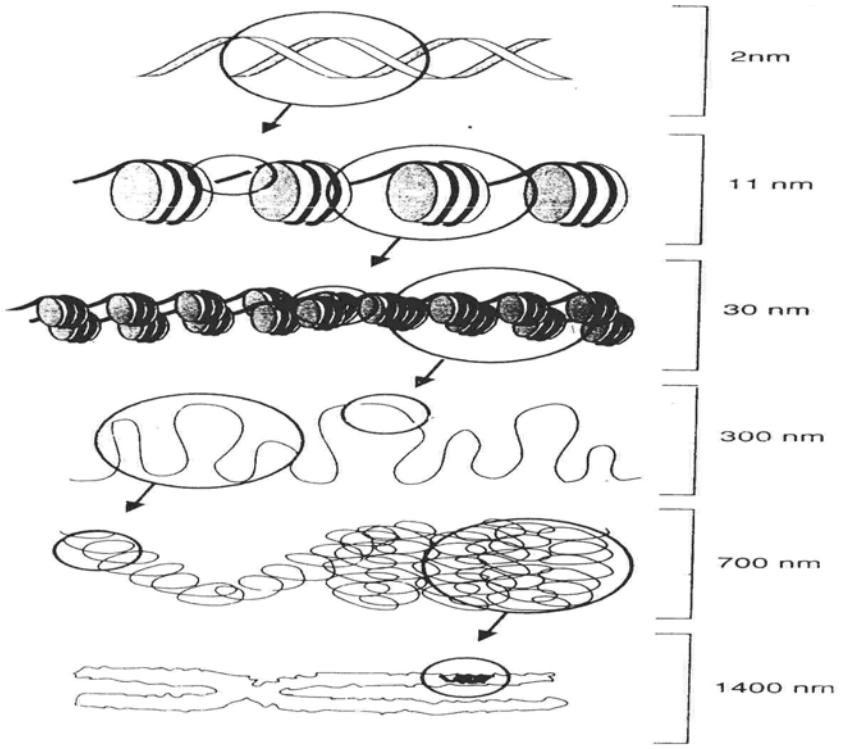


**Figure 1.** Packing of DNA inside nucleosomes.

- The metaphase chromosome (The active chromosome) is formed by a condensation process occurring during the prophase of mitosis through coiling and compaction of the looped domain structure. In this condensed state the loops are held together by protein interactions forming a network that is held in a helical fashion along the axis of the chromosome.
- During the prophase and the metaphase, the chromosomes exhibit alternating dark and light bands under appropriate staining conditions .These bands reflect the differential folding of clusters of looped domains and also define regions of the genome that have different properties and functions.

## The special features of the chromosomes

The chromatin is the name given to the material of which the chromosomes are made i.e. a combination of DNA and histone proteins. Each chromatin stains lightly and is believed to contain genes which are actively expressed .The chromosome bands define alternating partitions of euchromatin with differing properties.

### *R bands*

Are areas that stain light and they contain the highest gene density.

### *G bands*

Are areas that stain dark and contain relatively fewer genes than R bands.

### *The centromere*

Appears as a constricted area of the metaphase chromosome. It consists of specific DNA sequences that bind proteins which can be identified by their antigenic properties .They are known to be responsible for the movement of the chromosome at cell division .The centromere divides the chromosome into short and long arms designated P for (petit) and G for (grand ) respectively.

### *Telomeres*

These are DNA sequences found at the ends of chromosomes, which are required to maintain chromosome stability .Chromosomes without telomeres tend to recombine with other chromatin segments and are generally subject to breakage ,fusion and eventual loss .They consist of similar DNA sequence (TTAGGG) which is tandemly repeated in several thousand copies.

### *Satellites*

They are small segments of heterochromatin at the tip of the short arm (P arm) of the acrocentric chromosomes number 13, 14,15,21,22.

## The classification of normal chromosomes

- This is based on the international system for human cytogeneic nomenclature (ISCN).The normal human karyotype consists of 23 pairs of chromosomes :22 homologous pairs of autosome , and one pair of X chromosomes(XX or XY).The autosomes by convention are divided into seven groups arranged by size and position of the centromere.
- The metaphase chromosomes are divided longitudinally into two sister chromatids held together at the centromere which delineates the chromosome into a short arm (p) and a long arm (g).
- The position of the centromere is used in the morphologic description of the chromosomes e.g. Metacentric chromosomes have central centromeres. Submetacentric and acrocentric chromosomes have slightly or markedly shifted centromeres to one end.
- Each chromosome has alternating dark and light bands .These bands are numbered started from the centromere progressing to the telomere. High resolution banding resolves bands to sub bands. These are numbered as a subset e.g.18q22.1, 18q22.2; 18q22.3.These bands have constant morphology between members of a homologous pair of chromosomes and between normal individuals. A change in their morphology is usually associated with abnormal clinical presentation.

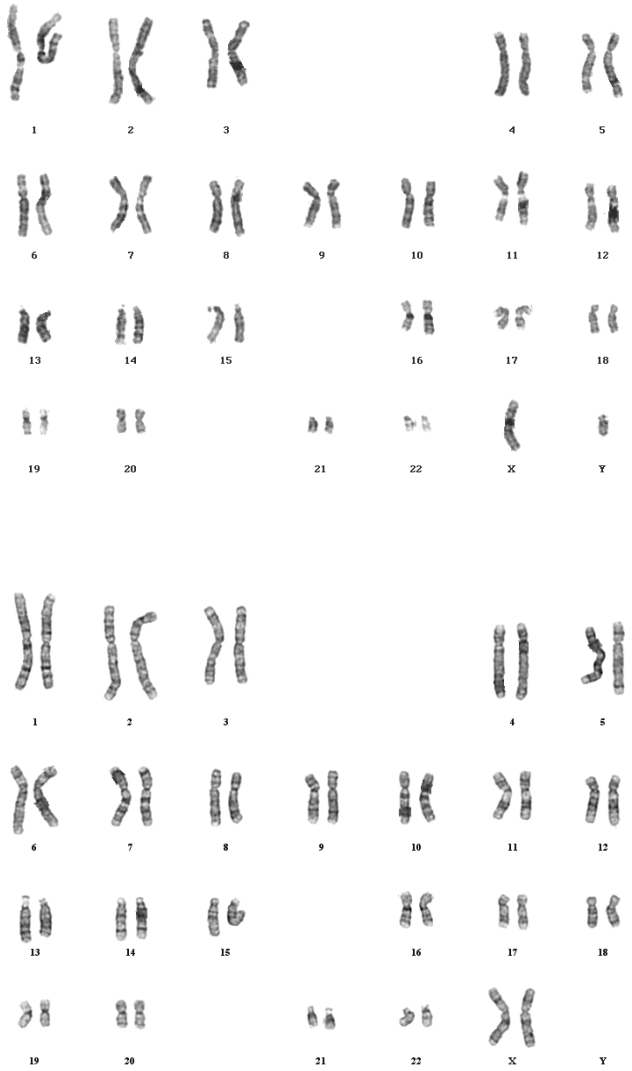


**Figure 2.** The Classification of normal chromosomes (2a. normal male and 2b. normal female).
*Courtsey of Prof. Mohamad El-Sawy.*

## Chromosomal abnormalities

1. **Triploidy:** three copies of all chromosomes.
2. **Monosomy: Autosomal:** single copy of one autosome.
   **Sex chromosome:** single sex chromosome.
3. **Trisomy: Autosomal:** three copies of an autosome.
   **Sex chromosome:** extra sex chromosome.
4. **Deletion: Autosomal:** partial Monosomy of one autosome.
   **X chromosome:** partial Monosomy of an X chromosome.
5. **Duplication: Autosomal:** partial trisomy.

## Suggested Readings

1. Watson J, Alberts B, Bray D, et al. Molecular Biology of the cell. New York: Garland Publishers, 1994.
2. Darnell J, Lodish H, Baltimore D. Molecular Cell Biology, 3rd edn. New York: Scientific American Books, 1995.