Nucleosome ,chromatin and karyotyping

Chromatin is specific to eukaryotic chromosomes, formed by DNA and histone proteins in. Its primary functions include packaging DNA to fit within the cell nucleus, protecting the DNA from damage, and facilitating essential cellular processes such as cell division and DNA replication. Additionally, chromatin plays a vital role in controlling gene expression.

Structure of Chromatin (DNA + 4 HISONE protein)

- Nucleosomes is the fundamental units of chromatin. Each nucleosome consists of:
- Histone Dimers: The histone proteins in nucleosomes are arranged in pairs, known as Dimers: The two types of dimers are: H2A-H2B dimers and H3-H4 dimers these together form the octameric core, around which the DNA is wrapped. About 147 base pairs of DNA that are wrapped around the histone octamer. The DNA wraps around the histones in approximately 1.6 turns.

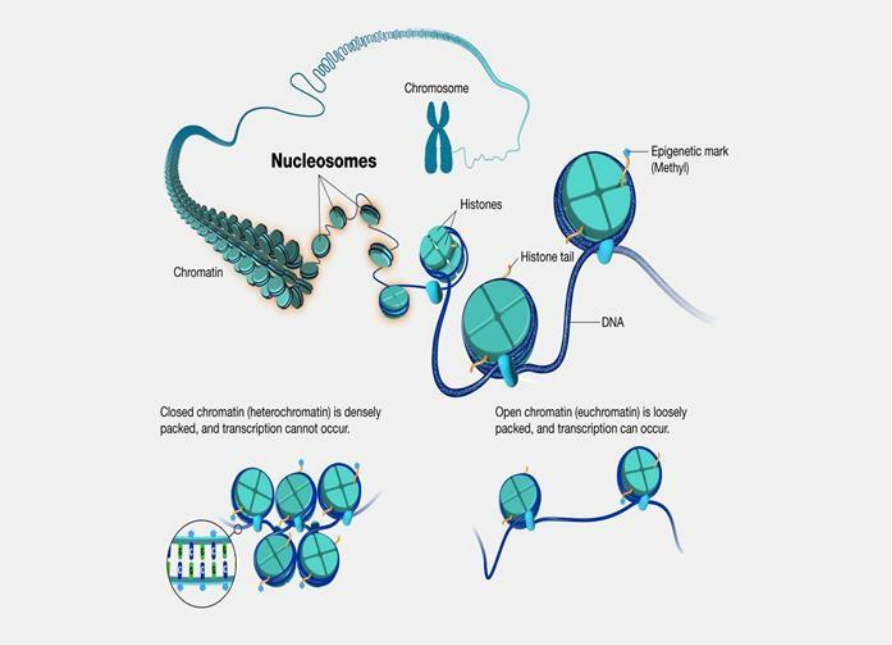

Figure (1) chromatin and nucleosome

- ❖ There are 3 levels of chromatin organization depends on the stage of the cell cycle.
  - During interphase : Euchromatin, Heterochromatin
  - During cell division : higher-level DNA packaging.

A. During Interphase: - Chromatin is loosely packed to allow access for RNA and DNA polymerases to transcribe and replicate DNA. Chromatin during interphase is visible as euchromatin and heterochromatin that depending on the activity of the genes present on the DNA:

- Euchromatin contain active genes that are loosely packaged and associated with RNA polymerases.
- Heterochromatin: Contains inactive genes that are more tightly packaged with structural proteins.

Euchromatin:	Heterochromatin
1- Under an electron microscope appears as a light-staining area.	1. Under an electron microscope appears as a dark-staining area.
2. The less coiled part of chromosomes.	2.highly condensed part of chromosome
3. Metabolically active it contain active genes	3.Metabolically inactive it contain inactive genes
4. **acetylated DNA**	4. methylated DNA
5. ONE type	5. two types constitutive and facultative

Figure (2) comparison between heterochromatin and euchromatin .

B. **During cell division**: The Higher-level DNA packaging represents the most compact form of DNA packaging and it occurs mainly during the metaphase of cell division to form chromosomes (metaphase chromosome).

❖ **Sex chromatin or Barr body:**

✓ In females, one of two X chromosome is highly condensed and forms a Barr body (or sex chromatin), visible in the interphase nucleus as a tightly coiled mass about 1µm in diameter. The other X chromosome remains uncoiled and is not visible. The Barr body is genetically inactive and can be easily stained for observation under a light microscope.

✓ Barr bodies in squamous epithelial cells of the buccal cavity are visible as small granules attached to the nuclear envelope

✓ Barr bodies in blood smears, can appear as a drumstick-like appendage attached to the nuclei of neutrophil leukocytes.

➢ The study of sex chromatin is important in medicine for determining genetic sex in ambiguous cases, such as in hermaphroditism. sex chromatin is essential for identifying chromosomal anomalies like:

- Klinefelter's syndrome (XXY) : Male phenotype
- Turner's syndrome (XO): Female phenotype

✓ Males have 22 pairs of autosomes and 1 pair of sex chromosomes (X and Y). The X chromosome is uncoiled, *so no Barr body is present in normal male somatic cells.*

❖ Karyotyping is the process of organizing and pairing all the chromosomes in an organism to create a complete picture of its genome. This involves using specific staining techniques that highlight the unique features of each chromosome, making them easier to identify.

➢ Karyotypes are used in medical genetics to diagnose birth defects, genetic disorders, and cancers. So Clinical cytogeneticists analyze human karyotypes for three main reasons:

1. To identify large genetic abnormalities in DNA.
2. to Check Chromosome Numbers, Karyotypes help find conditions like aneuploidy, such as Down syndrome.
3. To look for subtle changes like deletions, duplications, translocations, or inversions.

❖ *Preparing Karyotypes from Mitotic Cells*

Karyotypes are made from mitotic cells during the metaphase stage of the cell cycle, when chromosomes are most condensed.

Different tissue types can provide these cells:

1. Tumor biopsies or bone marrow samples for cancer diagnoses
2. Amniotic fluid or chorionic villus samples for prenatal diagnoses
3. Peripheral blood or a skin biopsy for other diagnoses.

❖ ***Steps to Generate a Karyotype:***

1. Cell Culture: Cells from the specimen are cultured for a short time to allow growth.
2. Colchicine is added to stop the cells at metaphase by disrupting the mitotic spindle.
3. The cells are treated with a hypotonic solution to make their nuclei swell and burst.
4. The nuclei are fixed with a chemical, placed on a glass slide, and stained to reveal structural features of the chromosomes.

This process allows for the analysis of chromosomes for abnormalities.

❖ *Organizing Chromosomes in Karyograms According to international conventions*

1. Human autosomes, or non-sex chromosomes, are numbered from 1 to 22, in descending order by size, with the exceptions of chromosomes 21 and 22, the former actually being the smallest autosome.
2. The sex chromosomes are generally placed at the end of a karyogram.
3. Within a karyogram, chromosomes are aligned along a horizontal axis shared by their centromeres.
4. Individual chromosomes are always depicted with their short p arms at the top, and their long q arms at the bottom.

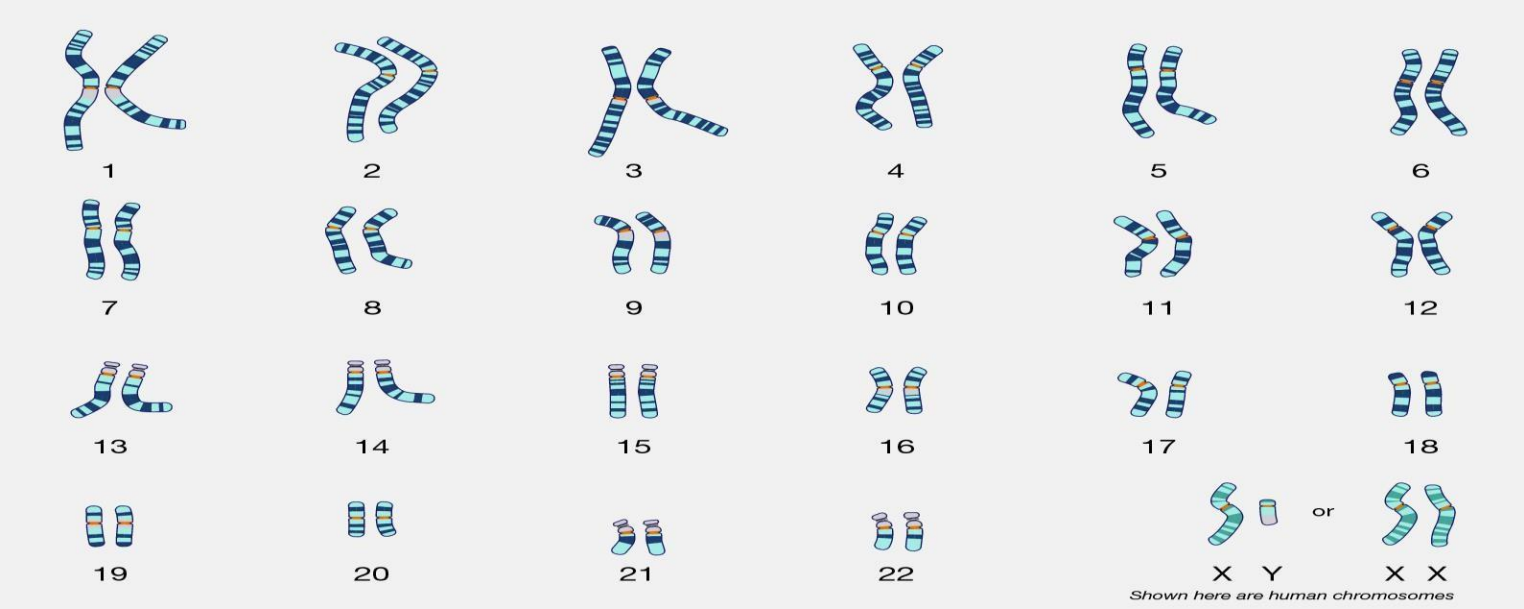

Figure (3) karyogram and banding