Heterochromatin, Types organisation formation and Significance

Heterochromatin - It is a form of chromatin that is densely packed and is found in the nucleus of Eukaryotic cells.

Heterochromatin is a condensed structure and it does not enable DNA and RNA polymerase to access the DNA, thus prevents DNA replication and transcription. The amount of Heterochromatin is about 10% of the human chromosome while the 90% part accounts for Euchromatin which is loosely packed part of chromatin allowing the DNA to be replicated and transcribed.

Structure of Heterochromatin -

The DNA of eukaryotes is ~~formed~~ forms the chromatin, which is a complex formed of DNA and proteins. The proteins found in DNA are called histones, around which DNA is wrapped. Specifically the DNA (200 base pairs) is coiled around sets of eight histones (Octamer) comprising two copies of each of the following H_2A, H_2B, H_3 and H_4. These units made of histone and DNA coiled around them are called nucleosomes. Nucleosomes in turn connects to one another through DNA strings called linker DNA

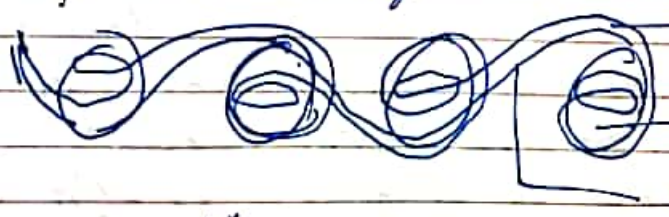

fig showing arrangement of DNA in a nucleosome

Euchromatin → The most loosely packed chromatin is called Euchromatin, also known as beads on a string because it resembles like a beads (nucleosome) and string (DNA)

Heterochromatin is a more tightly condensed form of euchromatin and is also known as 30 nm fibre because the diameter is about 30 nm Euchromatin are faintly stained by G-Stain (Giemsa) while the heterochromatin is darkly stained part of chromatin. In Metaphase stage of cell division it is highly condensed and active.

The DNA of the heterochromatin is not actively replicated or transcribed as DNA is not exposed and therefore the regulatory proteins and polymerase cannot reach it. while the linker DNA in the Euchromatin is exposed and accessible to Polymerases and other proteins in order to be replicated and transcribed, the DNA in the heterochromatic conformation is tightly coiled around the nucleosome and does not allow access to transcriptional elements.

Types of Heterochromatin — There are two types of heterochromatin

1. Constitutive
2. Facultative

Constitutive heterochromatin is a stable form of heterochromatin, it does not loosen up to form euchromatin, and contains repeated sequence of DNA called Satellite DNA, it can be found in centromeres and telomeres, and is usually involved in structural functions.

Faultative heterochromatin, is reversible its structure can change depending on the cell cycle and is characterized by another kind of repeated DNA sequences known as Line sequences. An example of faultative heterochromatin is that it changes its structural conformation with the cell cycle is the inactivated X chromosome (Barr bodies) of females.

Function of Heterochromatin

Heterochromatin has been associated with several functions, from gene regulation to the protection of chromosome integrity some of the important functions are -

(1) protection of naked double stranded DNA ends that would damage leading to cell cycle arrest, DNA repair of ~~Of~~ or destruction of the fragment by endonucleases in bacterial cell.

(2) Heterochromatin helps in epigenetic inheritance since when a cell divides the two daughter cells contain heterochromatin within the same region of DNA.

(3) It helps in variation since a part of heterochromatin looses or encroaches the adjacent genes or needs genes from the extremes eg chromatin domains.

(4) Transcriable material of Euchromatin may be repressed by possition effect and can give rise to gene expression varying from cell to cell.

Centric heterochromatin –

Centric heterochromatin is a tightly packed form of DNA that makes the active centromeres in most of the higher organisms, the centromere is present in both mitotic and interphase chromosomes centric heterochromatin is usually formed on alpha satellite DNA in humans, centric heterochromatin domains are flanked by pericentric heterochromatin.

Diagram Showing centric heterochromatin

Telomeric Heterochromatin → Telomeres are nucleoprotein structures that protects the ends of linear chromosomes and from being detected as double strand DNA breaks these chromosome ends are made up of telomeric repeats (GGGTTT/CA) organised in tandem, followed by an array of non coding DNA elements also the sub telomeric regions, these telomere associated sequences (TAS) are species specific and consist of a coding and a non coding regions the non coding region of telomeric heterochromatin is composed of six different blocks of repetitive sequences located between the telomere and the coding regions.

Organisation of heterochromatin – The formation and maintenance of heterochromatin depends upon chromosomal localization nuclear localization and the presence and density of repeated DNA elements. Chromosomal regions that contain a high density of repeated DNA elements organized in clusters such as telomeres and centromeres are the primary targets for the formation of heterochromatin. These regions remain condensed throughout the cell cycle and are known as constitutive heterochromatin and HC found at loci interspersed with euchromatin containing promoter regions are called facultative heterochromatin

It has been suggested that histones and their modification play an important role in assembly of heterochromatin. The increase in the acetylation or methylation of specific histone proteins (eg H_3K_9ac, H_3K_4me and $H_3K_{36}me$) invariably correlates with transcriptional activity, a decrease in acetylation is correlated with suppressed transcriptional state.

Therefore heterochromatin is associated with histone hypoacetylation, the methylation of H_3K_9 or H_4K_{20} and ~~Sumoylation~~ Sumoylation of the four histones are the characteristic heterochromatin markers.

Methylation of specific lysine residues in the amino acid terminal ends of core histones is critical for establishment maintenance and slicing of chromatin domains in chromosome centromeric and telomeric regions.

Significance of heterochromatin —

Heterochromatin has been associated with several functions -

(1) Gene regulation
(2) Protection of chromosomal integrity
(3) It helps in speciation.
(4) Protection of centromere and telomere.
(5) It helps an important role in chromosome ~~segg~~ Segregation during cell division.
(6) Rapid change in heterochromatin helps in isolation of populations by various mechanisms.

Difference between Heterochromatin and Euchromatin.

1) Tightly packed form of DNA called heterochromatin	loosely packed form of DNA called Euchromatin.
2) High DNA density	Low DNA density
3) Darkly stained	lightly stained
4) Found at the periphery of nucleus in Eukaryotic cells	Found in the inner body of the nucleus of prokaryotic as well as Eukaryotic cells
5) No transcriptional activity	Actively participate in transcription
6. They are compactly coiled	They are loosely coiled
7. They are late replicative	They are early replicative
8) Genetically inactive	Genetically active
9) Regions of HC is sticky	Regions of EC is non sticky
10. Phenotype remains unchanged of an organism.	Variation may be seen due to the effect in DNA during the genetic process.
11 It permits gene expression regulation and maintains the structural integrity of cell.	It results in genetic variation and permits transcription.