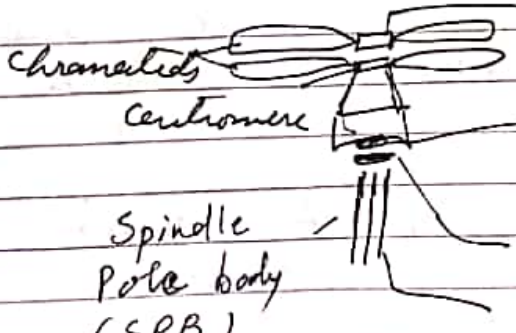
PG Sem 1
CC3
Unit-1

Centromere, Kinetochore, Telomere and its organization- ①

Centromere – Centromeres are chromosomal domains at which the Kinetochore, a protein complex is situated, which is required for correct seperation of chromosomes during mitosis and meiosis, is assembled. The centromere is situated at any point of two chromatids for their assembly.

Centromere function recognized the proper coordination of several sub functions such as Kinetochore assembly, Sister chromatid cohesion, binding of Kinetochore microtubules, orientation of Sister Kinetochores to opposite Spindle poles, and their movements towards the Spindle poles.

The centromere is a region of the chromosome that is responsible for its segregation at mitosis and meiosis. Centromeres are therefore essential for genetic stability and there are examples in which defective centromere leads to chromosomal abnormalities causing birth defects and cancer. The centromere is made up of heterochromatin and and proteins associated with central core DNA. At metaphase stage of cell division CENP is a component of inner plate in the human centromere. The Kinetochore remain attached to it which is also a protein structure



Dig - Showing organisation of centromere

Methylation of Histones H_3 and H_4 and methylation of lysine 9 of histone H_3 are required for heterochromatin formation and for proper Chromosome segregation in several different organism. The centromere is a portion of a chromosome where mitotic spindle fibres attach to pull sister chromatids during cell division.

Functions of centromere - The centromere of the chromosome provides a binding site for the mitotic spinelle fibre that attach with each sister chromatid and pull them to opposite ends of the parent cell. They are responsible for successful division of the cell

Centromeric dysfunction leads to problems in chromosome sorting leading to miscarriage miscarriage, in which inherited centromere disorders may result in early embryonic death. Centromere dysfunction is also suspected to play a role in cancer cells which display massive chromosome imbalance of the type that would be expected if the sorting of chromosomes during cell division fails.

Types of centromere

① Point Centromere - Point centromeres are centromeres where mitotic spindle fibres are attached to a specific sequence of DNA.

② Regional centromeres - Human and most eukaryotic cells have this type of centromere.

There are centromeres where mitotic spindle binding is determined by a combination of DNA and Protein working together to signal the location of a centromere.

KINETOCHORE – A Kinetochore is a disc shaped protein structure associated with duplicated chromatids in eukaryotic cells where the spindle fibres attach during cell division to pull sister chromatids apart. The Kinetochore assembles on the centromere and links the chromosome to microtubule polymers from the mitotic spindle during mitosis and meiosis. Its proteins also help to hold the sister chromatids together and play a role in chromosome etiting

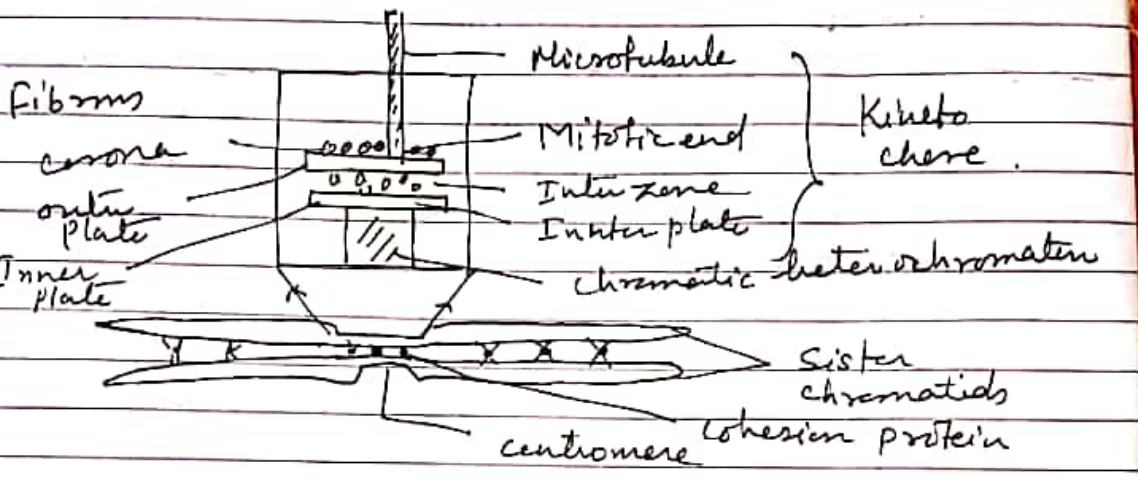
Structure of Kinetochore – The Kinetochore contains two regions

1/ An inner Kinetochore, which is tightly associated with the centromeric DNA and assembled in a specialized form of chromatin that persists throughout the cell cycle.

2/ An outer Kinetochore, which interacts with microtubules, the outer Kinetochore is a very dynamic structure with many identical components, assembled and functional only during cell division.

The Kinetochore is made up at least 19 different proteins conserved between the Eukaryotic species, a histone H3 variant (CENP or CENH3) which helps the Kinetochore to associate with DNA. other proteins attach to the microtubules of the spindle fibre. there are also

motor Proteins - including dynein and Kinesin which generates forces that move chromosomes during mitosis. other proteins as ~~Mad2~~ Mad 2 monitor the microtubule attachment as well as the tension between sister Kinetochore and activate the spindle check point to arrest the cell cycle when it is absent.



Kinetochore structure and components in vertebrate cells.

Functions of Kinetochore - Kinetochore functions include anchoring of chromosome to MTs in the spindle verification of anchoring, activation of the spindle checkpoint and participation in the generation of force to propel chromosome movement during cell division

The microtubules are made up of α and β tubulin alternating between growing and shrinking phases a phenomenon known as dynamic instability. MTs are highly dynamic structures responsible for Pairing of homologous chromosomes, Sister Kinetochore mono orientation Protection of centromeric cohesion and spindle pole body cohesion and duplication.

TELOMERE – Telomeres are nucleoproteins Structure at the end of each chromosome. The nucleic acid sequence of telomeres is TTAGGG hexamer repeat. The number of hexamer repeats can vary greatly from very few to thousands of repeats with most repeated telomere length varying from 4-11 kilobases in humans. Several proteins CTRF1, TRF2, POT1, TIN2, TPP1, RAP1 and Tankyase are associated with telomere DNA to form the Shelterin complex which interacts with enzymes such as telomerase and other proteins, required for proper telomerase maintenance and function. Shortening of telomeres may increase excessively with age and lead to telmerase end function, chromosomal instability and accelerated senescence..

Telomeres may become dysfunctional if base damage or/DNA Strand breaks in telomere sequence. It may be due poor nutrition and dietary intervention has a potential role to improve telomere integrity

In 1930, Hermann Muller was the first scientist to note that the ends of chromosome had unique properties Muller named these ends Telomeres based on their Position on chromosome. Telomeres play an essential role in stabilizing the ends of chromosomes but they do not contain active genes. Instead Telomere contains an array of highly repeated DNA sequences and specific binding proteins that form a unique structure at the end of the chromosome.

Function of Telomere – The function of telomere is to protect the ends of chromosomes They prevent one chromosome from binding

to another DNA (DNA is sticky).
They do not have any genetic information so during DNA replication everytime a small portion of DNA is lost with each round of cell division, So the telomeres protect the DNA having genetic information they are not lost during this process.

Organization of Telomere- Telomeres are essential for integrity of chromosomes forming a cap like structure to protect the ends of eukaryotic linear chromosomes.

Telomeric DNA consists of the single stranded, guanine rich 3' overhang at the extreme ends of chromosomes, flanked by the double stranded, region of telomeric repeats, several proteins are present to maintain telomere structure and for performance of telomeric function

Telomeric DNA is synthesized by the enzyme telomerase complex, and their length is controlled by positive and negative regulators for the telomerase.

Telomeres are made of transcriptionally repressed, non nucleosomal chromatin and are often localized near the nuclear margin.

The telomeric cap structure prevents DNA damage checkpoint and repair mechanisms from treating telomeric breaks.

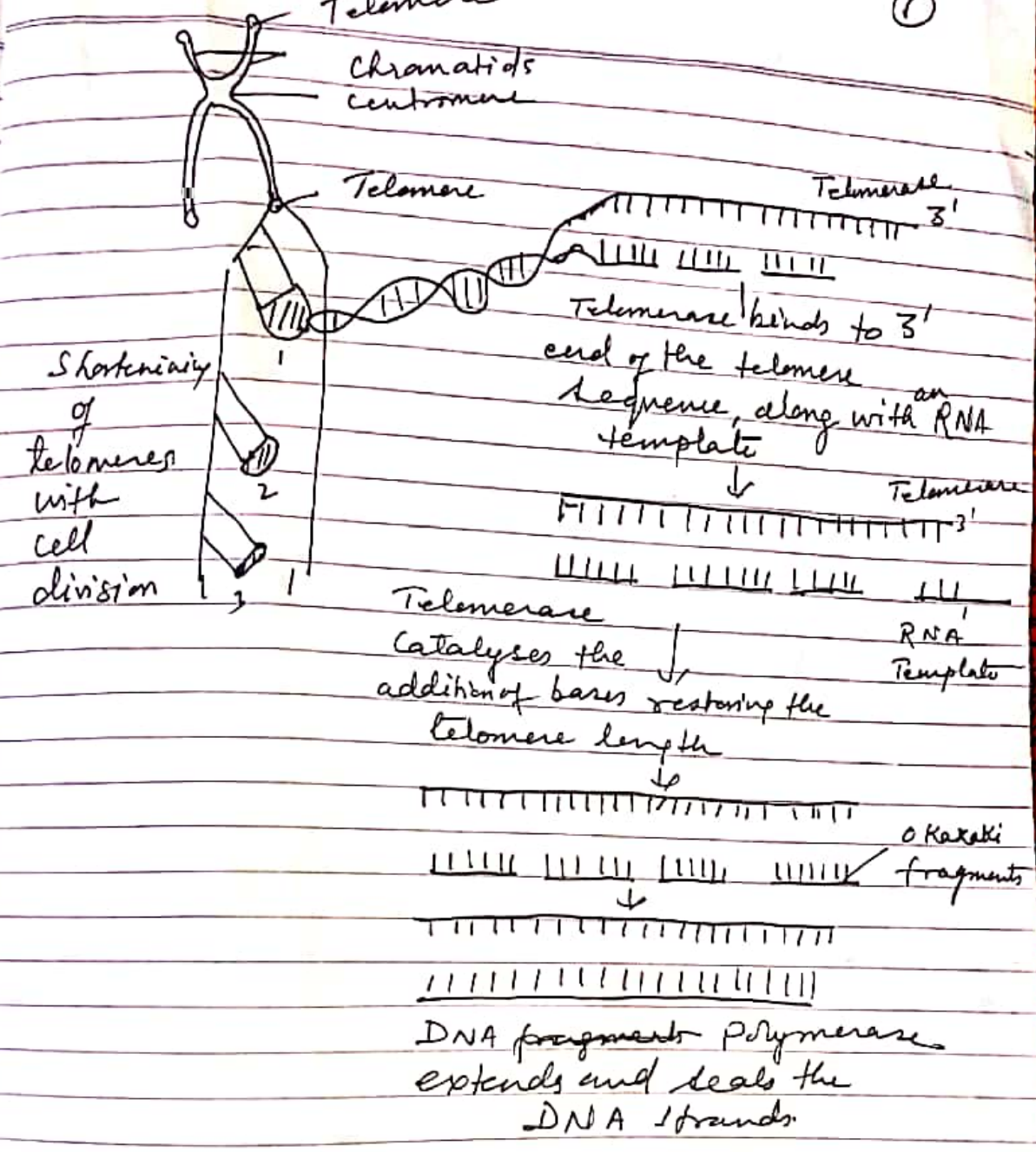


fig- Synthesis or formation of telomere by enzyme Telomerase.

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