

Kinetochores and its Role in Maintaining Genomic Stability During Cell Division

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DESCRIPTION

The kinetochore plays a pivotal role in ensuring the accurate segregation of chromosomes during cell division, which is critical for maintaining genomic stability. Genomic stability refers to the integrity of a cell's genetic material, ensuring that each daughter cell receives the correct number of chromosomes and preventing errors that can lead to diseases such as cancer.

The kinetochore is a large protein complex that forms at the centromere of each chromosome, a specialized region that holds the two sister chromatids together. Directly associated with the centromeric DNA, it anchors the kinetochore complex. Interacts with spindle microtubules, forming attachments that are crucial for chromosome movement.

The kinetochore's primary function is to mediate the attachment of chromosomes to the spindle microtubules. These microtubules form from the mitotic spindle, a structure responsible for pulling chromosomes apart during cell division. Each kinetochore binds to microtubules from opposite poles of the spindle, allowing for the equal distribution of chromosomes into the two daughter cells. Proper attachment is essential for accurate chromosome segregation. During metaphase, chromosomes align at the metaphase plate, an imaginary plane equidistant between the two spindle poles. The kinetochore ensures that each chromosome is properly oriented, with microtubules pulling from both poles. This alignment is critical to avoid errors like aneuploidy (an abnormal number of chromosomes), which can lead to cell dysfunction or disease.

The Spindle Assembly Checkpoint (SAC) is a surveillance mechanism that monitors whether chromosomes are correctly attached to the spindle. The kinetochore plays a key role in this checkpoint. If any chromosome is not properly attached, the SAC halts the progression of cell division to prevent the separation of unaligned chromosomes. This ensures that cells do not proceed until all chromosomes are correctly positioned, reducing the risk of genomic instability. Once all chromosomes are properly aligned and attached to the spindle, the SAC is

satisfied, and the cell proceeds to anaphase. In this phase, the kinetochore plays a vital role in the separation of sister chromatids. Microtubules pull the chromatids apart toward opposite poles of the cell. If the kinetochore is not functioning correctly, this process can result in incorrect chromosome segregation, leading to Chromosomal Instability (CIN), a hallmark of many cancers.

Chromosomal instability is a condition in which chromosomes are unevenly distributed during cell division. The kinetochore ensures that the chromosomes are evenly divided by maintaining proper tension and attachment to spindle fibers. Defects in kinetochore function can result in the misalignment or missegregation of chromosomes, which can trigger genomic instability and contribute to tumorigenesis. In addition to its role in chromosome segregation, the kinetochore is involved in signaling pathways that help repair errors during cell division. For example, if a kinetochore is not properly attached to the microtubules, repair proteins are recruited to correct the attachment before the cell proceeds through division. Kinetochore malfunction can lead to aneuploidy, which is a common feature of many cancers. Abnormal kinetochore-microtubule attachments can drive tumorigenesis by increasing genetic diversity in cancer cells. Mutations in kinetochore proteins can cause developmental disorders due to improper chromosome segregation during embryonic development.

CONCLUSION

The kinetochore is indispensable for accurate chromosome segregation during mitosis and meiosis. By ensuring proper attachment to spindle fibers, facilitating chromosome alignment, and enabling the spindle assembly checkpoint, the kinetochore helps maintain genomic integrity. Dysregulation of its function can lead to chromosomal instability, contributing to a range of diseases, particularly cancer. The molecular mechanisms behind kinetochore function is critical for both basic cell biology and the development of therapeutic strategies to treat diseases linked to genomic instability.

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