

Project Title

Dissecting Mechanisms and Functions of Centromere positioning in Neural Stem Cells

Type of Cancer

Not Site-Specific Cancer

Area of Research

Cancer Initiation: Alterations in Chromosomes

Cells are highly ordered. There is a place for everything and when all is well, everything is in its place. The cell's nucleus is no different. DNA is packaged into the nucleus in a particular way. The physical location of different regions of DNA within the nucleus helps determine how many proteins are made from the genes on that part of the DNA. DNA positioning is also important for repairing DNA damage. Disruptions of these processes can lead to cancer. While we know that DNA organization is very important, there is still much we do not understand. Cells use many strategies to organize DNA. One of these is how they position centromeres. Centromeres are a special region of DNA on each chromosome that is needed for cell division. In many diverse organisms, from yeast to mammals, centromeres are organized as clusters and are positioned at specific locations in the nucleus when the cell is not dividing. We do not understand the details of how and why cells position centromeres this way. In one study, centromere positioning was altered in cancer cells compared to healthy cells, but we do not know if disruption of centromere localization can cause cancer. In this research, I will work to uncover how and why centromeres are positioned in the fruit fly brain stem cell model system, which will provide a foundation for determining if disrupted centromere localization can cause cancer. Our lab previously showed that centromere positioning requires protein filaments called microtubules. This provides an excellent starting point. To find out what other proteins are needed, I will look to see if I can alter where centromeres are positioned by disrupting other proteins that are likely candidates for connecting microtubules to centromeres. I will then investigate why centromere positioning is important for cells. I will disrupt centromere positioning and then will look to see what changes. These changes might include how cells split up DNA when they divide and/or the positioning of other non-centromeric DNA regions. I will use a microscope and fluorescent DNA to see if either of these possibilities occurs. The results from this work will help us better understand organization of the nucleus. Knowing what proteins are required and why the cell needs to position centromeres could be helpful for understanding how cancer develops.



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