Researchers determine the composition of centromeric chromatin

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The Stowers Institute's Gerton Lab has provided new evidence to clarify the structure of nucleosomes containing Cse4, a centromere-specific histone protein required for proper kinetochore function, which plays a critical role in the process of mitosis. The work, conducted in yeast cells, was published in the most recent issue of *Molecular Cell*.

The centromeric nucleosome acts as a guide for the position of the kinetochore. The kinetochore attaches the chromosome to a microtubule for chromosome segregation. It is essential that chromosome segregation is carried out with high fidelity, since errors in this process can produce cells which contain an abnormal number of chromosomes. In humans, these types of errors are hallmarks of many types of cancer, and therefore are thought to play a significant role in tumor formation, malignancy, and metastasis.

For many years, researchers assumed that centromeric nucleosomes were structurally like other nucleosomes — "octamers" with two copies each of four different histone protein subunits with DNA wrapped around the outside. Recently, two alternative models for the structure of centromeric nucleosomes have been proposed. The first suggests that two of the histone protein pairs normally found in the centromere are replaced by the Scm3 protein, creating a hexameric nucleosome made up of six subunits. The second model suggested that centromeric nucleosomes contain a single molecule of each of the four proteins, forming a tetrameric structure called a hemisome.

The Gerton Lab provides evidence for a model in which Cse4-containing nucleosomes are, in fact, octamers. A variety of unbiased methods was used to test the three different models, including genetic, biochemical, and cell biological approaches. In the end, the octamer model was the only one consistent with all of the current experimental results.

"These data support a new model for the structure of centromeric nucleosomes and reinforce the importance of both structure and function of octameric nucleosomes in the epigenetic propagation of centromeric chromatin," said Raymond Camahort, Ph.D., formerly a Postdoctoral Research Associate and lead author on the paper. "In order to better understand how centromeric nucleosomes are formed, we must understand their composition. This work has answered a critical question of structure."

"Many lines of evidence indicate that centromeric chromatin is evolutionarily conserved from yeast to man," said Jennifer Gerton, Ph.D., Associate Investigator and senior author on the paper. "The octameric structure for centromeric nucleosomes may be universal. Our studies in budding yeast help to shed light on mechanisms of centromere propagation and chromosome transmission that are needed to maintain human health."

Source: Stowers Institute for Medical Research