Slicing chromosomes leads to new insights into cell division

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(PhysOrg.com) -- By using ultrafast laser pulses to slice off pieces of chromosomes and observe how the chromosomes behave, biomedical engineers at the University of Michigan have gained pivotal insights into mitosis, the process of cell division.

Their findings could help scientists better understand genetic diseases, aging and cancer.

Cells in plants, fungi, and animals—including those in the human body—divide through mitosis, during which the DNA-containing chromosomes separate between the resulting daughter cells. Forces in a structure called the mitotic spindle guide the replicated chromosomes to opposing sides as one cell eventually becomes two.

"Each cell needs the right number of chromosomes. It's central to life in general and very important in terms of disease," said Alan Hunt, an associate professor in the Department of Biomedical Engineering and an author of a paper describing these findings published in Current Biology.

"One of the really important fundamental questions in biology is how do chromosomes get properly segregated when cells divide. What are the forces that move chromosomes around during this process? Where do they come from and what guides the movements?"

Hunt's results validate the theory that "polar ejection forces" are at play. Scientists had hypothesized that the direction and magnitude of these

forces might provide physical cues guiding chromosome movements. In this capacity, polar ejection forces would play a central role separating chromosomes in dividing cells, but no one had established a direct link until now.

Polar ejection forces are thought to arise out of the interaction between protein motors on the arms of chromosomes that push against cells' microtubules. Microtubules are long, thin tubes that form a central component of the cytoskeleton and the mitotic spindle. They serve as intracellular structural supports and as railways along which molecular motors move cargoes such as chromosomes.

Hunt's group hypothesized that polar ejection forces should be proportional to the chromosome's size, and therefore could be predictably changed by altering the size of the chromosomes. Using newts as a model organism, they cut off pieces of the chromosomes' arms.

"We asked what the relationship is between the size of the fragment we removed and the direction the chromosome moved," Hunt said. "Not only did we observe a relationship, we established that polar ejection forces were in fact a direct cue that guided chromosomal movements in mitosis."

To achieve this, Hunt performed "nanoscale surgery," as he calls it, taking advantage of the unprecedented precision of femtosecond pulses of laser light. A femtosecond is one billionth of one millionth of a second. The chromosomes he altered were only micrometers long, and the slices across the chromosomes were only nanometers thick. A nanometer is one-billionth of a meter, about a million times thinner than a human hair.

Understanding how chromosome guidance occurs allows scientists to

determine how failures lead to genetic diseases, aging and cancer. When cells don't properly divide, they usually die. But survival can cause cancer or aging-related disorders. Likewise, genetic diseases such as Down's syndrome result from improper chromosome segregation.

Mitosis, Hunt says, is one of the most important targets of chemotherapy.

"By knowing how chromosomes move, we can better understand how these drugs interfere with those movements and we can design experiments to screen for new drugs," Hunt said. "It will also allow us to have a better handle on what makes these drugs work. There are a lot of drugs that interfere with mitosis, but only a few are good for cancer therapy."

More information: The paper is called, "The Distribution of Polar Ejection Forces Determines the Amplitude of Chromosome Directional Instability." It is published in the May 26 print edition of *Current Biology.*

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