

Insect genomes' analysis challenges universality of essential cell division proteins

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Cell division, the process that ensures equal transmission of genetic information to daughter cells, has been fundamentally conserved for over a billion years of evolution. Considering its ubiquity and essentiality, it is expected that proteins that carry out cell division would also be highly conserved. Challenging this assumption, scientists from Fred Hutchinson Cancer Research Center have found that one of the foundational proteins in cell division, previously shown to be essential in organisms as diverse as yeast, flies and humans, has been surprisingly lost on multiple occasions during insect evolution.

Faithful [cell division](#) relies on centromeres, chromosomal sites that are designated for attachment to the machinery that will pull the two copies of chromosomes following replication ('sister chromatids') to opposite poles and different [daughter cells](#). Observed in light microscopy studies as early as in the 1880s, chromosomes ready for segregation appear X-shaped with the centromere commonly identifiable as a constriction between sister chromatids. Subsequent studies have revealed that centromeres are highly diverse both in length and sequence of their underlying DNA, ranging from tiny point centromeres in yeast to megabase long stretches of repeats in humans. Despite this diversity, the common denominator of all centromeres is a DNA-packaging protein, CenH3, which has been found and shown to be essential for cell division in all species studied so far.

In a study published this month in the open-access journal *eLife*, researchers from Malik and Henikoff labs upend this dogma about

CenH3 essentiality. The study began with their interest in the unusual chromosomal architecture of some insect lineages, in which centromeres are organized along the entire length of chromosomes akin to 'railroad tracks' (referred to as 'holocentric' chromosomes) instead of the canonical X-shape. "We initially became interested in butterflies and moths because of their unusual centromere structure that we wanted to investigate using CenH3 as a marker," said study lead Ines Anna Drinnenberg, Ph.D., researcher at Fred Hutch. "It was very unexpected that searches for homologs in their genomes did not reveal any hits."

Recognizing that these 'railroad track' chromosomes had also been observed in other insects like aphids, lice, earwigs and dragonflies, Drinnenberg and her colleagues searched through both available genome sequences as well as generated comprehensive lists of gene repertoires by sequencing live insects collected from the wild with the help of entomologist Dakota deYoung from the University of Washington. They found that all holocentric insects appeared to be missing CenH3 while all monocentric insects (i.e., containing X-shaped chromosomes) including flies, bees, beetles, cockroaches, stick insects and mayflies still possessed CenH3. It thus appeared that transitions from monocentric to holocentric [chromosomes](#) in insects rendered CenH3 non-essential, ultimately leading to its loss in species of insects that comprise 16% of named biodiversity. "Our report completely revises the notions of gene essentiality in a process that is of fundamental importance to all eukaryotic organisms," added Harmit Malik, Ph.D., researcher in the Basic Sciences division at Fred Hutch. "To find that insect species have replaced the very foundation of centromere definition was quite surprising. It presents a unique opportunity to understand what kind of process may have facilitated this loss."

In addition to its important implications for the basic biology of cell division, findings such as these exceptional CenH3-deficient centromeres also provide insights into what types of changes might lead

to cell division defects that result in chromosomal imbalances, or aneuploidy, frequently observed in cancer cells.

Provided by Fred Hutchinson Cancer Research Center

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