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Repetitive but not redundant

Satellite DNA found at centromeres promotes correct spindle–chromosome attachments.

Like a parachute jump, mitosis can go badly wrong unless every connection is sound. The repetitive DNA sequences located at centromeres help secure mitotic links, Bassett et al. show (1). Contradicting previous evidence that the sequences are expendable, the study indicates that they help attract proteins necessary to repair faulty chromosome connections.

Centromeres ensure that mitotic spindle fibers correctly fasten to kinetochores. Although no specific nucleotide sequence marks the centromeres, several features distinguish these structures from the rest of the chromosome. The protein CENP-A supplants the standard H3 histone in centromeric nucleosomes, for example. Aurora B kinase and other passenger proteins gather on the inner centromere, ready to break any improper connections to the spindle. The centromere also usually carries long stretches of repetitive, or satellite, DNA, in which particular short sequences recur multiple times. Whether repetitive DNA contributes to chromosome separation remains unresolved. Some studies suggest that centromeres work fine without it (2).

Bassett et al. were able to probe satellite DNA's function thanks to a human cell line in which the centromere on chromosome 4 has shifted along one arm by about 25 million base pairs (3). This relocated centromere, or neocentromere, lacks the repetitive DNA, which remains at the original position. "We can monitor what's happening at the old site and the new site on the same chromosome," says senior author Ben Black.

What happens is a migration of centromere-associated proteins to the new site. Researchers already knew that CENP-A makes the move. Bassett et al. showed that the CENP-A nucleosome-associated complex also transfers to the neocentromere. So do several other recently discovered CENPs, including CENP-O and CENP-P. By stiffening nucleosomes, CENP-A appears to establish the new centromere without help from repetitive DNA.

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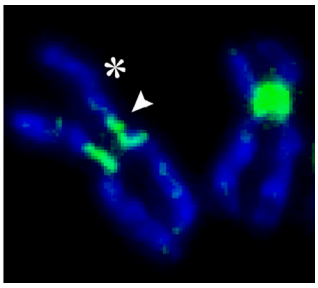
The picture for aurora B is more complex. Although some aurora B collects at the neocentromere, the researchers also detected the kinase spread along the chromosome arm. They were curious about whether this altered distribution would upset mitosis. At first glance, it seemed to have no effect—the cells typically divide in culture without chromosomal chaos. However, Bassett et al. found that chromosomes with dispersed aurora B were only one-fifth as likely as control chromosomes to fix incorrectly attached spindle fibers. In cells with the neocentromere, much of the aurora B inappropriately shuts down—the kinase shows only one-fourth as much activity as in normal cells.

The results suggest that repetitive DNA does have a function: helping to position the inner centromere to fix mistaken mitotic attachments. "It's a surprise that aurora B [localization] is not the same for this variant chromosome as on all the normal chromosomes," says Black. "It requires a certain chromatin context that isn't there at the neocentromere." Repetitive DNA could provide that context. "If repetitive DNA is making a bed for the aurora B kinase, that might explain why all centromeres have it," Black says. A topic for further investigation is what entices aurora B to settle down on repetitive DNA.

Instead of a normal inner centromere, this cell line has one that works just well enough to get by, Black says. Whether that sloppiness triggers health problems remains unclear, he says. The girl who was the source of the cells showed developmental delay, but other members of her family didn't, despite having the same displaced centromere (3).

Although centromere relocation is rare in the human population, it has happened frequently during mammalian evolution (4) and might cement differences between recently diverged species. If chromosome 4's neocentromere persists over evolutionary time, Black says he suspects that the repetitive DNA would migrate to the new location.

Focal Point



Emily Bassett (left), Ben Black (center), Kevan Salimian, and colleagues took a close look at protein positioning on a human chromosome whose centromere had moved. Most of the centromere components shifted to the new location (asterisk), but aurora B kinase spread out along the arm of the chromosome (left), likely because the repetitive DNA remained at the old centromere location. In the control chromosome on the right, aurora B clusters at the original centromere.

1. Bassett, E.A., et al. 2010. *J. Cell Biol.* doi:10.1083/jcb.201001035.
2. Wade, C.M., et al. 2009. *Science.* 326:865–867.
3. Amor, D.J., et al. 2004. *Proc. Natl. Acad. Sci. USA.* 101:6542–6547.
4. Murphy, W.J., et al. 2005. *Science.* 309:613–617.