Kinetochores expand their reach

Kinetochores are thought to assemble in a hierarchical order (2). Inner kinetochore proteins, such as CENP-C and CENP-T, first bind to centromeric chromatin, which is marked by the variant histone CENP-A. These proteins then recruit outer kinetochore proteins involved in microtubule attachment and spindle checkpoint signaling. The inner and outer layers of kinetochores can be distinguished by electron microscopy, but the organization of individual proteins within these layers remains uncertain. David Wynne and Hironori Funabiki, from The Rockefeller University in New York, decided to examine kinetochores using 3D structured-illumination microscopy. “Not many studies have looked at kinetochores using super-resolution microscopy, so we wanted to see what kinds of structures we could visualize,” Funabiki explains.

The researchers looked at the assembly of kinetochores on sperm chromosomes added to Xenopus egg extracts. “The surprising thing was that several outer kinetochore proteins showed a massive expansion when the extracts were treated with nocodazole,” Funabiki says. These proteins—including the checkpoint proteins Bub1, BubR1, and Mad1, as well as proteins, such as CENP-E and dynein, involved in lateral microtubule attachment—formed long, thin filaments that extended more than a micron away from centromeric chromatin marked by CENP-A. Wynne and Funabiki saw a similar, transient expansion of these proteins in unperturbed egg extracts at the beginning of mitosis.

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Kinetochores attach chromosomes to the mitotic spindle. After binding initially to the sides of spindle microtubules, they form stable attachments to microtubule plus ends so that chromosomes can be segregated to the spindle poles during anaphase. In addition, kinetochores recruit the spindle assembly checkpoint proteins that prevent cells from entering anaphase if their chromosomes aren’t attached to the spindle correctly. Although the function of individual kinetochore proteins is fairly well understood, how their assembly and disassembly is orchestrated to coordinate the kinetochore’s different functions remains unclear. Wynne and Funabiki use super-resolution microscopy to reveal that, in the absence of microtubule attachment, a subset of kinetochore proteins form extended filaments that could help activate the spindle checkpoint and capture microtubules (1).

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