Mitosis without wind

The relatively minor effects of interfering with a kinesin that mediates polar ejection forces suggests that kinetochores may be smarter than once thought. This conclusion comes from a report on page 1135 from Levesque and Compton. Their antibody experiments target a human kinesin motor called Kid that sticks to chromosome arms and is thought to mediate chromosome movement out along spindle microtubules. This polar ejection force has been proposed as a mechanism for pushing chromosomes away from spindle poles and thus aligning chromosomes on the metaphase plate.

The importance of Kid and the polar ejection force has been shown in fly germ cells mutant for the Nod kinesin, and in frog extracts, where depletion of Kid resulted in widespread wandering of chromosomes away from in vitro assembled metaphase plates. Levesque and Compton set out to see if Kid was equally important in a mitotic rather than meiotic system.

After injection of Kid antibodies into cells with monopolar spindles, chromosomes clustered tightly around the pole, whereas after control injections chromosomes kept a polite distance from the pole because of polar ejection forces. When the authors inhibited Kid in cells with bipolar spindles, most chromosomes moved to the metaphase plate correctly. The chromosome arms trailed toward the poles, but nevertheless, the chromosomes moved in the right direction, and only 17.5% of cells had chromosome disorganization sufficient to cause a noticeable cell cycle delay. Delayed cells tended to have one or more sister chromatid pairs hung up very close to one pole.

The relatively small numbers of problems suggests that mitotic kinetochores can usually be captured even by microtubules from a very distant pole, and once captured are smart enough to sense the midpoint of the spindle without the help of polar ejection forces. The kinetochore microtubules, like a rope in a tug-of-war, may be subject to forces that are proportional to the length of the microtubule, so that the opposing forces will cancel out when a chromosome reaches the metaphase plate.

From nuclear pore to kinetochore

Nuclear proteins are turning up in some odd places lately. First, the nuclear-transport factor Ran was implicated in spindle formation. Then, the mitotic checkpoint proteins Mad1 and Mad2 turned up at the nuclear pore, in a switch with the mRNA export factor hRae1, which appeared with the mitotic checkpoint protein mBUB1 at the kinetochore. Now, Belgareh et al. report that two structural nuclear pore complex constituents also localize to the kinetochore (page 1147).

Belgareh et al. were interested in characterizing the human version of a budding yeast nuclear pore subcomplex that is involved in mRNA export. They identified hNup133 by homology, and identified three other members of the subcomplex through immunoprecipitation experiments.

The surprise came in the localization studies, when both antibody staining and GFP fluorescence indicated that at least two of these nucleoporins are found at kinetochores from prophase through to late anaphase.

This simple observation has many possible interpretations, none of which (as yet) comes with any significant supporting evidence. First, nucleoporins at the kinetochore could act to seed the formation of a specific subset of nuclear pores at the end of mitosis, while the nuclear envelope reforms around chromosomes. Second, the nucleoporins could have some unspecified function at the kinetochore, although a role in spindle formation is not obvious as none of the nucleoporins under discussion has the FG repeats characteristic of proteins that link indirectly to Ran.

Finally, the nucleoporins may visit the kinetochore merely to pick up mitotic checkpoint proteins, so that those checkpoint proteins can be sequestered at the nuclear pores during the following cell cycle. Why that might be necessary is anyone’s guess.