

Journal club



TO CUT OR NOCUT IN MITOSIS

During mitosis, several morphologically distinct events must occur in the right order. For example, chromosome segregation must be complete before cytokinesis. Two papers on this mitotic coordination, one by Norden *et al.* and the other by Mendoza *et al.*, stirred a memory of a discussion that I had with my graduate mentor, Professor Mitsuhiro Yanagida.

Studying fission yeast Cut1 (cell untimely torn 1; now known as separase or separin, the protease that cleaves sister chromatid linkages), I naively thought that, after anaphase is triggered, there is no feedback between chromosome segregation and cytokinesis. One evening in 1994, Yanagida-sensei suggested to me that Cut1 may be a component of the checkpoint that delays cytokinesis in the presence of

“ Yanagida-sensei suggested ... that Cut1 may be a component of the checkpoint that delays cytokinesis in the presence of unsegregated chromosomes. ”

unsegregated chromosomes. This would explain why *cut1* mutants showed the *cut* phenotype, in which cytokinesis takes place over the unseparated chromosomes. I pushed aside this idea, however, as *cut* phenotypes were so prevalent in other fission yeast mutants, such as the DNA topoisomerase II mutant *top2*.

More than a decade later, I was stunned by the report from Norden *et al.*, demonstrating the existence of just such a checkpoint, NoCut, in budding yeast. In the study by Mendoza *et al.*, the same group further showed that the non-catalytic function of Esp1 (the budding yeast separase) is actually important for the NoCut checkpoint. Their results indicate that the separase-Cdc14 early anaphase release (FEAR) pathway promotes recruitment of the protein kinase increase-in-ploidy 1 (*Ipl1*; also known as Aurora B) to the spindle midzone, which activates this checkpoint in the presence of unsegregated

chromosomes. Interestingly, unlike the case in fission yeast, NoCut inhibits completion of cytokinesis in the budding yeast *top2* mutant. So, I had a good reason to miss this checkpoint in fission yeast, but my supervisor had the right perspective. A study by Steigemann *et al.* suggests that a similar checkpoint exists even in human cells, although in this case the direct involvement of separase in the NoCut checkpoint remains an open question.

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The author declares no competing financial interests.

ORIGINAL RESEARCH PAPERS Norden, C. *et al.* The NoCut pathway links completion of cytokinesis to spindle midzone function to prevent chromosome breakage. *Cell* **125**, 85–98 (2006) | Mendoza, M. *et al.* A mechanism for chromosome segregation sensing by the NoCut checkpoint. *Nature Cell Biol.* **11**, 477–483 (2009) | Steigemann, P. *et al.* Aurora B-mediated abscission checkpoint protects against tetraploidization. *Cell* **136**, 473–484 (2009)