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**Mutant yeast provides new insight into how reproductive cells can fail**

*Analyzing brewer’s yeast genes gives a better understanding of the role of a key protein*

Researchers affiliated with RIKEN have uncovered what happens at two crucial points in the chain of events during reproductive cell division, and they said in a recent report that they know better now why the tenuous thread of new life may suddenly break. Published in *Genes & Development*, a leading U.S. genetic research journal, their study offers fresh insight into issues that have perplexed geneticists since the days of Gregor Mendel.

To elucidate the processes of early reproductive cell division, the researchers focused on mutant strains of *Saccharomyces cerevisiae*, a yeast that is a frequent subject of genetic studies, not to mention its duties in making bread, wine and beer. It is useful in studying the cell cycle because it is easy to culture and shares the complex internal cell structure of plants and animals. It was also the first organism of its genome type to be genetically sequenced, thus laying open the yeast's DNA structure and permitting researchers to target specific genes with a lot of "what if?" sort of questions.

Thanks to its short life cycle, brewer's yeast, as it is commonly known, lends itself to procedures in which researchers create yeast cell variations, or 'mutants,' to permit turning on and off the expression of individual genes to determine what happens. This was the approach used by scientists at the University of Tokyo, Osaka University and others working in cooperation with RIKEN.

In their paper they cite and expand on research into the cyclin-dependent protein kinase, Cdc7, which has been found to play a key role in the splitting of DNA strands when reproductive cells divide. By modifying yeast cells to limit the activity of Cdc7, they found that cell division could not take place normally at the stage of initial DNA strand division and recombination and, with almost certain lethal effect, when the reproductive cells are ready to convert to normal cells. In humans, this would be at the point when bone, organs, hair and skin begin to form.
What fails, the researchers concluded, is the all-important regulatory effect of phosphorylation, which is compromised at those crucial two points, causing the ordered process of cell division to break down. Phosphorylation has been previously shown to serve two purposes: to activate each already-assembled pre-replication DNA complex, and to prevent new complexes from forming. This ensures that every portion of the cell's DNA structure will be replicated only once. The researchers noted that previously reported "hot spots" are where the breakdown was especially likely to occur.

Such findings add to the accumulating body of knowledge on both normal and abnormal cell development as well as show the precision of increasingly sophisticated analytical techniques to determine what takes place on the genetic level at the start of new life.

The study was reported by a research team including Kunihiro Ohta at RIKEN's Discovery Research Institute in the city of Wako near Tokyo. Published in Genes & Development, a peer-reviewed journal affiliated of the Genetics Society, the paper can be viewed online at http://www.genesdev.org.

Original work:
Cdc7-dependent phosphorylation of Mer2 facilitates initiation of yeast meiotic recombination.
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