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GENOME INSTABILITY

The more, the merrier

Eukaryotic cells have several copies of genes encoding RNA products, such as ribosomal RNA, but many of these are not transcribed, and their function is unclear. Ide *et al.* now reveal that ribosomal DNA (rDNA) repeats are essential for maintaining genome integrity.

Saccharomyces cerevisiae has ~150 copies of rDNA on chromosome XII, which are maintained at high levels through a gene amplification system. In this study, the authors generated *S. cerevisiae* strains with different numbers of rDNA copies. Low copy strains showed higher levels of rDNA transcription and, as a result, were more sensitive to the DNA-damaging agent methyl methanesulphonate (MMS) than high copy ones. Furthermore, low copy strains had more homologous recombination (HR) intermediates (such as Holliday junctions) than high copy strains following MMS treatment and could not progress to G2 phase of the cell cycle, which indicates that in these strains DNA damage triggers incomplete replication. These defects were due to compromised HR repair; as the copy number-dependent sensitivity to MMS was abolished in strains mutated for HR proteins, the authors conclude that HR is impaired by the high transcription levels of rDNA.

Interestingly, HR mutants show synthetic lethality with cohesion mutants (that is, strains in which sister chromatids are not held together, which is required for HR), suggesting that the encoded proteins collaborate during HR. Indeed, sister chromatids in low copy strains were separated immediately after DNA replication began. The defect in sister chromatid cohesion increased the DNA damage sensitivity of low copy strains, as artificial tethering of sister chromatids enhanced their viability following MMS treatment. The separation phenotype of sister chromatids was due to the reduced association of rDNA with condensin — a complex involved in chromosome assembly and segregation during mitosis and meiosis, sister chromatid cohesion in yeast and DNA damage repair. Consistent with this, loss of condensin had no effect in the low copy strain but increased the MMS sensitivity of the high copy strain, highlighting its role in DNA repair in the presence of high copy numbers of rDNA.

> “multiple copies of rDNA are required for efficient HR repair during replication”

Together, these findings indicate that multiple copies of rDNA are required for efficient HR repair during replication because they facilitate the association of sister chromatids with condensin during DNA replication.

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ORIGINAL RESEARCH PAPER Ide, S. *et al.* Abundance of ribosomal RNA gene copies maintains genome integrity. *Science* **327**, 693–696 (2010)