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Does genetic information ow from RNA to DNA in a more general fashion than anticipated? Is the central dogma of molecular biology o en reversed to let RNA repair DNA damage or even recode genes on chromosomes? We recently discovered that RNA serves as a template to repair DNA double-strand breaks (DSBs), either indirectly, in the form of complementary DNA (cDNA), or directly, in the form of transcript-RNA in budding yeast. We found that transfer of genetic information from RNA to DNA occurs with an endogenous generic transcript in cis, and is thus a more common mechanism than previously anticipated. With the advent of CRISPR RNA-guided DNA endonuclease enzymes, there is marked interest in understanding the pathways to facilitate accurate genome engineering events. While ribonucleases (RNases) H1 and H2 blo DSB repair by RNA, the recombination protein Rad52 is a key factor for this repair mechanism. DSB repair by RNA requires Rad52 but not the recombination protein Rad51, RecA homolog, or Rad59, which has homology with the yRad52 N-terminal domain (NTD). Upon overexpression of yRad52,yeast or hRad52 NTD, we observed a signi cant increase in the frequency of DSB repair by RNA. A 68-fold increase was obtained when hRad52 NTD was expressed in cells defective for RNase function that was lacking the yeast RAD52 gene, indicating that hRad52 could catalyze DSB repair by RNA also in human cell Moreover, in the absence of SAE2 or EXO1 genes, which are important for DNA end resection, the frequency of DSB repa by RNA was either increased or not changed, respectively. ese results support an RNA-dependent mechanism of DSB repair mediated by Rad52 that catalyzes a reaction in which RNA invades a broken double-stranded DNA in conditions of limited end resection. Our results suggest that transcript RNA, like non-coding RNA, may have a signi cant role in genome stability and genome modi cation, much more prominent than previously anticipated.

Biography

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