

3rd International Conference on

Molecular Biology & Nucleic Acids

August 27-28, 2018 | Toronto, Canada



Francesca Storici

Georgia Institute of Technology, USA

Mechanisms of RNA-guided DNA repair and modification

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. By removing the function of ribonucleases (RNases) H1 and H2, which cleave RNA in RNA-DNA hybrids, 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. DSB repair by RNA requires the recombination protein Rad52 but not Rad51 or Rad59. Upon overexpression of yRad52, yeast or human Rad52 N-terminal domain (NTD), the frequency of DSB repair by RNA increased up to of a factor of 68. These results indicate that human Rad52 could potentially catalyze DSB repair by RNA also in human cells. Moreover, in the absence of SAE2 or EXO1 genes, which are important for DNA end resection, the frequency of DSB repair by RNA was either increased or not changed, respectively. DSB repair by RNA occurs in the absence of a bona fide reverse transcriptase (RT) enzyme. Nevertheless, overexpression of RT stimulates DSB repair by RNA. These 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 (Figure 1). While the recombination protein Rad52 is a key factor for RNA-templated DNA repair of DSBs, RNA can modify DNA even without the induction of a DSB in a Rad52-independent manner. Our results suggest that transcript RNA, like non-coding RNA, may have a significant role in genome stability and genome modification, much more prominent than previously anticipated.

Biography

Francesca Storici is Professor in the School of Biological Sciences at Georgia Tech. She received her Ph.D. in Molecular Genetics from the International School of Advanced Studies in Trieste, Italy (1998). She was a postdoctoral fellow at the National Institute of Environmental and Health Sciences (NIEHS, NIH) (NC) till 2007, and then research assistant professor at the Gene Therapy Center of the University of North Carolina at Chapel Hill, NC. She joined the Georgia Institute of Technology as an assistant professor in 2007 and became Distinguished Cancer Scientist of the Georgia Research Alliance. In 2013 she was promoted to Associate Professor with tenure. In 2016, she became Howard Hughes Medical Institute Faculty Scholar. In 2018, she was promoted to Professor. Her research is on DNA damage, repair and gene editing.

storici@gatech.edu

Notes: