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# PAPER OF THE MONTH • NOVEMBER 2020


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## Genome-wide R-loop analysis defines unique roles for DDX5, XRN2, and PRMT5 in DNA/RNA hybrid resolution


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DDX5, XRN2, and PRMT5 have been shown to resolve DNA/RNA hybrids (R-loops) at RNA polymerase II transcription termination sites at few genomic loci. R-loops pose a major threat for the cell as the lack of their resolution can lead to DNA breaks causing genomic instability. R-loops associated with a variety of diseases that exhibit genomic instability, including myelodysplastic syndromes, neurological disorders, and cancer.

For this paper, the Richard lab performed genome-wide R-loop mapping using classical DNA/RNA immunoprecipitation and high-throughput sequencing (DRIP-seq) of loci regulated by DDX5, XRN2, and PRMT5. The authors observed hundreds to thousands of R-loop gains and losses at transcribed loci in DDX5-, XRN2-, and PRMT5-deficient U2OS cells. R-loop gains were characteristic of highly transcribed genes located at gene-rich regions, whereas R-loop losses were observed in low-density gene areas. DDX5, XRN2, and PRMT5 shared many R-loop gain loci at transcription termination sites, consistent with their coordinated role in RNA polymerase II transcription termination. DDX5-depleted cells had unique R-loop gain peaks near the transcription start site that did not overlap with those of siXRN2 and siPRMT5 cells, suggesting a role for DDX5 in transcription initiation independent of XRN2 and PRMT5. Moreover, the accumulated R-loops at certain loci in siDDX5, siXRN2, and siPRMT5 cells near the transcription start site of genes led to antisense intergenic transcription. The findings define unique and shared roles of DDX5, XRN2, and PRMT5 in DNA/RNA hybrid regulation.


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