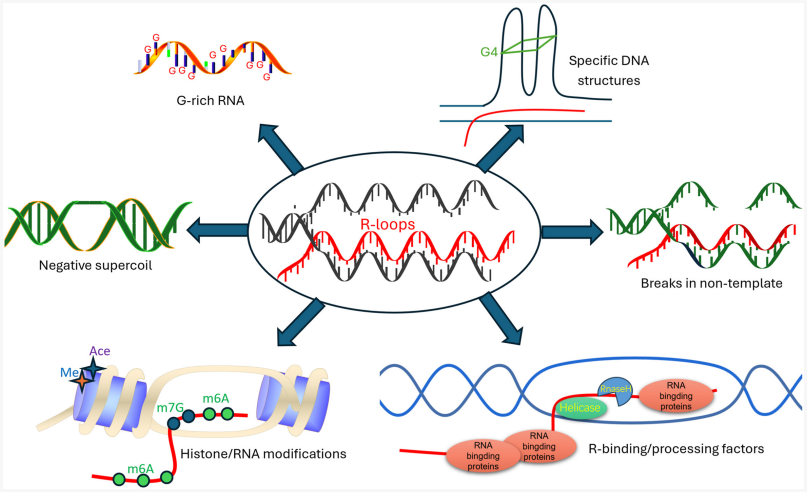
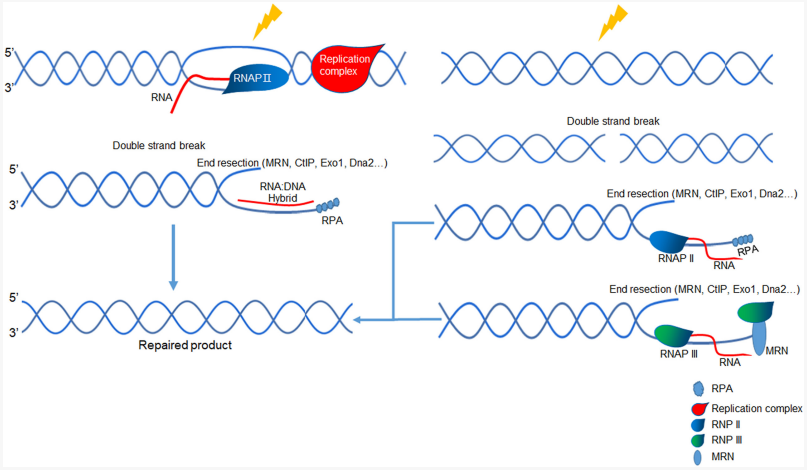
R-Loops Play Dual Role in Genome Stability and Disease

SHANNON, CLARE, IRELAND, April 20, 2025 /EINPresswire.com/ --
This new review article highlights the pivotal and paradoxical role of R-loops in maintaining genomic stability while simultaneously posing risks to it. These three-stranded nucleic acid structures, composed of an RNA:DNA hybrid and a displaced DNA strand, are now recognized not merely as byproducts of transcription but as essential regulatory elements in gene expression, DNA replication, and repair mechanisms.

The article traces the evolution of R-loop research, illuminating how sophisticated detection techniques have transformed our understanding of their biological functions. From early antibody-based imaging to high-throughput sequencing methods like DRIP-seq and R-ChIP, the field has advanced rapidly. These tools have revealed the extensive presence of R-loops at key genomic regions such as promoters, terminators, and double-strand break (DSB) sites, positioning them as significant actors in the DNA damage response.



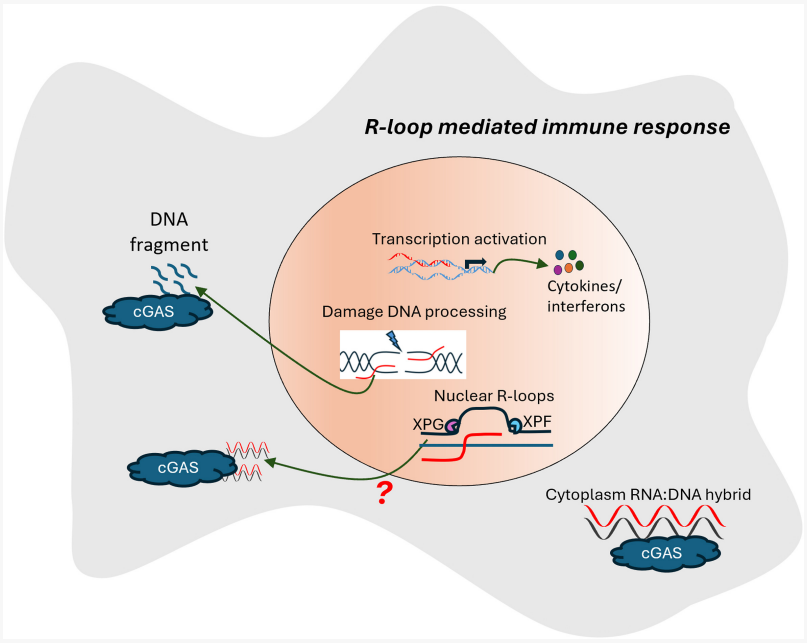
The factors contributing to R-loop formation. Several factors contribute to R-loop formation, including RNA components, specific DNA structures, histone and RNA modifications, RNA-binding proteins, and helicases.



Mystery of RNA:DNA hybrid formation at double-strand break (DSB) site.

A central focus of the article is the dual nature of R-loops. Under controlled conditions, they play protective roles—regulating gene activity, terminating transcription, and facilitating repair through homologous recombination. However, when dysregulated, R-loops become hazardous.

They can obstruct replication forks, induce transcription-replication collisions, and provoke DSBs, ultimately threatening genome integrity. These pathological consequences are amplified in the context of mutations in repair-related genes like BRCA1 and BRCA2, underlining their relevance in diseases such as cancer and neurodegeneration.



R-loop mediated immune response.

The article draws attention to the influence of non-coding RNAs, including lncRNAs, circRNAs, and enhancer RNAs, in modulating R-loop formation. These RNA species can either stabilize or destabilize R-loops, thus influencing chromatin structure and transcriptional dynamics. Additionally, the interplay between R-loops and RNA modifications like m6A and m5C further adds to the complexity of their biological impact, especially in DNA repair pathways.

The emerging connection between R-loops and immune responses are also explored, showing how they can activate pathways like cGAS-STING, linking genomic surveillance to inflammatory signaling. This cross-disciplinary significance makes R-loops a promising frontier for therapeutic intervention, especially in diseases driven by genome instability.

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Reference

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