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Insights Into the Role of CircRNAs: Biogenesis, Characterization, Functional, and Clinical Impact in Human Malignancies

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Circular RNAs (circRNAs) are an evolutionarily conserved novel class of non-coding endogenous RNAs (ncRNAs) found in the eukaryotic transcriptome, originally believed to be aberrant RNA splicing by-products with decreased functionality. However, recent advances in high-throughput genomic technology have allowed circRNAs to be characterized in detail and revealed their role in controlling various biological and molecular processes, the most essential being gene regulation. Because of the structural stability, high expression, availability of microRNA (miRNA) binding sites and tissue-specific expression, circRNAs have become hot topic of research in RNA biology. Compared to the linear RNA, circRNAs are produced differentially by backsplicing exons or lariat introns from a pre-messenger RNA (mRNA) forming a covalently closed loop structure missing 3' poly-(A) tail or 5' cap, rendering them immune to exonuclease-mediated degradation. Emerging research has identified multifaceted roles of circRNAs as miRNA and RNA binding protein (RBP) sponges and transcription, translation, and splicing event regulators. CircRNAs have been involved in many human illnesses, including cancer and neurodegenerative disorders such as Alzheimer's and Parkinson's disease, due to their aberrant expression in different pathological conditions. The