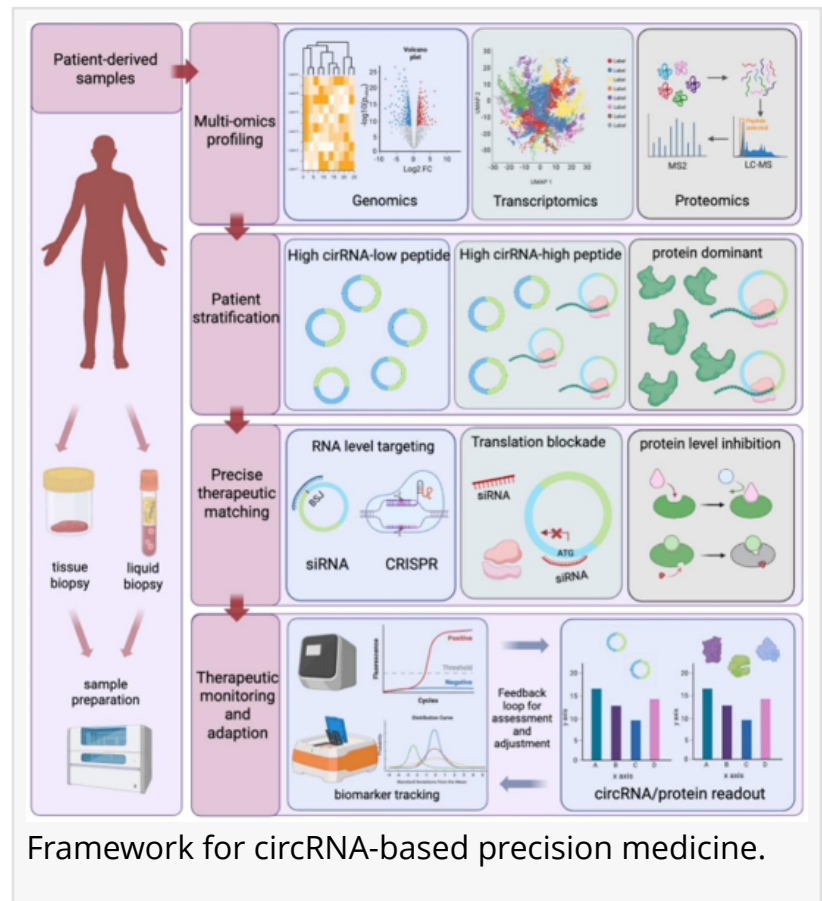


Closing the loop on disease: How circular RNAs are reshaping diagnosis and therapy

FAYETTEVILLE, GA, UNITED STATES, May 19, 2026 /EINPresswire.com/ -- [Circular RNAs \(circRNAs\)](#), once dismissed as harmless splicing errors, are now recognized as powerful regulators of human health and disease. This review synthesizes recent breakthroughs showing that a subset of these stable, closed-loop molecules can be translated into functional proteins, overturning their traditional classification as non-coding RNAs.

Traditional biomarkers, including many protein-based indicators, often fail to capture the dynamic regulatory changes that drive disease progression and influence treatment responses. Although Circular RNAs (circRNAs) are exceptionally stable, highly tissue-specific, and readily detectable in blood and other biofluids, their clinical adoption has been slow. Key barriers include the absence of standardized measurement methods, variability in RNA extraction protocols, and lingering uncertainty about whether many circRNAs are truly functional or merely splicing noise. Based on these challenges, deeper investigation into circRNA biology, standardized detection pipelines, and therapeutic engineering is urgently needed to unlock their full clinical potential.

A team at Sunnybrook Research Institute and the University of Toronto has published (DOI: [10.1093/pcmedi/pbag011](https://doi.org/10.1093/pcmedi/pbag011)) a comprehensive review in [Precision Clinical Medicine](#) (2026, Volume 9, Issue 2). The work outlines how circRNAs can be selectively targeted at both the RNA and protein levels, offering a dual-layer approach to intervention. The authors also examine how synthetic circRNAs are being engineered as stable, programmable therapeutics, and they discuss the delivery systems—from lipid nanoparticles to viral vectors—that will be essential for bringing these treatments into clinical practice.



Framework for circRNA-based precision medicine.

The review highlights multiple innovative strategies now under development. Antisense oligonucleotides designed to target unique back-splice junctions can suppress disease-driving circRNAs without disturbing their cognate linear messenger RNAs, solving a major specificity problem. CRISPR-Cas13 systems offer programmable RNA degradation and have been successfully applied in large-scale circRNA screening platforms. Meanwhile, engineered synthetic circRNAs—delivered via lipid nanoparticles or adeno-associated virus vectors—can produce sustained protein expression that often outlasts conventional messenger RNA therapies. Remarkably, some circRNAs undergo rolling-circle translation, generating repetitive protein products, as shown for circEGFR in glioblastoma, where the resulting protein variant sustains tumor-driving signaling. Others, such as a peptide encoded by circCDYL, exacerbate cardiac hypertrophy, while a protein derived from circFBXW7 suppresses glioma tumorigenesis. The authors also emphasize circRNAs' clinical potential as liquid biopsy biomarkers. For example, plasma levels of hsa_circ_0000190 correlate with immunotherapy response in lung cancer, and serum circAHSA1 tracks gastric cancer progression and lymph node metastasis. Importantly, the first human trial of a circRNA therapeutic—RXRG001 for radiation-induced dry mouth—is already underway, marking a major translational milestone.

“What excites us most is that circRNAs combine stability, specificity, and function in one single package,” the authors said. “They’re not just molecular sponges anymore—many of them actually produce proteins that actively drive disease. That gives us two distinct ways to intervene: we can knock down the circular RNA itself, or we can go after the protein it makes. And because their closed-loop structure resists breakdown, they’re ideal for long-lasting therapies or as stable biomarkers you can easily detect from a simple blood test. We’re really just beginning to explore what they can do.”

These findings pave the way for circRNA-based diagnostics and therapeutics across oncology, cardiology, and neurology. Liquid biopsy panels measuring circulating circRNAs could enable early cancer detection, real-time treatment monitoring, and risk stratification for heart failure patients. Engineered circRNAs expressing therapeutic proteins offer durable, low-immunogenicity alternatives to messenger RNA vaccines and protein replacement therapies. Looking ahead, artificial intelligence-driven tools may help predict which circRNAs are truly translatable, accelerating target discovery and validation. As delivery systems continue to improve, circRNA drugs could become a mainstay of precision medicine—closing the loop from non-invasive diagnosis to targeted, durable treatment in a single molecular platform.

References

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