

EDITORIAL

Cartilage Repair in 2025: Hope, Hype, or Horizon?

Mostafa Shahrezaee, MD ¹; Reza Heidari, PhD ²¹ Trauma and Surgery Research Center, AJA University of Medical Sciences, Tehran, Iran² Medical Biotechnology Research Center, AJA University of Medical Sciences, Tehran, Iran*Overview of Current Cartilage Repair Modalities*

Cartilage injury and degeneration are among the most prevalent musculoskeletal disorders, affecting more than 500 million people worldwide.¹ Autograft transplantation provides an effective treatment for focal cartilage defects, particularly in younger patients; however, its use is limited by donor-site morbidity, restricted graft availability, and biomechanical mismatch.^{2,3} Conventional approaches to cartilage repair include autologous chondrocyte implantation (ACI), bone marrow stimulation or microfracture, stem cell transplantation, and artificial cartilage or biomaterial implants.⁴ Although ACI is considered a major milestone, it frequently results in fibrocartilage with inferior biomechanical properties compared to native tissue. Stem cell-based therapies hold promise due to their multipotency and paracrine effects, yet challenges persist regarding cell engraftment, immunogenicity, and potential tumorigenicity.^{5,6} Microfracture techniques stimulate endogenous repair by creating access channels to the bone marrow; however, they also predominantly generate fibrocartilage, which deteriorates over time.⁴ These limitations have accelerated the shift toward biologically driven, patient-specific regenerative strategies.

Innovations and Technologies in 2025

The landscape of cartilage regenerative medicine has advanced rapidly with the emergence of innovative technologies. Three-dimensional (3D) bioprinting enables the in situ fabrication of patient-specific constructs with precisely organized cellular and extracellular matrix components.^{7,8} Extracellular vesicles (EVs), particularly exosomes, have attracted significant attention as cell-free therapeutics capable of modulating inflammation, enhancing chondrocyte proliferation, and promoting matrix synthesis.⁹ Recent bioengineering strategies have further refined EV targeting, cargo loading, and functional performance, thereby increasing their therapeutic potential. Moreover, genetic engineering tools such as CRISPR are being

investigated to upregulate chondrogenic pathways, while advanced hydrogels and smart biomaterials provide enhanced mechanical support and controlled delivery of bioactive molecules.

Hope

Early clinical evidence indicates that advanced therapies, including engineered exosomes, 3D-bioprinted scaffolds, and combination approaches, may alleviate pain, improve joint function, and promote more effective tissue regeneration—while minimizing the risks of immune rejection and tumorigenicity associated with stem cell transplantation.¹⁰ Advances in high-throughput omics technologies and targeted drug delivery are enabling more precise, patient-tailored interventions, offering the potential for improved clinical outcomes through personalized therapeutics.^{11,12}

Hype

Despite encouraging progress, much of the current enthusiasm remains speculative. Many emerging strategies are still confined to preclinical or early-phase clinical trials. Existing studies frequently involve small sample sizes and short follow-up durations, making it difficult to draw definitive conclusions regarding long-term safety and efficacy.¹³ Furthermore, high production costs, the absence of universally accepted manufacturing standards, regulatory uncertainty, and an incomplete understanding of underlying biological mechanisms continue to hinder large-scale clinical translation. Consequently, inflated expectations in both academic and commercial arenas may overshadow the need for rigorous validation and increase the risk of premature clinical adoption.

Horizon

Looking ahead, the convergence of bioengineering, systems biology, and omics-based precision medicine approaches is poised to transform cartilage repair.¹⁴ Combinatorial strategies—integrating cell-derived exosomes, bioactive scaffolds, gene therapies, and smart nanomedicine—are

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being developed to tackle the multifaceted challenges of cartilage regeneration. Expanding the scale and rigor of clinical trials will be essential for defining best practices, establishing standardized protocols, and ensuring long-term safety. Ultimately, the field is moving toward fully integrated, minimally invasive, and patient-specific regenerative solutions; however, achieving these goals will require both scientific rigor and regulatory clarity.

Conclusion

In 2025, the field of cartilage repair stands at the intersection of promising breakthroughs, inflated expectations, and a future rapidly shaped by technological innovation. While engineered exosomes, bioprinting, and combination therapeutics hold the potential to redefine clinical outcomes, substantial barriers remain before these approaches can be established as standard of care. Sustained research efforts, rigorous clinical validation, and careful translation from laboratory to bedside will be essential for advancing from symptomatic management to true cartilage regeneration for patients worldwide.

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