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A REVIEW ON NANOMATERIALS FOR CARTILAGE REPAIR: INNOVATIONS IN SCAFFOLD DESIGN AND DRUG DELIVERY

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Article History	Abstract
Received on: 04-06-2025 Revised on: 22-07-2025 Accepted on: 16-09-2025	Cartilage damage and osteoarthritis remain major clinical challenges due to the tissue's poor self-healing capacity and limited regenerative potential. Conventional treatments fail to restore native function, underscoring the need for advanced therapeutic strategies. Nanomaterials have emerged as promising candidates for cartilage repair because of their ability to mimic the extracellular matrix, provide structural support, and enable targeted drug delivery. This review highlights recent innovations in nanomaterial-based scaffolds and drug delivery systems for cartilage regeneration. Nanofibers and nanoscaffolds reproduce the fibrous structure of cartilage, while nanoparticles enable controlled release of growth factors, anti-inflammatory drugs, and genetic material. Hydrogels reinforced with nanomaterials offer injectable, bioactive environments, and nanocomposites provide mechanical stability alongside bioactivity. Advances in scaffold design, including biomimetic architectures, biofunctionalization, and 3D bioprinting, are enhancing integration and functional outcomes. Preclinical studies have demonstrated encouraging results in vitro and in vivo, while early clinical trials indicate translational potential. Future perspectives include the development of personalized 3D-printed scaffolds, multifunctional smart nanomaterials, and integration with regenerative medicine approaches. Collectively, nanotechnology represents a transformative platform for durable and functional cartilage repair. Keywords: Nanomaterials, Cartilage repair, Nanoscaffolds, Drug delivery, Osteoarthritis, Tissue engineering.
	
	

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Introduction

Cartilage injuries, particularly in osteoarthritis (OA) and following trauma, remain a significant clinical challenge due to the poor self-healing capacity of cartilage, which is avascular and exhibits limited cellular turnover. Such degenerative diseases result in chronic pain and disability, affecting hundreds of millions worldwide, and place significant socio-economic and healthcare burdens on societies [1]. Conventional treatments, such as pain management, anti-inflammatory drugs, physical therapy, and surgical approaches like microfracture or autologous chondrocyte implantation, often result in reparative cartilage of inferior quality and do not halt the degenerative process [2]. Nanomaterials offer promising avenues in cartilage repair due to their ability to mimic the nanoscale architecture of the extracellular matrix (ECM), thus

fostering chondrocyte adhesion, proliferation, and differentiation [3]. Their high surface area, tunable surface chemistry, and controllable degradation enable the precise local delivery of growth factors and anti-catabolic agents, which can enhance tissue regeneration while reducing systemic side effects [4]. Additionally, nanocomposite scaffolds offer enhanced mechanical strength and flexibility, which are essential for load-bearing applications commonly encountered in articular cartilage [5]. Recent advances highlight innovative uses: nanoparticle-enriched hydrogels simulate the native cartilage microenvironment, thereby improving integration and bioactivity [6]. Magnetic nanomaterials enable the remote activation of mechanotransduction pathways and the alignment of cells within scaffolds, thereby enhancing functional repair [7]. More broadly, nanomedicine is enabling integrated regenerative strategies, including diagnostics, repair, and monitoring that were previously unattainable [8].

Cartilage Biology and Repair Challenges

Articular cartilage is a specialised connective tissue that lines the ends of long bones in synovial joints. Its primary functions are to provide a smooth, low-friction surface for articulation

and to distribute mechanical loads during movement, thereby protecting the underlying bone. Structurally, cartilage is composed of a sparse population of chondrocytes, which are the only resident cell type, embedded within an abundant extracellular matrix (ECM). The ECM is rich in type II collagen that provides tensile strength and a highly hydrated network of proteoglycans, which impart elasticity and resistance to compressive forces. This unique structural organisation allows cartilage to function as a shock absorber and to sustain repetitive mechanical stresses without significant wear [9].

Despite its essential biomechanical function, articular cartilage has a very limited ability for self-repair. A significant barrier is its avascular, aneural, and alymphatic nature, which restricts nutrient diffusion and impedes cellular recruitment to injured sites. Consequently, chondrocytes show minimal mitotic activity, and once the cartilage is damaged, endogenous repair mechanisms are inadequate. Injuries that only penetrate the cartilage layer generally fail to heal and tend to progress into degeneration, often leading to osteoarthritis, one of the most common musculoskeletal disorders worldwide [10,11].

To overcome these biological limitations, researchers have focused on tissue engineering approaches, particularly the development of scaffolds to support cartilage repair. An ideal scaffold must closely mimic the native cartilage microenvironment both structurally and functionally. This includes being biocompatible to avoid adverse immune responses, mechanically stable to withstand the compressive and shear stresses of the joint, and porous to facilitate nutrient exchange, vascular infiltration from surrounding tissue, and cellular migration [12]. Furthermore, scaffolds should be bioactive, promoting chondrocyte adhesion, proliferation, differentiation, and matrix production. In addition, they should be biodegradable, breaking down at a controlled rate so that the newly synthesised tissue gradually replaces the scaffold [13-16]. A scaffold that meets these biological and mechanical requirements would not only restore cartilage structure but also re-establish long-term joint function.

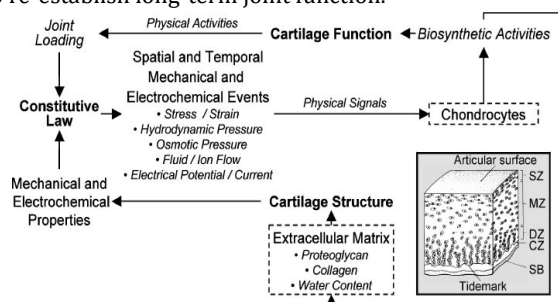


Figure 1: Structure and function of articular cartilage

Nanomaterials in Cartilage Tissue Engineering

Nanofibers and Nanoscaffolds

Nanofibers created through electrospinning or 3D printing closely imitate the fibrous structure of the native extracellular matrix (ECM). They provide physical cues that promote chondrocyte growth and extracellular matrix deposition, thereby supporting the regeneration of cartilage. Electrospun PLGA nanofibers, for example, have been shown to facilitate the multilineage differentiation of mesenchymal stem cells within a 3D environment [17]. Likewise, collagen–chitosan

nanofibers enhanced ECM mimicry and offered improved mechanical strength for cartilage scaffolding [18].

Nanoparticles

Nanoparticles act as targeted carriers for growth factors, anti-inflammatory drugs, or genetic material. For example, chitosan nanoparticles encapsulating TGF- β 1 achieved sustained release and significantly enhanced the chondrogenesis of mesenchymal stem cells [19]. Lipid nanoparticles delivering non-steroidal anti-inflammatory drugs (NSAIDs) have also demonstrated the ability to reduce cartilage degradation in osteoarthritis models. Metallic nanoparticles, including silver and gold, are further explored for their intrinsic anti-inflammatory and antioxidant properties, as well as their potential as theranostic agents [20].

Hydrogels with Nanomaterials

Hydrogels provide a hydrated, injectable, and bioactive environment for cartilage regeneration. When reinforced with nanoparticles, they combine structural support with controlled drug release. For instance, PEG-based hydrogels with silica nanoparticles have been shown to improve stiffness while maintaining chondrocyte viability [21]. Likewise, hyaluronic acid hydrogels with PLGA nanoparticles enabled localised release of insulin-like growth factor-1 (IGF-1), promoting matrix synthesis and improved repair outcomes in cartilage defects [22].

Nanocomposites

Nanocomposites integrate polymers with nanoparticles to yield scaffolds that balance mechanical strength, bioactivity, and biodegradability. A chitosan–hydroxyapatite nanocomposite demonstrated enhanced compressive strength and superior cell adhesion, making it suitable for load-bearing cartilage regions [23]. Collagen–silica nanocomposites similarly provided a synergistic improvement in both mechanical support and biological recognition cues, which are critical for long-term integration with host tissue [24].

Table 01: Examples of Nanomaterials in Cartilage Repair

Nanomaterial Type	Example	Application in Cartilage Repair
Nanofibers & Nanoscaffolds	PLGA electrospun nanofibers	Scaffold for chondrocyte culture
	Collagen–chitosan nanofibers	Tissue engineering scaffold
Nanoparticles	Chitosan nanoparticles loaded with TGF- β 1	Growth factor delivery
	Lipid nanoparticles carrying NSAIDs	Anti-inflammatory therapy
Hydrogels with Nanomaterials	PEG hydrogel with silica nanoparticles	Injectable scaffold
	Hyaluronic acid hydrogel with PLGA nanoparticles	Controlled drug delivery
Nanocomposites	Chitosan–hydroxyapatite nanocomposite	Scaffold material
	Collagen–silica nanocomposite	Hybrid scaffold

Scaffold Design Innovations

Scaffold design has evolved from providing only structural support to acting as an active participant in cartilage regeneration. Modern scaffolds are increasingly developed to mimic the native extracellular matrix (ECM), facilitate cell-matrix interactions, and regulate biochemical signalling.

A significant innovation is the development of biomimetic scaffold architectures that replicate the nano-topography, porosity, and stiffness of native cartilage. The nanoscale arrangement of collagen fibres and proteoglycans in articular cartilage is crucial for directing chondrocyte activity. By reproducing these microstructural features, scaffolds can enhance cell adhesion, proliferation, and matrix synthesis. Furthermore, interconnected porosity enables the transport of nutrients and oxygen, which is essential for maintaining cell viability in avascular tissues such as cartilage [25].

Scaffold functionalization has further enhanced regenerative potential. By incorporating bioactive peptides (e.g., RGD), growth factors (such as TGF- β and BMPs), or gene delivery systems (plasmids, siRNA), scaffolds act as therapeutic delivery platforms in addition to structural frameworks. This dual role transforms scaffolds into bioactive matrices capable of activating signalling pathways, enhancing chondrogenesis, and directing tissue-specific responses [26].

Emerging fabrication methods such as 3D bioprinting and electrospinning have revolutionized precision scaffold engineering. 3D printing enables patient-specific scaffolds that match defect geometry, while electrospinning generates nanofibrous matrices that resemble the fibrillar ECM of cartilage. Both approaches offer precise control over pore size, fiber alignment, and spatial distribution of bioactive cues, improving integration and functional outcomes [27].

Another exciting frontier is the development of “smart” or responsive scaffolds. These scaffolds adapt to local microenvironmental changes, such as pH shifts, enzymatic activity, or temperature fluctuations, and can release therapeutic molecules on demand. This enables spatiotemporal control of growth factor or drug release, ensuring that bioactive signals are delivered at the most effective time and concentration [28]. Collectively, these innovations are transforming scaffolds into dynamic, multifunctional platforms that combine mechanical support with biological regulation, holding immense promise for durable and functional cartilage regeneration.

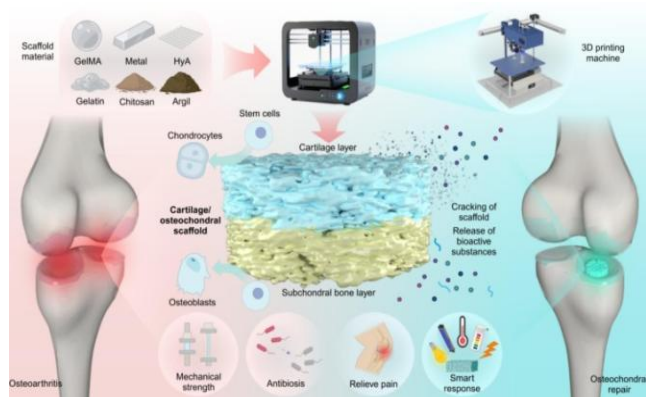


Figure 02: 3D printing of scaffolds for articular cartilage/osteocondral regeneration

Nanomaterial-Based Drug Delivery in Cartilage Repair

Controlled Release of Growth Factors

Growth factors such as transforming growth factor- β (TGF- β), insulin-like growth factor-1 (IGF-1), and bone morphogenetic proteins (BMPs) play crucial roles in promoting chondrocyte proliferation, differentiation, and extracellular matrix (ECM) synthesis. However, their clinical application is limited due to rapid degradation, short half-life, and the need for high systemic doses to achieve therapeutic concentrations. Nanomaterials overcome these barriers by enabling sustained, localised, and bioactive delivery of growth factors directly to cartilage defects. For example, nanoparticles, nanofiber scaffolds, and hydrogel carriers have been utilised to encapsulate TGF- β or BMPs, thereby ensuring controlled release over extended periods and maintaining their bioactivity. This targeted delivery reduces systemic side effects while maximising regenerative outcomes, making nanocarrier-mediated growth factor release a powerful tool in cartilage tissue engineering [29].

Delivery of Anti-Inflammatory Drugs for Osteoarthritis

Osteoarthritis is characterized by chronic low-grade inflammation, with elevated levels of cytokines such as TNF- α , IL-1 β , and IL-6, along with increased COX-2 expression. These inflammatory mediators accelerate cartilage breakdown and impair repair processes. Conventional oral or systemic administration of anti-inflammatory drugs such as NSAIDs and corticosteroids is often associated with poor joint specificity and adverse systemic effects. Nanocarrier-based delivery systems—including PLGA nanoparticles, chitosan nanocarriers, liposomes, and solid lipid nanoparticles—have been developed to directly deliver anti-inflammatory agents to the cartilage microenvironment. Such systems prolong drug residence time within the joint cavity, improve penetration into dense cartilage tissue, and provide long-term suppression of inflammation. For example, curcumin-loaded liposomes demonstrated significant reduction of chondrocyte apoptosis and oxidative stress, while indomethacin-loaded chitosan nanoparticles reduced pro-inflammatory cytokine levels in preclinical models. [30, 31]

Gene Delivery Systems

Genetic strategies provide long-lasting therapeutic effects by directly altering the expression of key genes involved in cartilage degeneration and regeneration. Nanomaterial-based carriers such as cationic lipids, polymeric nanoparticles, dendrimers, and lipid-polymer hybrids have been utilised to deliver plasmid DNA, siRNA, and miRNA to chondrocytes and mesenchymal stem cells. For instance, siRNA-loaded nanoparticles can silence pro-inflammatory genes, such as NF- κ B and MMP-13, thereby reducing cartilage degradation. Conversely, plasmid DNA encoding TGF- β or SOX9 can stimulate chondrogenic differentiation. Importantly, nanocarriers protect nucleic acids from enzymatic degradation, enhance cellular uptake, and enable targeted release within the cartilage matrix. This makes nanomaterial-based gene delivery a promising approach for disease-modifying osteoarthritis therapy [32].

Cell-based Therapies with Nano-carriers

Cell transplantation, particularly with mesenchymal stem cells (MSCs), has emerged as a promising approach for cartilage regeneration due to their ability to differentiate into chondrocytes and secrete trophic factors that modulate the repair environment. However, challenges such as poor survival, low retention, and limited differentiation efficiency reduce their therapeutic impact. The integration of nanomaterials into cell-based therapies has provided solutions to these limitations. Nanofiber scaffolds (e.g., PLGA, PCL electrospun fibers) mimic the structure of the native ECM, improving MSC adhesion and guiding chondrogenic differentiation.⁷ Hydrogels functionalized with nanoparticles further enhance MSC survival by providing a 3D microenvironment and enabling controlled release of growth factors alongside cell delivery.⁸ In addition, innovative approaches such as magnetic nanoparticles combined with scaffolds have enabled remote control of MSC distribution and retention at defect sites. Exosome-loaded nanoparticles derived from MSCs have also shown the ability to deliver regenerative signals without direct cell transplantation, offering reduced immune rejection while maintaining bioactivity [33,34].

Table 2: Nanomaterial-Based Delivery of Anti-inflammatory Drugs in Cartilage Repair

Nanocarrier System	Example Drug	Application in Cartilage Repair
PLGA nanoparticles	Diclofenac, Celecoxib	Local suppression of inflammation in osteoarthritis
Liposomes / Solid lipid nanoparticles	Curcumin, Dexamethasone	Anti-inflammatory & antioxidant protection of chondrocytes
Chitosan nanoparticles	Indomethacin	Reduction of inflammatory cytokines (TNF- α , IL-1 β)
Gold / Silver nanoparticles	Experimental anti-inflammatory effects	Modulation of oxidative stress and inflammation

Table 3: Nanomaterial-Assisted Cell-Based Therapies in Cartilage Repair

Nano-Approach	Cell Type	Application
Nanofiber scaffolds (e.g., PLGA, PCL)	MSCs	Support chondrogenic differentiation
Nanoparticle-modified hydrogels (HA, PEG, collagen)	MSCs, chondrocytes	Cell encapsulation and sustained GF/drug release
Magnetic nanoparticles with scaffolds	MSCs	Cell guidance & retention at defect site
Exosome-loaded nanoparticles	MSC-derived exosomes	Delivery of regenerative signals without direct cell transplantation

Preclinical and Clinical Studies

In vitro Studies

In vitro investigations are the first step in evaluating the potential of nanomaterials for cartilage regeneration. These studies typically involve culturing primary chondrocytes or mesenchymal stem cells (MSCs) on nanofiber scaffolds, nanoparticle-modified hydrogels, or nanocomposites to assess cell adhesion, proliferation, viability, and differentiation. For example, electrospun PLGA nanofibers have been shown to enhance MSC chondrogenic differentiation, while nanocomposite hydrogels incorporating silica or hydroxyapatite nanoparticles improve mechanical strength and matrix deposition. In vitro assays also help determine the biocompatibility and cytotoxicity of nanomaterials before animal or clinical testing [35-37].

In vivo Animal Models

Preclinical animal models are essential for evaluating the regenerative efficacy and safety of nanomaterial-based scaffolds and drug delivery systems. Small animal models, such as mice and rats, are frequently used for mechanistic studies, while rabbit and goat osteochondral defect models provide valuable insights into load-bearing cartilage repair. For example, PLGA/chitosan nanoscaffolds implanted in rabbit knee defects promoted hyaline-like cartilage formation, and hydrogel-nanoparticle composites demonstrated improved integration with host cartilage in rat models. Large animal studies, such as those in sheep or pigs, further validate the biomechanical functionality and durability under physiological joint loading [38-40].

Clinical Trials and Translational Potential

Although still in the early stages, several clinical studies are beginning to explore nanomaterial-based strategies for cartilage repair. Most are pilot or Phase I/II studies focusing on safety, feasibility, and preliminary efficacy. For example, injectable hyaluronic acid hydrogels with nanoparticles have been investigated for osteoarthritis treatment, showing improvements in pain reduction and joint function. Similarly, nanofiber scaffolds seeded with autologous chondrocytes or MSCs are under evaluation for focal cartilage defects. Translational progress remains cautious, but preclinical success and favorable early clinical outcomes underscore the potential of nanotechnology to bridge the gap between laboratory research and clinical application [41-43].

Table 4: Examples of Preclinical and Clinical Studies in Nanomaterial-Based Cartilage Repair

Study Type	Nanomaterial Approach	Model/Setting
In vitro	Electrospun PLGA nanofibers	Human MSC culture
In vitro	Nanocomposite hydrogel with silica nanoparticles	Chondrocyte culture
In vivo	PLGA/chitosan nanoscaffold	Rabbit knee defect model
In vivo	Hydrogel-nanoparticle composite	Rat osteochondral defect
In vivo (large animal)	Collagen-nanohydroxyapatite scaffold	Sheep model
Clinical (pilot trial)	HA-nanoparticle injectable hydrogel	OA patients
Clinical (Phase I/II)	Nanofiber scaffold + autologous chondrocytes	Focal cartilage defects
Clinical (Translational study)	MSC-seeded nanoscaffold	OA patients

Future Perspectives

The future of nanomaterial-based cartilage repair is moving toward more personalized and multifunctional strategies. Personalized 3D-printed nanoscaffolds hold the potential to create patient-specific implants that precisely match defect geometry and mechanical requirements, while smart nanomaterials capable of dual functions—such as promoting regeneration and simultaneously delivering anti-inflammatory signals—could enhance therapeutic outcomes. The integration of artificial intelligence and computational modeling in scaffold design will enable predictive optimization of material properties and drug release kinetics, accelerating translational success. Furthermore, combining nanomedicine with regenerative medicine approaches, including stem cell and gene-based therapies, is expected to generate synergistic platforms that address both structural restoration and biological modulation, paving the way for durable and functional cartilage regeneration.

Conclusion

Nanomaterial-based strategies have opened new avenues for cartilage repair by combining structural mimicry with targeted therapeutic delivery. Preclinical evidence shows that nanofibers, nanoparticles, hydrogels, and nanocomposites can significantly enhance chondrocyte function, extracellular matrix deposition, and overall tissue regeneration. Clinical

studies, though limited, are beginning to validate safety and efficacy, marking an important step toward translation. The integration of 3D printing, smart responsive systems, and stem cell therapies with nanomaterials further strengthens their potential. While challenges related to long-term safety, scalability, and regulatory approval remain, nanotechnology offers a promising pathway toward effective, durable, and patient-specific solutions for cartilage regeneration.

Author Contributions

Atluri Divya Sri Madhavi, Bojja Naga Vennela, Chiriki Laxmi Vaishnavi, Chittela Pravallika, Dasari Maheswari, Kaki Tanmayi Sree, and Achanti Suneetha contributed to data collection, analysis, and manuscript preparation. Patibandla Jahnavi conceptualized, supervised, and finalized the manuscript.

Conflict of Interest

The authors declare that there is no conflict of interest

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References

- Sophia Fox AJ, Bedi A, Rodeo SA. The basic science of articular cartilage: structure, composition, and function. *Sports Health*. 2009 Nov;1(6):461–8.
- Huey DJ, Hu JC, Athanasiou KA. Unlike bone, cartilage regeneration remains elusive. *Science*. 2012 Nov 23;338(6109):917–21.
- Goldring MB, Goldring SR. Articular cartilage and subchondral bone in the pathogenesis of osteoarthritis. *Ann N Y Acad Sci*. 2010 Mar;1192:230–7.
- Makris EA, Gomoll AH, Malizos KN, Hu JC, Athanasiou KA. Repair and tissue engineering techniques for articular cartilage. *Nat Rev Rheumatol*. 2015 Jan;11(1):21–34.
- Benders KE, van Weeren PR, Badylak SF, Saris DB, Dhert WJ, Malda J. Extracellular matrix scaffolds for cartilage and bone regeneration. *Trends Biotechnol*. 2013 Mar;31(3):169–76.
- Chawla S, Kumar A, Admane P, Kumar V, Sharma A, Jaiswal AK, et al. Scaffold-based approaches for cartilage tissue engineering: current status and future directions. *Biomed Mater*. 2020 Apr 20;15(4):042001.
- Irawan V, Sung TC, Higuchi A, Ikoma T. Collagen scaffolds in cartilage tissue engineering and relevant approaches for future development. *Tissue Eng Regen Med*. 2018 Oct;15(5):673–97.

8. Gong T, Xie J, Liao J, Zhang T, Lin S, Lin Y. Nanomaterials and bone regeneration. *Bone Res.* 2015;3:15029.
9. Sophia Fox AJ, Bedi A, Rodeo SA. The basic science of articular cartilage: structure, composition, and function. *Sports Health.* 2009 Nov;1(6):461–8.
10. Huey DJ, Hu JC, Athanasiou KA. Unlike bone, cartilage regeneration remains elusive. *Science.* 2012 Nov 23;338(6109):917–21.
11. Goldring MB, Goldring SR. Articular cartilage and subchondral bone in the pathogenesis of osteoarthritis. *Ann N Y Acad Sci.* 2010 Mar;1192:230–7.
12. Makris EA, Gomoll AH, Malizos KN, Hu JC, Athanasiou KA. Repair and tissue engineering techniques for articular cartilage. *Nat Rev Rheumatol.* 2015 Jan;11(1):21–34.
13. Benders KE, van Weeren PR, Badylak SF, Saris DB, Dhert WJ, Malda J. Extracellular matrix scaffolds for cartilage and bone regeneration. *Trends Biotechnol.* 2013 Mar;31(3):169–76.
14. Chawla S, Kumar A, Admane P, Kumar V, Sharma A, Jaiswal AK, et al. Scaffold-based approaches for cartilage tissue engineering: current status and future directions. *Biomed Mater.* 2020 Apr 20;15(4):042001..
15. Irawan V, Sung TC, Higuchi A, Ikoma T. Collagen scaffolds in cartilage tissue engineering and relevant approaches for future development. *Tissue Eng Regen Med.* 2018 Oct;15(5):673–97.
16. Gong T, Xie J, Liao J, Zhang T, Lin S, Lin Y. Nanomaterials and bone regeneration. *Bone Res.* 2015;3:15029.
17. Li WJ, Tuli R, Huang X, Laquerriere P, Tuan RS. Multilineage differentiation of human mesenchymal stem cells in a three-dimensional nanofibrous scaffold. *Biomaterials.* 2005 Apr;26(25):5158–66.
18. Bhardwaj N, Kundu SC. Electrospinning: a fascinating fiber fabrication technique. *Biotechnol Adv.* 2010 May-Jun;28(3):325–47. doi:10.1016/j.biotechadv.2010.01.004.
19. Makadia HK, Siegel SJ. Poly lactic-co-glycolic acid (PLGA) as biodegradable controlled drug delivery carrier. *Polymers (Basel).* 2011;3(3):1377–97.
20. Zhang X, Reagan MR, Kaplan DL. Electrospun silk biomaterials for regenerative medicine. *Adv Drug Deliv Rev.* 2009 Nov;61(12):988–1006.
21. Gong T, Xie J, Liao J, Zhang T, Lin S, Lin Y. Nanomaterials and bone regeneration. *Bone Res.* 2015;3:15029.
22. Oliveira JT, Gardel LS, Rada T, Martins L, Gomes ME, Reis RL. Injectable gellan gum hydrogels with autologous cells for the treatment of cartilage defects in a rabbit model. *Tissue Eng Part A.* 2010 Sep;16(4):1091–101.
23. Basha RY, Doble M. Design of biocomposite materials for bone tissue regeneration. *Mater Sci Eng C Mater Biol Appl.* 2015 Mar;57:452–63. doi:10.1016/j.msec.2015.07.081.
24. Irawan V, Sung TC, Higuchi A, Ikoma T. Collagen scaffolds in cartilage tissue engineering and relevant approaches for future development. *Tissue Eng Regen Med.* 2018 Oct;15(5):673–97.
25. Qi Y, Zhao T, Yan W, Xu K, Shi Z, Wang J, et al. Biomaterials for the delivery of growth factors and drugs in cartilage tissue engineering. *J Control Release.* 2019;317:242–56. doi:10.1016/j.jconrel.2019.11.006.
26. Makadia HK, Siegel SJ. Poly lactic-co-glycolic acid (PLGA) as biodegradable controlled drug delivery carrier. *Polymers (Basel).* 2011;3(3):1377–97.
27. Bhardwaj U, Burgess DJ. A novel NF-kappaB inhibitor for treatment of inflammatory diseases. *J Control Release.* 2010;148(1):8–16.
28. Yan C, Zhang R, Gong W, Yin F, Wang H, Chen Y, et al. Curcumin-loaded liposomes suppress inflammation and apoptosis in chondrocytes to protect against osteoarthritis. *J Nanobiotechnology.* 2022;20:35.
29. Hu S, Chen X, Liang Y, Guo C, Yin Z, Luo Y, et al. Indomethacin-loaded chitosan nanoparticles enhance anti-inflammatory efficacy in osteoarthritis models. *Int J Pharm.* 2019;558:19–28.
30. Sharma A, Kaur K, Arora A, Tiwari A. Gene delivery systems for cartilage regeneration: current strategies and future directions. *Mol Pharm.* 2021;18(7):2488–2505.
31. Chen FH, Rousche KT, Tuan RS. Technology Insight: adult stem cells in cartilage regeneration and tissue engineering. *Nat Clin Pract Rheumatol.* 2006;2(7):373–82.
32. Wang X, Wang Y, Gou W, Lu Q, Peng J, Lu S. Role of mesenchymal stem cells in cartilage regeneration and bone repair. *Stem Cells Int.* 2017;2017:8835129.
33. Yan LP, Silva-Correia J, Oliveira MB, Vilela C, Pereira H, Sousa RA, et al. Bilayered silk/silk-nanoCaP scaffolds for osteochondral tissue engineering: in vitro and in vivo assessment. *Acta Biomater.* 2015;12:227–41.
34. Zhang S, Chuah SJ, Lai RC, Hui JHP, Lim SK, Toh WS. MSC exosomes mediate cartilage repair by enhancing proliferation, attenuating apoptosis and modulating immune reactivity. *Biomaterials.* 2016;156:16–27.
35. Li WJ, Tuli R, Huang X, Laquerriere P, Tuan RS. Multilineage differentiation of human mesenchymal

- stem cells in a three-dimensional nanofibrous scaffold. *Biomaterials*. 2005;26(25):5158–66.
36. Irawan V, Sung TC, Higuchi A, Ikoma T. Collagen scaffolds in cartilage tissue engineering and relevant approaches for future development. *Tissue Eng Regen Med*. 2018;15(5):673–97.
37. Basha RY, Doble M. Design of biocomposite materials for bone and cartilage tissue regeneration. *Mater Sci Eng C*. 2015;57:452–63.
38. Yan C, Sun J, Ding J, Chen X. Injectable nanocomposite hydrogel for cartilage tissue regeneration. *ACS Appl Mater Interfaces*. 2016;8(39):24281–92.
39. Hu S, Chen X, Liu M, Zhao Y, Shen J, Guo C, et al. Injectable silk fibroin hydrogel with mesoporous silica nanoparticles for cartilage regeneration. *ACS Appl Bio Mater*. 2020;3(5):3030–41.
40. Yan LP, Silva-Correia J, Oliveira MB, Vilela C, Pereira H, Sousa RA, et al. Bilayered silk/silk-nanoCaP scaffolds for osteochondral tissue engineering: in vitro and in vivo assessment. *Acta Biomater*. 2015;12:227–41.
41. Guo W, He Y, Zhang X, Lu W, Wang X, Guo Q. Clinical translation of advanced hydrogel-based systems for cartilage repair. *Bioact Mater*. 2021;6(10):3129–47.
42. Kon E, Filardo G, Di Martino A, Marcacci M. A novel nanostructured scaffold for cartilage regeneration: pilot clinical trial results at 1 year. *Clin OrthopRelat Res*. 2010;468(1):237–45.
43. Brittberg M, Recker D, Ilgenfritz J, Saris DB. Matrix-applied characterized autologous cultured chondrocytes versus microfracture: 2-year follow-up of a randomized study. *Am J Sports Med*. 2018;46(6):1343–51.