Journal of Multidisciplinary Healthcare

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Adipose-Derived Stem Cells for Cartilage Tissue Engineering: A Bibliometric Analysis of Trends and Themes

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Purpose: Adipose-derived stem cells (ADSCs) have shown great potential in cartilage tissue engineering (TE) due to their accessibility, high proliferation rate, and chondrogenic differentiation capacity. This study aims to systematically evaluate research trends, collaboration patterns, and emerging themes in ADSC-based cartilage TE through a bibliometric analysis, providing actionable insights to address knowledge gaps and advance the field.

Patients and Methods: A systematic search was conducted on the Web of Science Core Collection (WoSCC) database to identify publications related to ADSCs and cartilage TE. Bibliometric and visualized analysis was performed using VOSviewers (V 1.6.20), CiteSpace (V 6.3.R1) and Bibliometrix (R 4.3.3).

Results: A total of 436 English articles were analyzed, involving 2356 authors from 1532 institutions across 50 countries/regions, contributing to 189 journals. The annual growth rate of publications was 8.73%, peaking in 2021. China contributed the most articles (n=127, 29.1%), followed by the USA (n=65, 14.9%). Leading institutions included Kaohsiung Medical University and Duke University. *Tissue Engineering Part A* had the highest H-index (21) and the most publications (n = 26). Reis Rui L. and Gomes Manuela E. were among the most influential contributors. Keyword analysis revealed an early focus on "in-vitro" studies and "bone-marrow", which later transitioned to "chondrogenic differentiation", "growth", and "regeneration". Recent trends since 2020 include "3D printing", "mesenchymal stem cells", and "cartilage repair", reflecting the field's evolution towards advanced technologies and translational applications.

Conclusion: This bibliometric analysis provides valuable guidance for researchers, clinicians, and policymakers, emphasizing the necessity of addressing translational challenges and fostering global collaboration to develop clinically effective solutions for cartilage repair and regeneration.

Keywords: bibliometrics, research trends, cartilage repair, tissue engineering, adipose-derived stem cells, citespace, VOSviewer

Introduction

Cartilage is a specialized connective tissue that serves as a gliding interface in diarthrodial joints, enabling smooth joint movements and absorbing mechanical stress. Its unique structure provides limited structural support for embedded chondrocytes while maintaining its primary role in facilitating low-friction articulation in joints.[1] However, defects and diseases of cartilage, such as osteoarthritis and traumatic injuries, are highly prevalent and can significantly impact an individual's quality of life. These conditions are often accompanied by symptoms such as pain, stiffness, and restricted mobility.[2] Current therapeutic options, such as pharmacological treatments, physical therapy, and surgical interventions, are unable to fully restore cartilage function and structure, highlighting the unmet clinical need for more effective solutions.[3] This need has driven researchers to explore cartilage tissue engineering (TE), a field that seeks to develop

Received: 12 February 2025
Accepted: 29 April 2025
Published: 30 May 2025

functional cartilage substitutes by combining cells, scaffolds, and bioactive factors.[4] Cartilage TE leverages principles of regenerative medicine to mimic natural repair processes, offering promising avenues for cartilage repair and regeneration.[5]

To date, several cell-based therapies have been developed for cartilage repair. For example, autologous chondrocyte implantation (ACI), which uses expanded autologous chondrocytes, has been approved for clinical use in multiple regions, including the United States, Canada, and Europe. While ChondroCelect, the first ACI product approved in Europe, was later withdrawn from the market, other ACI-like products, such as MACI and Carticel, remain commercially available and widely used.[6] These therapies, while beneficial for focal cartilage repair, are not classified as tissue-engineered products but rely on autologous cell implantation.[7] As such, they represent an important step in cartilage repair but highlight the need for more advanced approaches to address broader cartilage defects.[8,9]

Among various cell sources explored for cartilage TE, adipose-derived stem cells (ADSCs) have garnered significant attention since the early 2000s due to their abundance,[4] ease of harvest, and ability to differentiate into chondrocytic, osteogenic, and adipogenic lineages.[10] ADSCs possess an autologous nature, which minimizes immune rejection risks, making them a promising candidate for regenerative medicine applications.[11] Despite their potential, challenges remain in translating ADSC-based therapies into clinical practice. These include optimizing cell differentiation protocols, developing effective scaffolds, and evaluating long-term outcomes.[12] Addressing these challenges requires a comprehensive understanding of the current research trends and themes in ADSC-based cartilage TE.

Bibliometric analysis is a valuable tool for quantitatively and qualitatively assessing published research articles to identify key trends, emerging themes, and future directions.[13] While bibliometric studies have been conducted in broader areas of tissue engineering and regenerative medicine,[14–16] there has been no bibliometric analysis focusing on ADSC-based cartilage TE. By analyzing publication trends, productive countries, institutions, journals, authors, and research themes, this study aims to provide insights into the current research landscape and predict future research hotspots. This work seeks to inform researchers and guide future efforts in advancing ADSC-based cartilage TE.

Material and Methods

Data Source and Literature Search Strategy

The bibliometric analysis was conducted using the Web of Science Core Collection (WoSCC), a widely utilized multidisciplinary database that provides high-quality citation data for bibliometric studies. WoSCC was chosen due to its comprehensive coverage of peer-reviewed journals and its focus on citation relationships, which are essential for bibliometric analysis.[17] The literature search was conducted on November 6, 2024, to ensure consistency and avoid database updates during the study. The search formula used was: TS = (“adipose derived stem cells” OR “adipose stem cells” OR “adipose tissue stem cells” OR “adipose tissue derived stem cells” OR “adipose derived mesenchymal stem cells” OR “adipose tissue derived mesenchymal stem cells” OR “adipose tissue mesenchymal stem cells” OR “adipose derived mesenchymal stromal cells” OR “adipose tissue derived mesenchymal stromal cells” OR “adipose derived adult stem cells” OR “fat tissue stem cells” OR “stem cells derived from adipose tissue” OR “stem cells from adipose tissue” OR “stem cells from fat” OR “stromal stem cells from adipose tissue” OR “mesenchymal stem cells derived from adipose tissue” OR “mesenchymal stem cells from adipose tissue” OR “stromal cells from adipose tissue”) AND TS = (cartilage tissue engineer*).[18–20] The Boolean search term “cartilage tissue engineer*” was used to include both “engineer” and “engineering”, ensuring comprehensive retrieval of relevant literature. Figure 1 illustrates the literature identification and screening process. A total of 492 studies were identified, and 436 studies were included after applying the following criteria: Inclusion criteria: 1. Peer-reviewed journal articles published in English; 2. Articles focusing on ADSC-based cartilage tissue engineering; 3. Studies containing experimental or quantitative bibliometric data. Exclusion criteria: Non-English articles (n = 6), reviews (n = 31), meeting abstracts (n = 5), duplicate records (n = 0), and other irrelevant documents (n = 14). The final dataset included publication year, citation counts, titles, countries/regions, institutions, journals, author details, and keywords.

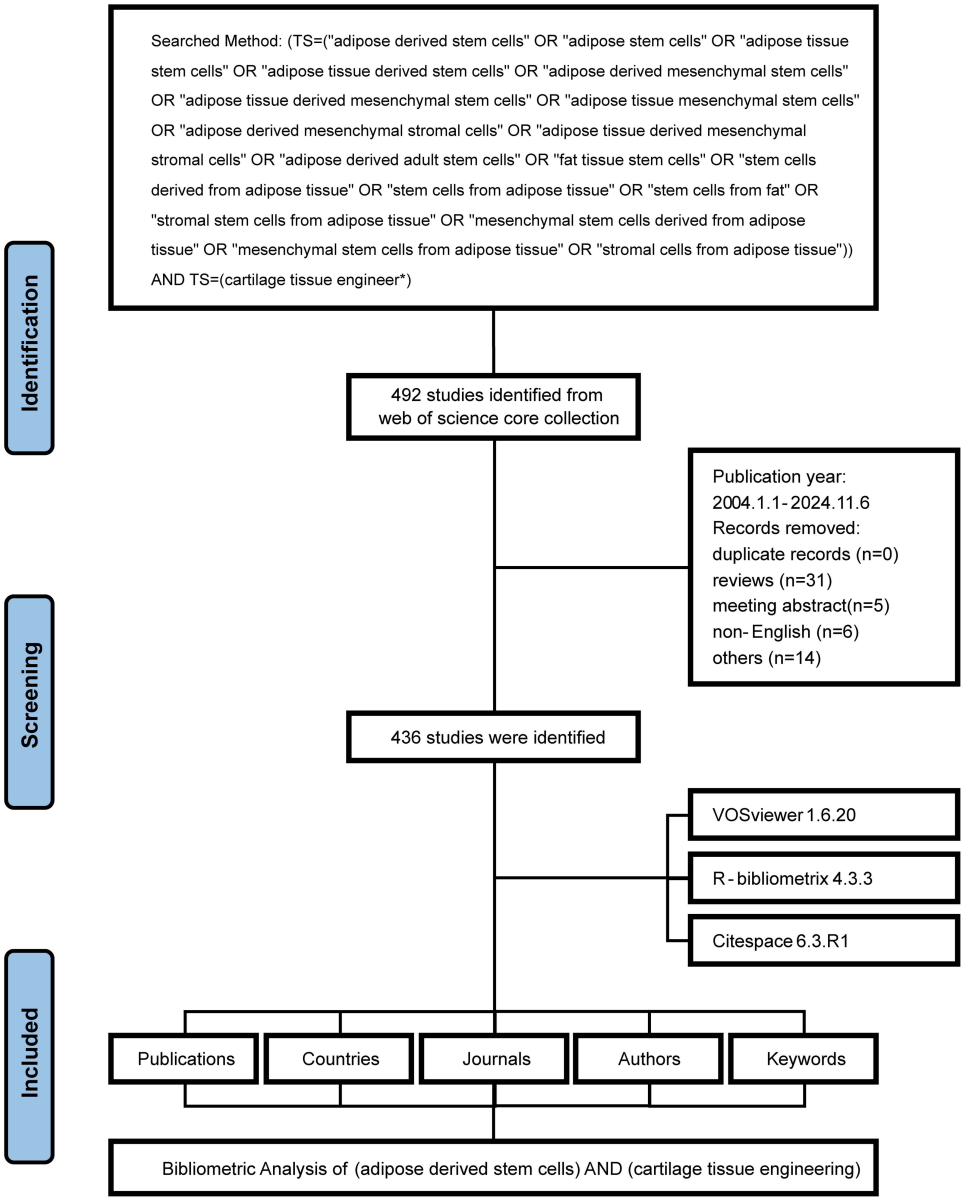

Figure 1 Flow diagram of the bibliographic retrieval process.

Statistical Analysis

Bibliometric indicators were computed using Microsoft Excel, and advanced analyses were conducted with VOSviewer (V1.6.20), CiteSpace (V6.3.R1), and R-bibliometrix (R 4.3.3) (https://bibliometric.com/), which have been validated in previous bibliometric studies and are widely recognized for their accuracy and reliability in analyzing large datasets.[21–23] VOSviewer generated co-occurrence maps and visualized collaborative networks of countries, institutions, and authors. Nodes represented entities, with size denoting frequency and color indicating clusters or average publication year.[21,24] CiteSpace produced time-zone maps to analyze research trends and emergent topics over time using keyword co-occurrence data.[22] By using keywords as node types and slicing the data annually, a visual timeline highlighted the top 5 keywords in each slice through a combined pruning method. The resulting maps displayed clusters of research topics, with size reflecting significance and color gradient indicating the duration of research activity over time.[23] R 4.3.3 calculated bibliometric indices (H-index, G-index, and M-index) for authors and institutions and generated additional visualizations.[25] The H-index, also known as the Hirsch index, is calculated by considering a researcher's papers sorted by the number of citations they have

received in descending order. The H-index is the largest number h such that the researcher has at least h papers each cited at least h times.[26] The G-index is computed similarly to the H-index but with different criterion. The papers are ranked in decreasing order of citations, and the G-index is the largest number g such that the top g papers together have received at least g^2 citations. This index provides a supplementary measure to the H-index and is often higher.[27] The M-index is a variant that considers the researcher's academic career duration. It measures the annual H-index since the researcher first published a paper.[28] This index helps to compare researchers with different career lengths more fairly by normalizing the H-index over time. In this study, authors' H-indices were retrieved directly from the WoSCC database. To evaluate journal influence, Journal Citation Reports (JCR) metrics such as the 2023 impact factor (IF) and 2023 quartile ranking (Q1-Q4) were employed. The IF reflects the average citations per article within a year, while quartile ranking categorizes journals into four impact groups, with Q1 denoting the highest tier.

Results

Overview of Publications

According to the search strategy, 436 publications regarding ADSCs for cartilage TE between 2004 and 2024 met the inclusion and exclusion criteria, and all of them were English articles (Figure 1). A total of 2356 authors, representing 1532 institutions across 50 countries or regions, contributed to the publications. These works were distributed among 189 journals and cited 14,945 references. Each publication averaged 7.01 co-authors and exhibited an international collaboration rate of 18.81%. Additionally, the publications covered 929 keywords, with an average of 37.98 citations per publication (Figure 2A). The top 50 most cited articles are listed in Table S1.

From 2004 to 2024, the annual growth rate of article publications in this field was 8.73%. In the early years (2004–2007), the annual number of publications was relatively low (below 5). From 2008 to 2021, the number of publications showed a fluctuating upward trend, reaching a peak in 2021 (43 articles). In the subsequent years (2022-–2024), a declining trend was observed (Figure 2B).

Distribution and Collaborative Networks of Countries

Among 50 countries or regions, China contributed the largest volume of articles (n = 127, 29.1% of the total) and ranked second in total citations (TC = 3586). The USA had the second volume of articles (n = 65, 14.9%), while ranked first in terms of total citations (TC = 5157). Also, the USA had the largest number of multiple country publications (MCP = 16), with a higher proportion (0.246) compared to China (0.110). Iran ranked third in the number of articles (n = 50, 11.5%) and fourth in total citations (TC = 950). South Korea ranked third in total citations (TC = 1176) (Figure 3A and Table S2).

Among 30 countries involved in international collaborations with a minimum of 2 articles, the USA is the center, with the highest strength in collaborations (total link strength = 47). It actively engaged in collaboration with international partners such as China (total link strength = 26, ranking second), the UK (total link strength = 16, ranking third), Iran (total link strength = 15), and South Korea (total link strength = 8) (Figure 3B).

Distribution and Collaborative Networks of Institutions

A total of 1532 institutions published research in this field. Among the top 10 institutions in terms of article count, Kaohsiung Medical University in China led with 64 articles, followed by the Duke University in the USA (n = 30) and the University Do Minho in Portugal (n = 27) (Figure 4A). Among the 98 institutions involved in international collaborations with a minimum of 2 articles, University of Tehran in Iran had the highest number of collaborations with others (total link strength = 20), followed by Shanghai Jiao Tong University in China (total link strength = 19) and Pasteur Institute of Iran (total link strength = 19) (Figure 4B).

Authors and Co-Authors

A total of 2356 authors contributed to these publications. Reis Rui L. led the high-impact authors with an H-index of 15, G-index of 17, M-index of 1.00, and the highest number of publications (TP = 17). Gomes Manuela E. followed with an

Figure 2 Analysis of the general information. (**A**) A summary of quantitative analysis of the publications. (**B**) Annual output of research from 2004 to 2024.

H-index of 11, G-index of 11, M-index of 0.73 and 11 publications (ranking third). In third place was Guilak Farshid, who recorded an H-index of 11, G-index of 13, M-index of 0.69, 13 publications (ranking second) and 1409 total citations (ranking second) (Table S3).

Among the 62 authors involved in international collaborations with a minimum of 2 articles, Guo, Quanyi had the highest number of collaborations with other authors (total link strength = 81), followed by Peng, Jiang (total link strength = 73) and Lu, Shibi (total link strength = 68) These three authors are the core of the most intensively communicating red research cluster. Additionally, authors within the green cluster also exhibited close collaboration (Figure 5).

Contributions and Collaborative Networks of Journals

The articles included have been published in 189 different journals. *Tissue Engineering Part A* (IF 2023 = 3.5, Q3) led the high impact journals with an H-index of 21, most publications (TP = 26) and 603 citations (ranking second). *Biomaterials* (IF 2023 = 12.8, Q1) followed closed with an H-index of 17, 17 publications (ranking third) and most citations (TC = 1611). Acta Biomaterialia (IF 2023 = 9.4, Q1) ranked third with an H-index of 13 (Table S4).

The co-occurrence network measured the frequency of joint citations among journals within the same articles, reflecting thematic convergence through strong links. Among 71 journals with at least 2 occurrences, the three key journals with the highest total link strength were *Tissue Engineering Part A* (total link strength = 113), *Biomaterials* (total link strength = 100), and *Acta Biomaterialia* (total link strength = 45) (Figure 6A).

The journal coupling network assesses interconnectedness by examining shared references in articles, with strong links indicating substantial overlap in these references and underscoring a common intellectual foundation. Among 71

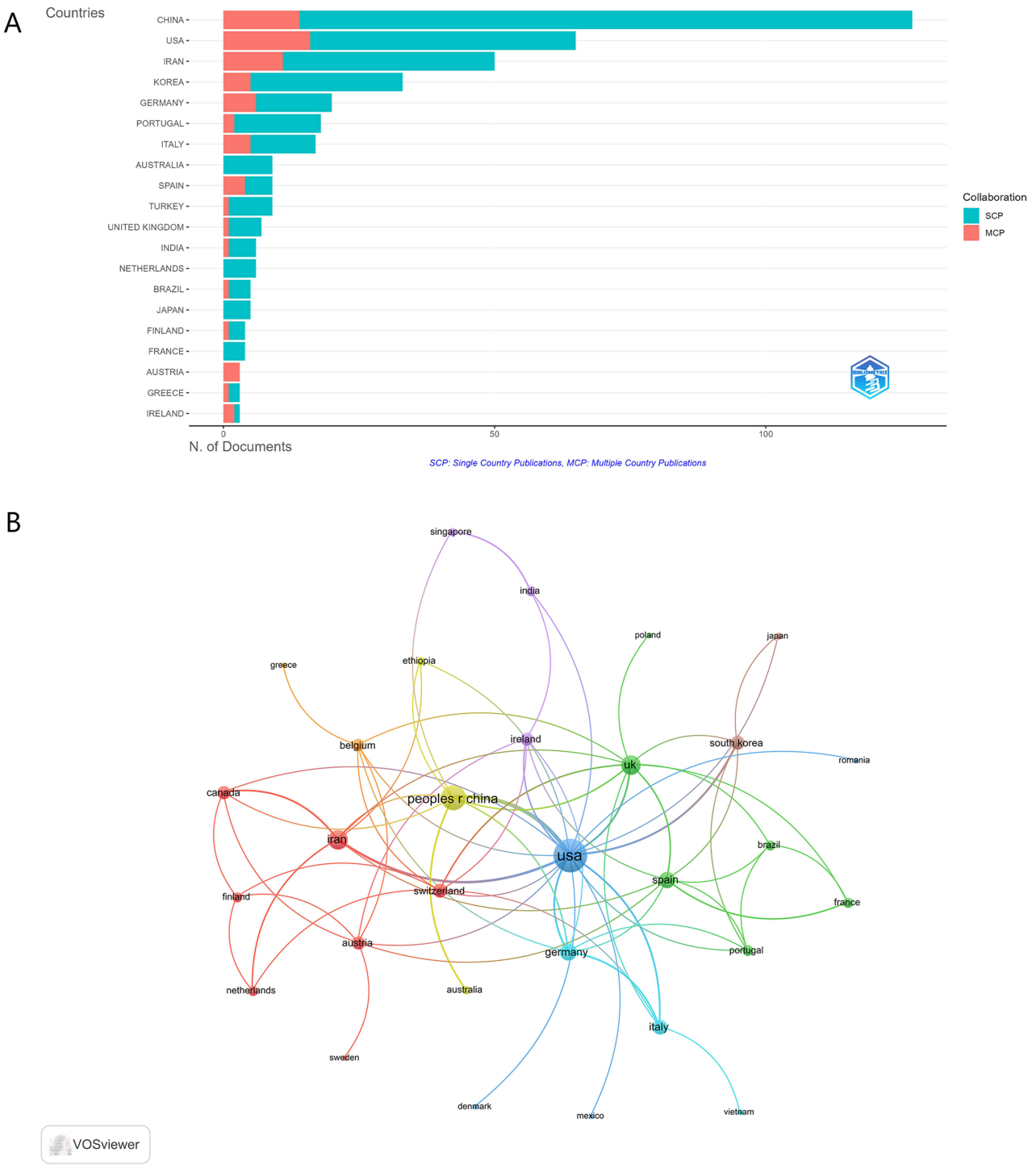

Figure 3 Analysis of countries. (**A**) Distribution of responding author's publications by country. (**B**) Visualization map depicting collaboration among different countries.

journals with at least 2 couplings, the three key journals with the highest total link strength were *Tissue Engineering Part A* (total link strength = 4764), *Biomaterials* (total link strength = 3254), and *Journal of Tissue Engineering and Regenerative Medicine* (total link strength = 2403) (Figure 6B).

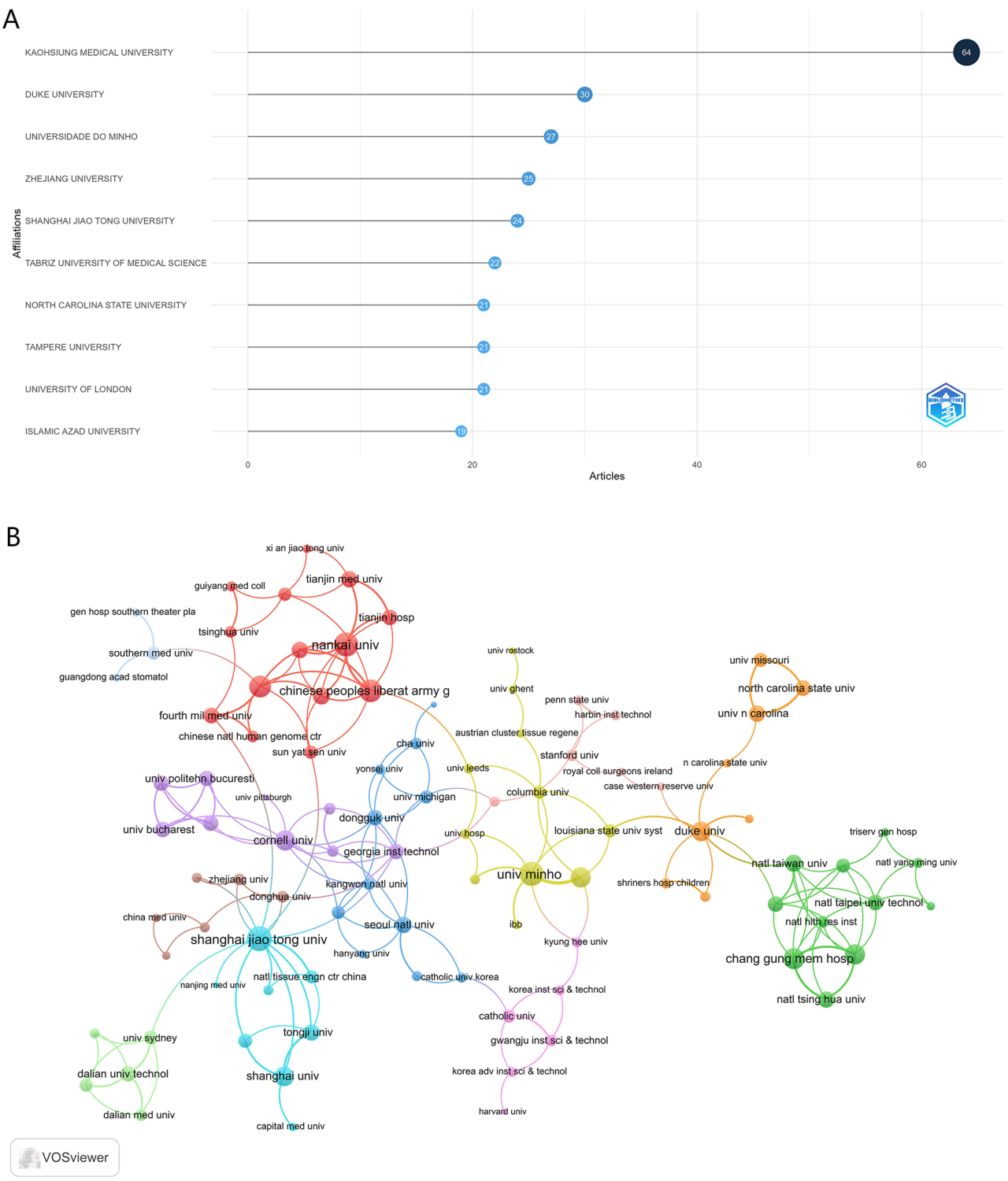

Figure 4 Analysis of institutions. (**A**) Top 10 institutions ranked by article count. (**B**) Visualization map depicting collaboration among different institutions.

Keyword Co-Existence Network and Burst Keywords

In total, 115 keywords with a minimum of 5 occurrences were identified for co-occurrence network analysis. These keywords were classified into different clusters as shown in Figure 7A. The blue cluster focuses on in-vitro experimentation related to bone and cartilage growth, including "in-vitro", "bone", "growth" and "culture". The red cluster

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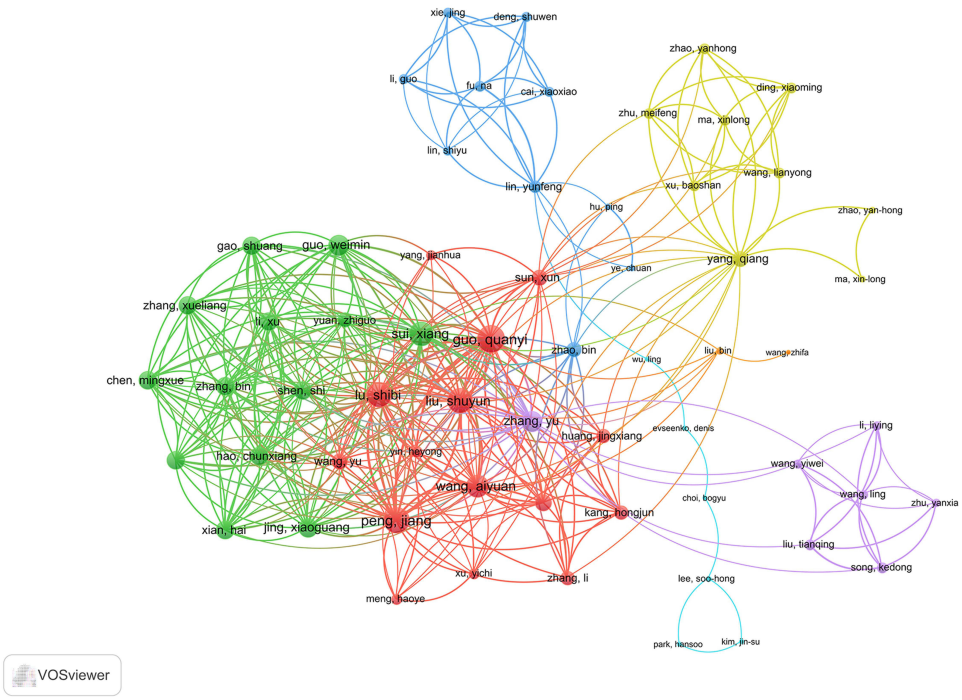

Figure 5 The visualization map depicting collaboration among authors.

emphasizes the regeneration of tissues, particularly through the use of scaffolds and the extracellular matrix in the fabrication process, such as "regeneration", "scaffolds", "extracellular matrix" and "fabrication". The green cluster revolves around the repair of tissues using stem cells, including "repair", "differentiation", "bone-marrow", and "chondrocytes". The purple cluster includes "tissue", "matrix", "in-vitro chondrogenesis", "induction", highlighting the induction of chondrogenesis. The yellow cluster focuses specifically on "stromal cells" and their "chondrogenic differentiation".

Subsequently, a plot was created based on the average time of occurrence of these keywords (Figure 7B). "In-vitro" was the keyword with the highest co-occurrence strength (strength = 630), emerging relatively early around 2014 (purple). Other notable keywords that appeared during the same period include "stromal cells" and "bone-marrow". Subsequently, around 2015–2016 (dark green), keywords with higher strength include "tissue", "differentiation", and "repair". Around 2017 (light green), "chondrogenic differentiation", "growth", and "regeneration" emerged. Around 2018 (yellow), keywords such as "extracellular matrix", "stem cells", and "scaffold" exhibited high co-occurrence intensity.

The top 20 keywords with the strongest citation bursts between 2004 and 2024 are listed in Figure 7C. From 2005 to 2015, the high strength burst keywords included "progenitor cells" (strength = 6.71), "gene expression" (strength = 5.46), and "in vitro chondrogenesis" (strength = 3.31). From 2015 to 2019, "osteoarthritis" (strength = 9.45) was the keyword with the highest burst strength, and this burst has continued to the present. Other burst keywords during the same period included "proliferation" (strength = 5.58) and "osteogenic differentiation" (strength = 4.81). In recent years (starting from 2020), the bursts of "3D printing" (strength = 3.35), "mesenchymal stem cells" (strength = 4.59) and "cartilage repair" (strength = 3.01) have consistently continued until now.

Discussion

This bibliometric analysis provides a comprehensive overview of the research trends, collaboration patterns, and key themes in ADSCs-based cartilage TE from 2004 to 2024. A total of 436 English publications were analyzed, representing the contributions of 2356 authors from 1532 institutions across 50 countries or regions. These findings highlight the global effort and the evolving landscape of ADSCs-based cartilage TE research.

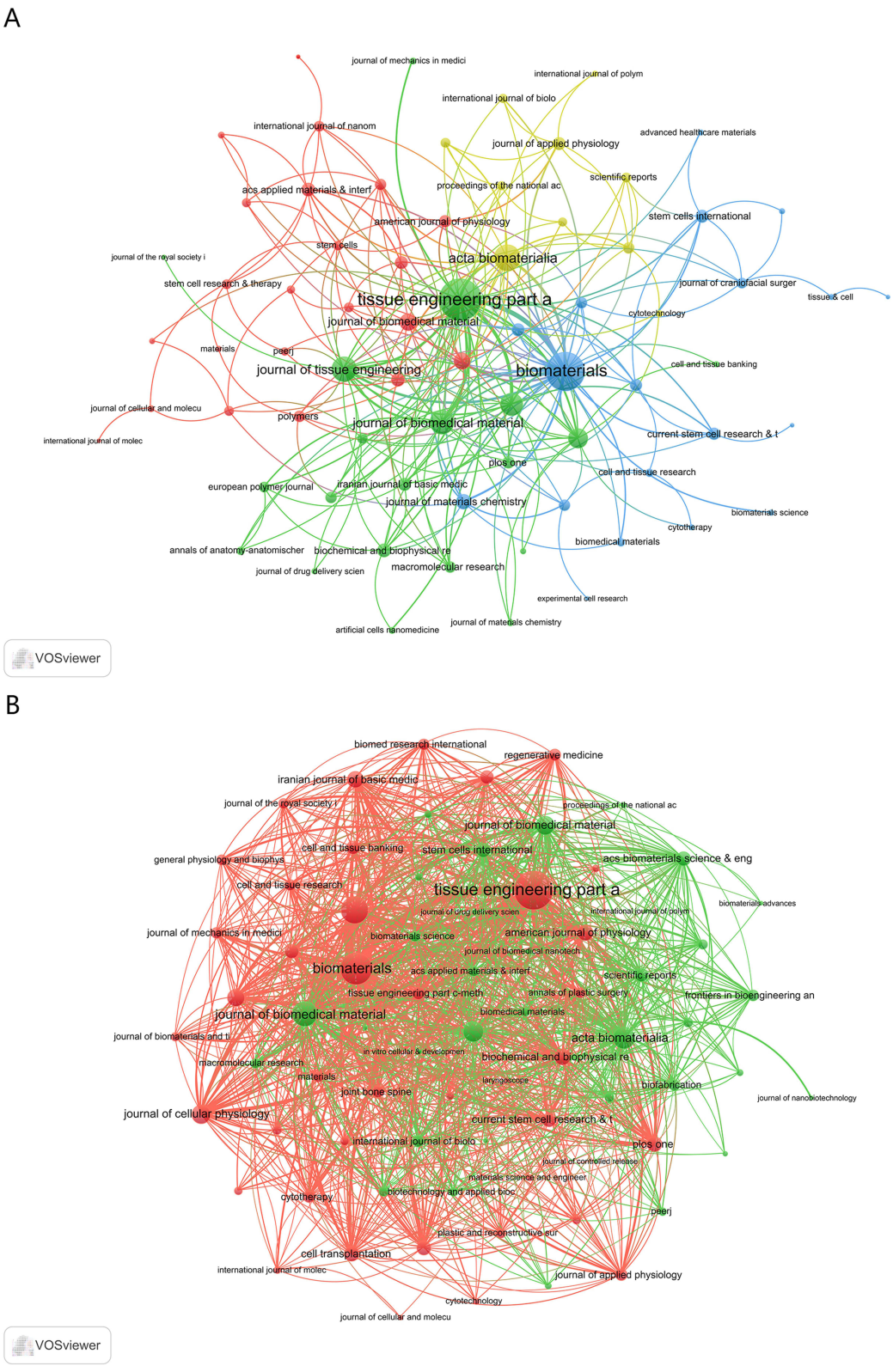

Figure 6 Analysis of journals. (**A**) The co-occurrence networks of journals. (**B**) The coupling networks of journals.

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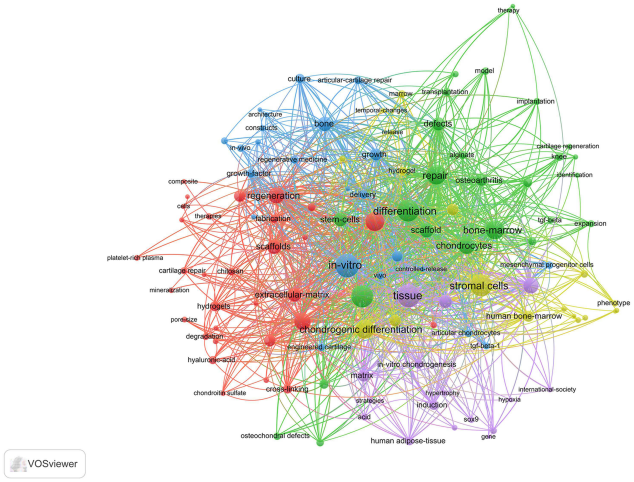
A



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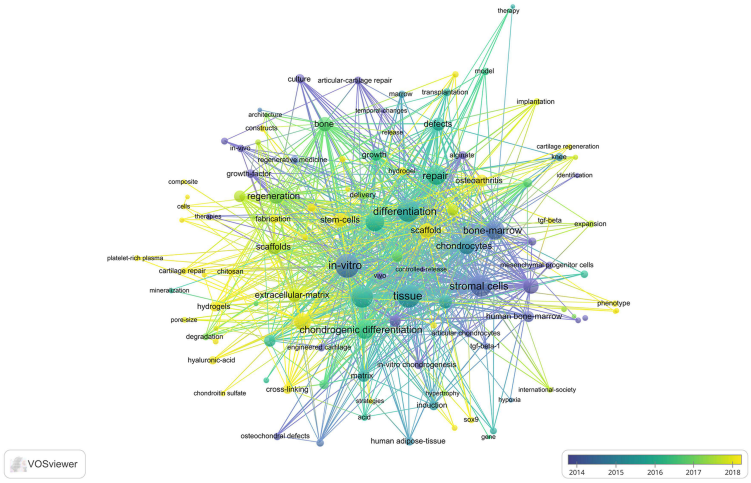

C

Top 20 Keywords with the Strongest Citation Bursts

Keywords	Year	Strength	Begin	End	2004 - 2024
gene expression	2005	5.46	**2005**	2010	
progenitor cells	2006	6.71	**2006**	2014	
human bone marrow	2006	3.15	**2006**	2014	
stromal cells	2004	3.19	**2009**	2012	
in vitro chondrogenesis	2010	3.31	**2010**	2012	
human adipose tissue	2012	2.92	**2012**	2013	
chondrocytes	2007	2.87	**2013**	2014	
regenerative medicine	2011	3.01	**2015**	2017	
matrix	2004	3.17	**2016**	2017	
defects	2009	3.17	**2016**	2017	
proliferation	2018	5.58	**2018**	2020	
osteogenic differentiation	2016	4.81	**2018**	2022	
stem cells	2008	4.33	**2018**	2019	
osteoarthritis	2019	9.45	**2019**	2024	
3d printing	2020	3.35	**2020**	2024	
biomaterials	2020	3.32	**2020**	2022	
cartilage regeneration	2010	2.92	**2020**	2022	
scaffolds	2012	5.79	**2021**	2022	
mesenchymal stem cells	2011	4.59	**2021**	2024	
cartilage repair	2015	3.01	**2021**	2024	

Figure 7 Analysis of keywords. (**A**) Visual analysis of keyword co-occurrence network by different clusters. (**B**) Visual analysis of keyword co-occurrence network by time. (**C**) Top 20 keywords with the strongest citation bursts.

The annual publication trend revealed a steady increase in research output from 2008 to 2021, reflecting growing interest and advancements in ADSCs-based cartilage TE. This surge likely stems from increased funding, technological advancements, and the expanding application of ADSCs in regenerative medicine. However, the subsequent decline in publications from 2022 to 2024 warrants further discussion. Possible explanations for this trend include funding shifts, changes in journal policies, or a saturation point in ADSC research. Additionally, the global impact of the COVID-19 pandemic may have disrupted research activities and publication processes during this period. Previous bibliometric studies have observed similar trends in other fields and have linked publication fluctuations to external factors such as funding cycles and global crises.[29,30]

The geographical distribution of publications highlights the dominance of China and the USA, which collectively account for a significant proportion of global research output. This prominence can be attributed to substantial investments in research, robust infrastructure, and active participation in international collaborations. Countries such as Germany, Japan, and South Korea also made notable contributions, underscoring their emphasis on tissue engineering and regenerative medicine. Despite these efforts, there remains room for improvement in fostering international collaboration, as evidenced by relatively low collaboration rates among some countries. Enhancing global partnerships could facilitate the sharing of resources and expertise, accelerating advancements in the field. At the institutional level, the analysis identified universities and research institutes as key contributors to ADSCs-based cartilage TE research. Institutions such as the Chinese Academy of Sciences and Harvard University were particularly prominent, reflecting their leadership in regenerative medicine and their ability to attract substantial funding and talent.

While total publication and citation counts provide valuable insights, normalizing citations by the number of papers offers a more meaningful metric for evaluating research influence. In this study, we calculated citations per paper (CPP) to assess the relative impact of research conducted in each country. The results revealed that countries like the USA and Germany exhibit high CPP values, reflecting their ability to produce influential and impactful research. Future studies could further explore the factors contributing to these variations, such as differences in research quality, funding availability, and publication strategies. Similar bibliometric studies have also demonstrated the importance of normalized metrics in evaluating research impact.[29,30]

The analysis of high-impact journals, including *Tissue Engineering Part A, Biomaterials*, and *Acta Biomaterialia*, underscores the field's focus on innovative methodologies, clinical applications, and biological mechanisms underlying ADSCs-based cartilage TE. These journals serve as platforms for disseminating groundbreaking research and fostering interdisciplinary collaboration. The identified research themes, including scaffold development, chondrogenic differentiation protocols, and growth factor applications, reflect the field's ongoing efforts to address the challenges of cartilage repair and regeneration.

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The most cited article by Hani et al focuses on chondrogenic differentiation of human adipose-derived adult stem (hADAS) cells in alginate, agarose hydrogels, and gelatin scaffolds. This article revealed that diverse biomaterials support this process and that altering their composition significantly impacts the mechanical properties of tissue-engineered cartilage constructs.[31] Furthermore, Farshid et al validates the hypothesis that individual hADAS cells are multipotent at a clonal level, with a significant proportion of clones differentiating into multiple lineages under specific in vitro conditions.[32] Bradley et al outlines the isolation, expansion, and chondrogenic differentiation of adipose-derived stem cells (ASCs) for tissue engineering approaches, detailing conditions and methods.[33] Collectively, these findings underscore the significant progress made in harnessing ASCs for cartilage tissue engineering, revealing their potential as a versatile and abundant source of stem cells for regenerative applications.

The analysis of keywords illuminates the evolution and focal points of research in this field. Early research efforts concentrated on "in vitro" studies within laboratory settings, encompassing the culturing of ADSCs and the observation

of their behavior, proliferation, and differentiation into cartilage cells.[34] The outcomes of these in vitro studies provided foundational data and insights into the potential of ADSCs for cartilage regeneration, paving the way for in vivo and clinical applications. During this period, stem cells derived from alternative sources like "bone marrow" were also extensively researched. Each of these diverse stem cell types exhibits unique advantages and disadvantages. ADSCs boast a higher proliferation rate and easier accessibility compared to bone marrow-derived stem cells (BMSCs), facilitating a more rapid and abundant cell supply for tissue regeneration.[35] Furthermore, the collection process for ADSCs is less invasive, reducing patient discomfort and potential complications. However, BMSCs have shown a superior capacity for differentiating into chondrocytes, the cells responsible for forming cartilage, which may make them more effective in promoting the formation of functional cartilage tissue.[36]

As research progressed, the subsequently emerging keywords collectively embody the functionalities of ADSCs in cartilage TE, which lies in leveraging the potential of "stem cells" to undergo chondrogenic differentiation, a process crucial for the "repair", "growth", and "regeneration" of damaged or diseased cartilage tissues.[10] Additionally, the emphasis on the "extracellular matrix" reflects the recognition of its crucial role in providing structural support and biochemical cues for cell growth and differentiation, while "scaffold" indicates advancements in creating suitable microenvironments to guide cell behavior and tissue formation.

The burst keywords further provide valuable insights into the dynamic evolution of research themes within the field. From 2005 to 2015, early research was characterized by a strong emphasis on the foundational aspects of stem cell biology. Keywords such as "progenitor cells" and "gene expression" indicate a focus on understanding the basic characteristics and mechanisms of ADSCs. The burst in "in vitro chondrogenesis" underscores the initial efforts to induce ADSCs to differentiate into chondrocyte-like cells, a crucial step in developing cartilage tissue engineering strategies. These bursts were necessary to establish a solid scientific foundation for subsequent advancements.

Transitioning to the period from 2015 to 2019, there was a significant shift in research focus. The keyword "osteoarthritis" reflects ADSCs could be a potential therapeutic option for the debilitating disease.[37] This burst continues to the present, underscoring the persistent and growing interest in developing effective treatments for osteoarthritis using ADSCs. Additionally, the bursts in "proliferation" and "osteogenic differentiation" indicate a broader exploration of ADSCs' regenerative capabilities and their potential for multilineage differentiation.

More recently, the burst in "3D printing" highlights the integration of advanced manufacturing techniques into tissue engineering, enabling the precise fabrication of complex cartilage structures. Li et al introduced a novel 3D-printed double-network hydrogel scaffold with tissue-specific decellularized extracellular matrix and human adipose-derived mesenchymal stem cell-derived exosomes. This scaffold promotes stem cell differentiation and accelerates simultaneous osteochondral tissue regeneration, offering a promising cell-free approach for stem cell therapy in treating injured or degenerative joints.[38] Fujimoto et al demonstrates the successful fabrication of scaffold-free constructs using 3D-printed ADSCs to generate chondrogenic and osteogenic tissues for the potential treatment of extensive bone defects without the use of artificial materials.[39] ADSCs have emerged as one of the most favored seed cells in 3D bioprinting of cartilage due to their abundance, excellent proliferation potential, low morbidity at harvest, and the absence of ethical constraints.[40]

While significant strides have been made from in vitro studies to in vivo applications, the ultimate goal—clinical translation—remains a critical focus. Recent years have seen the initiation of several clinical trials exploring the safety and efficacy of ADSC-based therapies for cartilage repair. For example, clinical trials (eg, NCT03539744[41] and NCT04293278[42]) are investigating the use of ADSCs in treating knee osteoarthritis and cartilage defects. These trials highlight the potential for ADSCs to transition from preclinical models to clinical applications. However, challenges such as variability in ADSC isolation protocols, scalability of cell production, regulatory hurdles, and the need for long-term safety and efficacy data remain significant barriers.[43] Moreover, the translation from basic research to clinical applications requires a multidisciplinary approach, including the development of standardized protocols for ADSC differentiation, scaffold fabrication, and the integration of advanced techniques such as 3D bioprinting. These advancements must also address challenges related to immune rejection and the replication of the native cartilage microenvironment. Despite these obstacles, the progress in ADSC-based therapies demonstrates promising potential for addressing unmet clinical needs in cartilage repair and regeneration.

In summary, research hotspots are transitioning from exploring ADSCs' basic biology and differentiation potential to developing innovative therapeutic strategies for cartilage repair and regeneration. The shift from laboratory-based studies to disease-specific therapies and clinical applications underscores the progress and maturity of the field. Addressing the remaining challenges will be essential for advancing ADSC-based cartilage TE and realizing its full clinical potential.

Limitations

This study is not without limitations. First, the keyword analysis relied on a threshold of at least five occurrences, which may have excluded emerging or niche topics with fewer mentions. Additionally, the interpretation of keyword trends depends on the accuracy and consistency of keyword usage in publications, which can vary among authors and journals. Second, this study only included English-language articles, potentially excluding important research published in other languages, especially from non-English-speaking countries, leading to a possible bias in the global research landscape. Third, the reliance on a single database (WoSCC) may have resulted in the omission of relevant studies indexed in other databases such as Scopus and PubMed. While WoSCC is widely used for bibliometric studies, incorporating multiple databases in future studies would provide a more comprehensive and balanced view of the research landscape. Another limitation is the lack of detailed analysis regarding clinical translation. While this study highlighted the progression from in vitro to in vivo research, the analysis did not delve into the transition to clinical settings. Clinical trials (eg, NCT03539744 and NCT04293278) investigating ADSC-based therapies for cartilage repair remain essential for bridging the gap between basic research and clinical application. Barriers such as variability in ADSC protocols, scalability of production, regulatory hurdles, and long-term safety concerns still pose significant challenges. Future bibliometric studies should incorporate data from clinical trials and translational research to better evaluate the progress and real-world impact of ADSC-based cartilage tissue engineering. By addressing these limitations, the field can advance further toward developing clinically effective solutions for cartilage repair and regeneration.

Conclusion

This bibliometric analysis offers a comprehensive overview of the research trends and themes in ADSCs-based cartilage tissue engineering (TE) from 2004 to 2024. The findings reveal key research hotspots, including the biological properties of ADSCs, optimization of tissue engineering methodologies, and advancements in clinical applications such as osteoarthritis treatment. Emerging frontiers, such as the integration of 3D printing and advanced scaffold technologies, highlight the innovative directions driving the field forward. For researchers, these insights provide a roadmap to focus on addressing persistent challenges, such as improving ADSC differentiation protocols, overcoming immune rejection issues, and developing scalable clinical solutions. Clinicians and policymakers can use this information to guide translational efforts, prioritize funding, and streamline regulatory pathways for ADSC-based therapies. By fostering interdisciplinary collaborations and leveraging the latest technologies, the field holds immense potential for delivering clinically effective solutions for cartilage repair and regeneration.

Data Sharing Statement

All data generated or analysed during this study are included in this published article.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This work was supported by an American Heart Association Postdoctoral Fellowship (grant no. 900337 to M.S.); the Niels Stensen Fellowship (to M.S.) and NIH/NHLBI grant nos. R35-HL145228 and P01-HL087123 (to I.T.).

Disclosure

The authors declare that they have no competing interests in this work.

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