

## Mapping the Global Research Status and Trends on Mesenchymal Stem Cell–Driven Tissue Engineering for Hand Reconstruction: A Bibliometric Study

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Cite this paper as: Andri Danika, Daffa Sadewa (2026) Mapping the Global Research Status and Trends on Mesenchymal Stem Cell–Driven Tissue Engineering for Hand Reconstruction: A Bibliometric Study. *Frontiers in Health Informatics*, Vol.15, No.1, 118-128

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### ABSTRACT

#### Introduction:

Reconstructing the hand remains a clinical challenge on account of complex hand anatomy and restoration of both structural stability and fine motor function. While conventional surgical techniques can restore anatomical structures, they often fail to accomplish true biological regeneration. Tissue engineering based on mesenchymal stem cells (MSCs) has therefore become an effective regenerative treatment approach for bone, tendon, cartilage and soft tissue defects of the hand. This study aimed to conduct a bibliometric analysis of the research trends and knowledge structures of MSC-based tissue engineering for hand reconstruction globally.

#### Methods:

A bibliometric analysis using publications obtained from Scopus and PubMed databases. A systematic search strategy using keywords related to mesenchymal stem cells, tissue engineering and hand-related musculoskeletal tissues was used. After screening and assessment of eligibility, 300 peer-reviewed articles were included. Publication trends, citation performance, top countries and institutions in this area, collaboration networks and keyword co-occurrence were studied using bibliometric tools.

#### Results:

The study showed a gradual rise in scientific output over the last twenty years, with a noticeable speedup in the past ten. Research activity was mostly located in countries with robust translational research infrastructure and interdisciplinary integration. Major research domains encompassed scaffold fabrication, biomaterial innovative developments, tendon and cartilage regeneration, and growth factor–mediated target pathways of signal transduction, indicating a full current trajectory toward translational relevance and early clinical translation.

#### Conclusion:

Mesenchymal stem cells (MSCs) based tissue engineering studies for hand reconstruction have seen rapid increase over the past years. This bibliometric analysis identifies significant research trends, collaboration dynamics, and potential future directions that can guide further scientific endeavors toward the development of regenerative therapies for complex hand injuries

**Keywords:** Mesenchymal stromal cells; Tissue engineering; Hand reconstruction; Regenerative medicine; Bibliometric analysis..

### INTRODUCTION

Breakthroughs in regenerative medicine have paved the way for restoration of complex musculoskeletal structures that are often resistant to resolution with traditional surgical strategies. Among these structures, the human hand poses a demanding reconstructive challenge because its function relies on the coordinated interplay of bones, tendons, cartilage, ligaments and soft tissues that afford both strength and fine motor control. Traditional reconstructive methods like tendon repair, grafting or fixation may restore anatomical continuity but do not necessarily regenerate native tissue structure and biomechanical properties. The search for better solutions has led to the development of biological strategies using mesenchymal stem cells (MSCs) in tissue engineering approaches aiming to transcend these limitations by

supporting biological repairs, not just structural ones. Regenerative approaches using MSC involve the integration of stem cell with biomaterial scaffolds as well as bioactive signalling molecules to recode and recreate microenvironment necessary for tissue healing. MSCs have become one of the most widely studied cell types suitable for musculoskeletal tissue engineering due to their multilineage differentiation potential and strong paracrine regenerative effects. As a result, MSC driven tissue engineering is now widely accepted as a beneficial direction to improve the results of hand reconstruction and other complex musculoskeletal injuries.<sup>1-6</sup>

Injuries and degenerative diseases of the hand, such as tendons, cartilage and bone, continue to be a significant global clinical challenge. Tendon injury, specifically, is one of the most prevalent musculoskeletal disorders seen in orthopaedic and reconstructive practice. Tendon tissue has a relatively poor ability to heal on its own, and post-injury healing is typically through the deposition of fibrotic scar tissue rather than regeneration of native tendon. This process may cause adhesive formation, restrict elasticity and joint range of motion, leading to hand dysfunction. Mesenchymal stem cells have thereby gained wide interest as a possible biological therapy to enhance healing outcomes in tendon and cartilage injuries. These cells can excrete a different type of tissues, such as tenogenic, chondrogenic and osteogenic lineages but also secreting multifunctionable growth factors and cytokines that play an important role towards modulation of inflammation stimulating angiogenesis and enhanced remodelling of extracellular matrix. Recently, the potential beneficial effects of MSC-based therapies on collagen fibres organization and biomechanical strength while decreasing postoperative adhesion formation during tendon repair have been reported in experimental and translational studies. Extracellular vesicles released from MSCs as well as secreted signalling factors have also been shown to be important components in regulating tissue regeneration and cellular communication during the processes of healing. Collectively, these findings serve to further inspire the burgeoning interest in MSC mediated regenerative strategy approaches to combat complex musculoskeletal injuries of the hand.<sup>7-12</sup>

The scientific literature surrounding MSC-based regenerative therapies has grown exponentially over the last 20 years, as investigations into this emerging area of research continue. This fast pace of growth is a direct reflection of the heteroclit structure underlying regenerative medicine; leading to collaboration between clinicians, biomedical engineers, molecular biologists and materials scientists. Nonetheless, the growing complexity and volume of literature further presents a challenge for traditional narrative reviews in discerning prominent research trajectories, consequential works, or novel topical areas. Bibliometric analysis offers a systematic and quantifiable method for assessing scientific publications by analyzing trends in publication volume, citation dynamics, and co-authorship networks. Using methods like citation analysis, keyword co-occurrence mapping, and institutional collaboration networks, bibliometric studies are able to identify the intellectual structure and development trajectory of a research area. Earlier bibliometric studies majorly indicated the emerging international trend in stem cell research of increased publicity and funding to regenerative medicine conducted globally. However, few studies have specifically analyzed the global research landscape of MSC-driven tissue engineering in hand reconstruction. Understanding how the field has evolved in terms of countries, institutions and research topics that have been most influential may inform future investigations and the clinical translation of regenerative therapies.<sup>13-16</sup>

Hence, the present study aims to perform a comprehensive bibliometric analysis of global publications related with mesenchymal stem cell-based tissue engineering for hand reconstruction. This study intends to investigate the publication trends over the years, identify the most productive country, and institution and author in this field along with leading journals. Moreover, collaboration networks of researchers and institutions will be examined for a better picture of scientific cooperation patterns in MSC-related regenerative research. Additionally, we will perform keyword co-occurrence analysis to explore the predominant themes and new research areas relevant to stem cell therapy, biomaterials and regeneration of hand tissues. The results of this bibliometric analysis are expected to depict a comprehensive overview of the current knowledge regarding MSC-mediated regenerative approaches for hand reconstruction and identify promising directions for future investigations in this domain.

## METHODS

### Search Strategy and Study Selection

#### Data Sources

The bibliometric study was performed using two large international scientific bases, Scopus and PubMed. These databases were chosen as they offer broad coverage across biomedical, engineering, and life science disciplines of the peer-reviewed literature; their citation indexing has also been found to be rational and reliable while their metadata is standardized thereby making them have extensive use in bibliometric studies. Use of both databases enabled exhaustive identification of publications relevant to mesenchymal stem cell-based tissue engineering and regenerative strategies for hand reconstruction.

#### Search Strategy

A systematic search strategy was created to recognized publications on mesenchymal stem cells, tissue

engineering and hand-related musculoskeletal supportive regenerative medicine. We searched, with a focus on maximizing sensitivity while keeping some relevance to the research topic, by combining Keywords and Synonyms using Boolean operators. The main search string contained the following words:

( ("mesenchymal stem cell\*" OR "mesenchymal stromal cell\*" OR MSC OR MSCs OR "bone marrow mesenchymal stem cell\*" OR BMSC OR BMSCs OR "bone marrow stromal cell\*" OR "adipose-derived stem cell\*" OR ADSC OR ADSCs OR "adipose-derived mesenchymal stem cell\*" OR "multipotent stromal cell\*" OR "mesenchymal progenitor cell\*" OR "mesenchymal precursor cell\*") AND ("tissue engineering" OR "regenerative medicine" OR "regenerative therapy" OR "cell therapy" OR "stem cell therapy" OR scaffold\* OR biomaterial\* OR "biological scaffold\*" OR "bioengineered scaffold\*" OR "tissue regeneration" OR "tissue repair" OR "3D bioprint\*" OR bioprinting OR hydrogel\* OR "extracellular matrix") AND (hand OR wrist OR finger\* OR digit\* OR phalanx OR phalange\* OR tendon\* OR ligament\* OR cartilage OR chondral OR bone OR osteochondral OR musculoskeletal) )

The search was performed on title, abstract and author keywords in databases with the article type are meta-analysis, randomized controlled trial, and systematic review. The last search was conducted in March 2026 and included 14 years publications listed in the databases up to the date of the last search.

### Eligibility Criteria

A bibliometric analysis was performed on studies selected using inclusion and exclusion criteria. Eligible publications were peer-reviewed original research articles and review articles pertaining to mesenchymal stem cells or mesenchymal stromal cells used in the context of tissue engineering or regenerative medicine. Studies were included that evaluated fashioning musculoskeletal tissues that would be applicable to hand reconstruction, such as tendon, cartilage, bone or digit regeneration. We only included articles published in English and indexed by Scopus or PubMed. Conference abstracts, editorials, letters and book chapters were excluded from the analysis. Furthermore, non-regenerative medicine studies or those with a focus on a different organ system were excluded. We additionally excluded duplicate records retrieved from both databases, prior to screening.

### Screening Process

All records retrieved were exported from each of the databases and then passed through a multistaged screening process. First, we searched for and removed duplicate records. Title review was initially used to screen the remaining publications and exclude studies clearly unrelated to the research topic. Then, title and abstract screening was performed to determine if the publications were relevant to mesenchymal stem cell-based tissue engineering in musculoskeletal structures related anatomical structures of the hand. If there was no agreement or uncertainty regarding inclusion after reviewing the abstract, the full text of articles flagged for eligibility were reviewed and judged on whether they met the inclusion criteria. The final dataset used for bibliometric analysis included only the studies satisfying all of the eligibility criteria.

### Data Extraction, Visualization, and Analysis

#### Data Extraction

The bibliographic information of the eligible publications was extracted directly from the selected databases. The extracted metadata consisted of publication title, authors, year of publication, journal name, author affiliations, country of origin, keywords and citation counts and reference lists. This data was exported in readily parsable formats for bibliometric analysis and visualization purposes.

#### Bibliometric Indicators

Various bibliometric indicators were used to analyze the scientific landscape and development of mesenchymal stem cell-driven tissue engineering for hand reconstruction. This involved analyzing annual publication output to assess trends and research productivity over time, as well as citation analysis to identify influential publications in the field. Furthermore, country-based and institution-based productivity was assessed to avert the champions of this area of research. They also explored scientific cooperation by analyzing authorship patterns and collaboration networks among researchers and institutions. Moreover, keyword co-occurrence analysis mapped thematic hotspots and emerging trends in MSC-based regenerative medicine for the hand-related musculoskeletal tissues.

#### Analytical Tools

One specialized bibliometric software (VOSviewer) were used for bibliometric analysis and visualization. We used VOSviewer to create visual network maps showing the relationships among authors, institutions, countries and keywords. This enabled the identification of clusters that represented these closely related fields and their collaborative networks. Descriptive bibliometric analyses and calculation of several bibliometric indicators such as trends in publications, citation metrics and productivity rankings were performed using Biblioshiny, which is the web interface of the Bibliometrix package operating in the R programming environment.

#### Detailed Analysis

The findings were analysed in steps to systematically assess the bibliometric dataset. Descriptive statistical analysis was firstly conducted to determine annual publication trends and general research productivity. Secondly, a citation analysis was conducted to determine very cited articles and influential journals in the field. Third, the collaboration networks of authors, institutions and countries were analysed to reveal patterns in scientific cooperation. Finally, keyword co-occurrence analysis was undertaken to detect main research trends and emerging topics within mesenchymal stem cell–based regenerative medicine for hand reconstruction. Visualization maps produced by VOSviewer were utilized to graphically represent the intellectual structure of research landscape as well as clusters of related domains within individual fields.

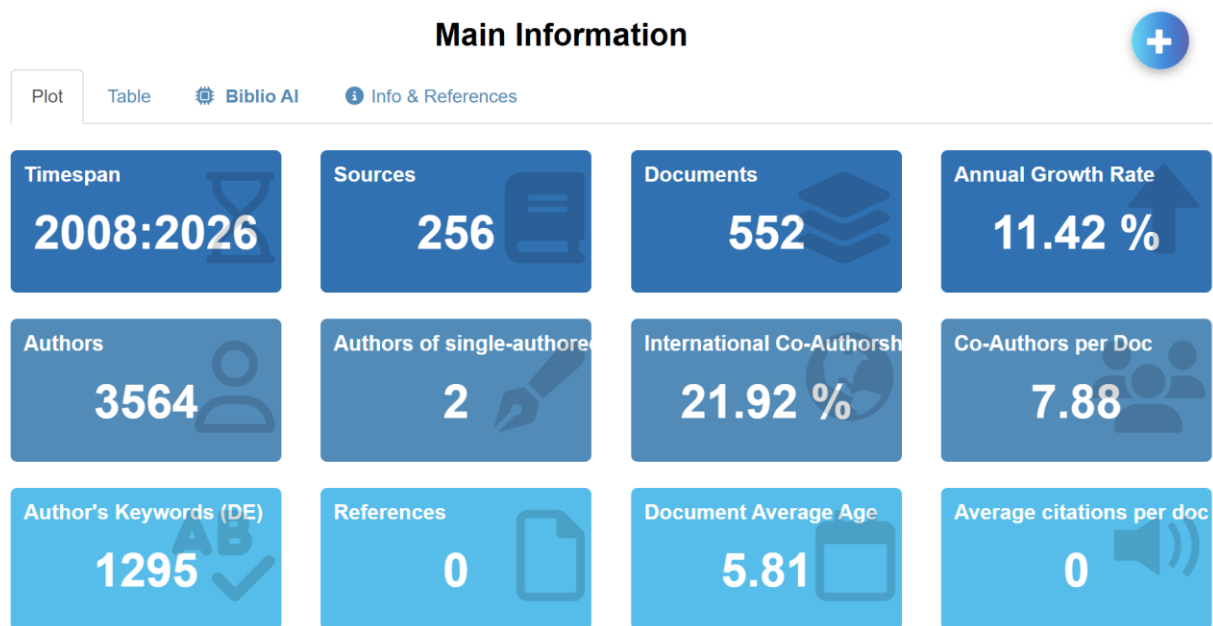
## RESULTS

### Description of Included Studies

A total of **552 publications** related to mesenchymal stem cell–based tissue engineering and regenerative approaches for hand and musculoskeletal reconstruction were retrieved from the Scopus and PubMed databases. After removing duplicate records and applying the predefined eligibility criteria, all eligible studies were included in the final dataset for bibliometric analysis.

The included studies consisted primarily of **randomized control trial, systematic review, and meta-analysis**, reflecting both experimental and translational investigations within the field. These publications explored various aspects of MSC-based regenerative strategies, including stem cell differentiation, scaffold fabrication, biomaterial development, extracellular vesicle signaling, and clinical applications in musculoskeletal tissue repair. The bibliographic metadata extracted from the selected publications—including authorship, institutional affiliations, country of origin, citation counts, and keywords—were subsequently analyzed using bibliometric tools such as VOSviewer and Biblioshiny.

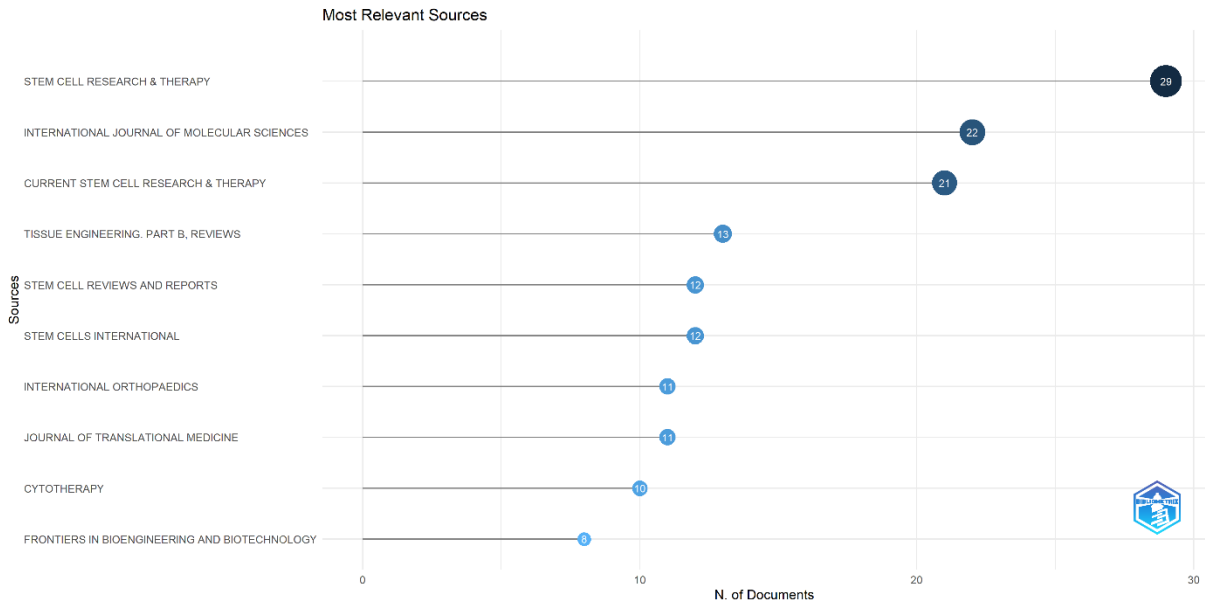
### Publication Trends



Analysis of annual publication output demonstrated a **progressive increase in scientific production** related to MSC-based tissue engineering over the past two decades. The number of publications remained relatively low during the early years of the field but began to increase steadily after 2008. A particularly notable rise in research output was observed during the **last 14 years**, indicating accelerating global interest in regenerative medicine and stem cell–based therapeutic strategies.

The upward trend reflects rapid developments in stem cell biology, biomaterial engineering, and translational regenerative medicine. Increased research funding and interdisciplinary collaboration between clinicians, biomedical engineers, and basic scientists have likely contributed to the expansion of this research area.

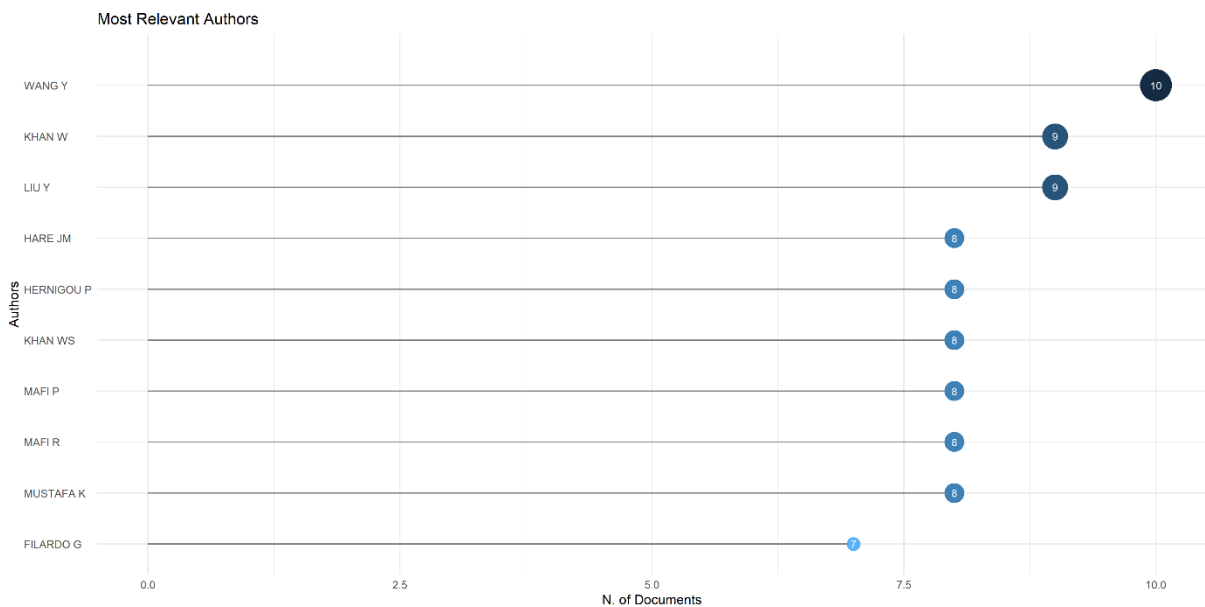
### Top Journals



The analysis identified several journals that contributed substantially to the dissemination of research on mesenchymal stem cell-based tissue engineering. The most productive journals included leading publications in the fields of regenerative medicine, biomaterials, and orthopedic research. These journals serve as major platforms for the dissemination of scientific findings related to stem cell therapy, biomaterial scaffolds, and musculoskeletal regeneration.

High-impact journals publishing studies in this field frequently focus on interdisciplinary topics integrating stem cell biology, tissue engineering technologies, and clinical translational research. The prominence of these journals reflects the interdisciplinary nature of MSC-based regenerative medicine.

### Top Authors and Co-Authorship Networks



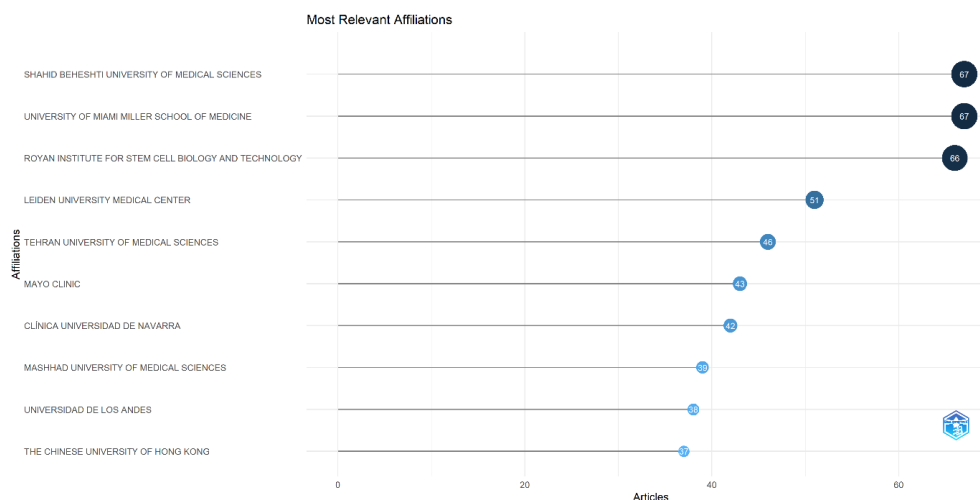
The bibliometric analysis identified several highly productive authors who have made significant contributions to MSC-based tissue engineering research. These authors have produced multiple publications addressing key aspects of regenerative medicine, including stem cell differentiation, scaffold-based tissue engineering, and translational therapeutic applications.

Co-authorship network analysis conducted using VOSviewer revealed collaborative clusters of researchers



working within similar thematic areas. These collaboration networks highlight the interdisciplinary nature of the field and demonstrate the importance of international cooperation in advancing regenerative medicine research.

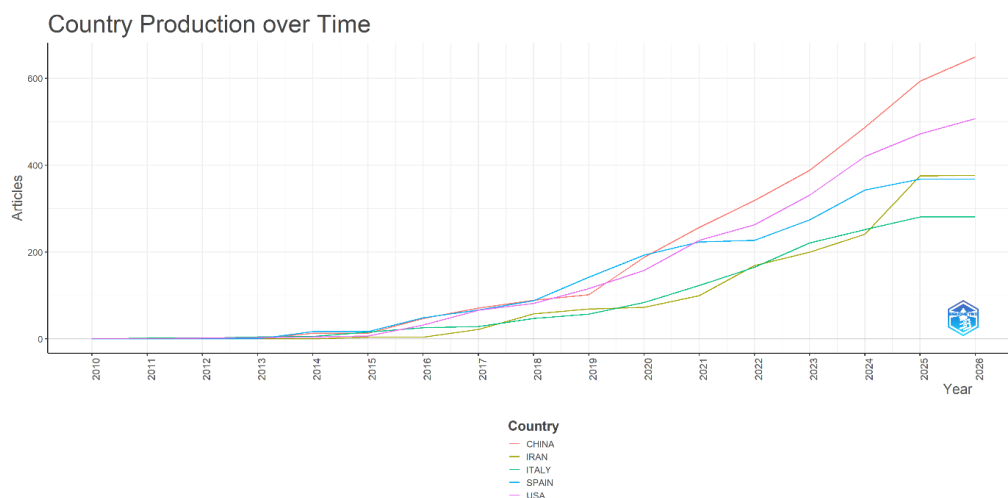
### Top Institutions



Institutional productivity analysis showed that several academic and research institutions have played a leading role in the development of MSC-based tissue engineering research. The most productive institutions were predominantly universities and research centers with strong programs in regenerative medicine, biomedical engineering, and translational research.

Institutional collaboration networks demonstrated extensive partnerships among research institutions, particularly those located in countries with well-established biomedical research infrastructure. Such collaborations facilitate knowledge exchange and accelerate the development of innovative regenerative therapies.

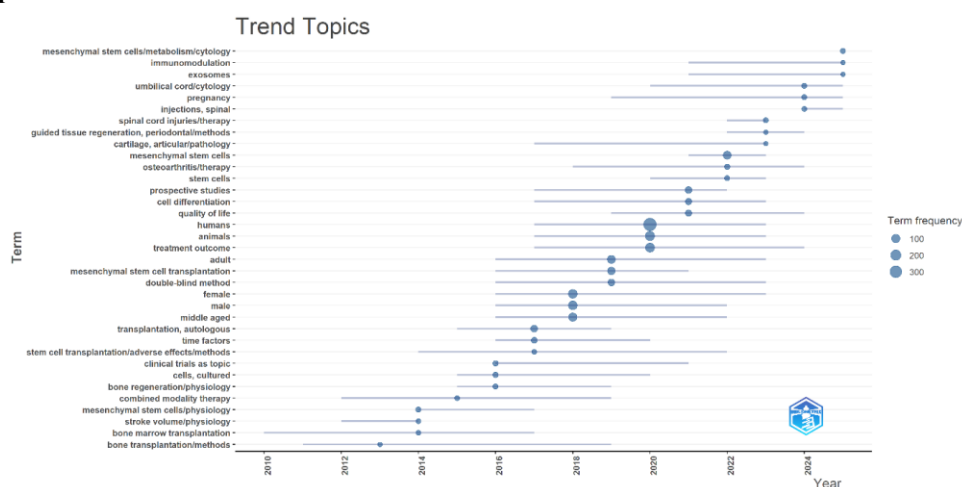
### Top Countries



Country-level analysis revealed that research output in MSC-based tissue engineering is concentrated in a number of scientifically advanced nations with strong investment in biomedical research. Countries such as the **United States, China, and several European nations** were among the most productive contributors to the literature.

International collaboration networks indicated that cross-border research partnerships play a significant role in advancing the field. These collaborations often involve joint projects between academic institutions, research laboratories, and clinical centers focusing on regenerative medicine and tissue engineering.

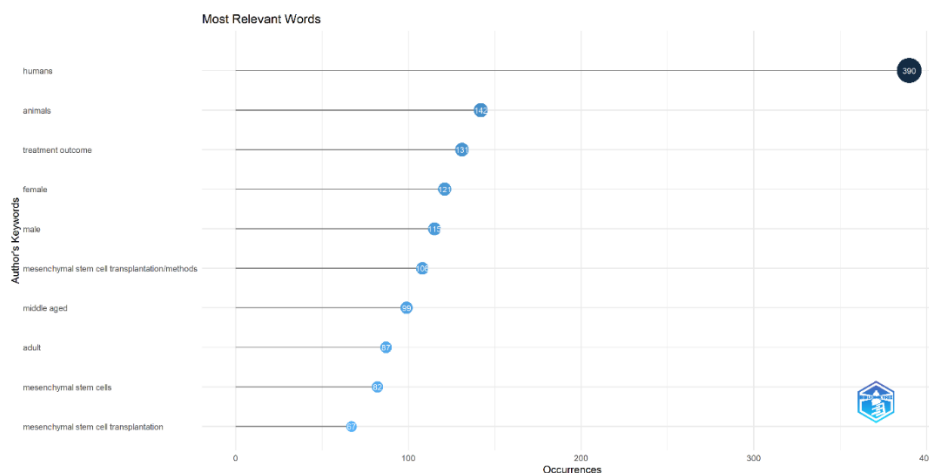
### Trend Topics



Trend topic analysis conducted using Biblioshiny revealed the evolution of research topics over time. Earlier studies primarily focused on bone transplantation, bone marrow transplantation, mesenchymal stem cells physiology. In contrast, more recent publications increasingly emphasize translational and clinical applications.

Emerging topics identified in recent years include mesenchymal stem cells/metabolism/cytology, immunomodulation, exosomes.

### Prominent Topics



Keyword analysis identified several prominent themes that dominate the research landscape. The most frequently occurring keywords included **“humans,” “animals,” “treatment outcome,” “female,” “male,” “mesenchymal stem cell transplantation/methods”**.

These keywords reflect the interdisciplinary nature of MSC research, integrating concepts from stem cell biology, biomaterial science, and clinical regenerative therapy in humans and animals.

### Underdeveloped Topics

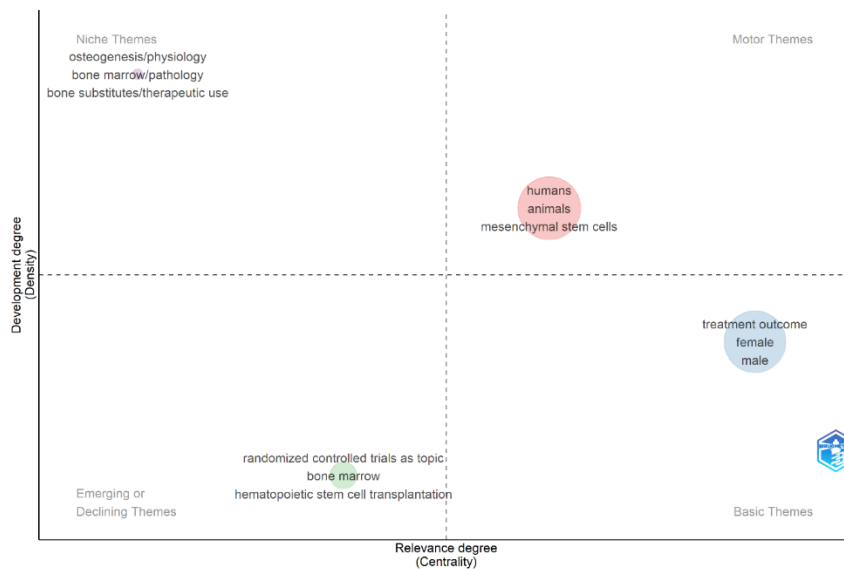
Terms	Frequency
cell- and tissue-based therapy	13
hematopoietic stem cell transplantation	13
stroke volume	14
osteoarthritis knee/therapy	15
osteogenesis	15
mesenchymal stem cells/cytology/metabolism	16
pilot projects	16
platelet-rich plasma	16
rats	16
regenerative medicine	16

Previous 1 2 3 4 5 Next

In contrast, several topics appeared less frequently in the keyword network analysis, suggesting potential areas for future investigation. These underrepresented themes may include **cell and tissue based therapy, hematopoietic stem cells, osteoarthritis knee/therapy, and regenerative medicine**.

Identifying these underdeveloped topics may provide valuable insights for future research directions and highlight potential opportunities for innovation within the field.

### Thematic Map



The thematic map generated using Biblioshiny provided a conceptual overview of the research structure within MSC-based tissue engineering. The map categorized research themes according to their **centrality and density**, allowing identification of motor themes, emerging themes, niche topics, and basic themes within the scientific landscape.

Motor themes typically included well-developed topics such as **humans, animals, and mesenchymal stem cells** while emerging themes were associated with newer research directions such as **randomized controlled trials as topic, bone marrow, and hematopoietic stem cell transplantation**.

## DISCUSSION

This bibliometric analysis serves as a global overview of the scientific landscape regarding mesenchymal stem cell (MSC)-based tissue engineering for hand reconstruction. The findings showed a significant and consistent growth of research productivity in the last 14 years, especially in the last decade. Such expansion demonstrates the clear global interest in regenerative medicine and recognition of MSCs as promising therapeutic agents for musculoskeletal repair and tissue regeneration. The increasing number of publications also reflects that the field has shifted from mostly exploratory experimental studies to more translational and clinically relevant studies.<sup>2,17</sup> The trends in publication are indicative of the collaborative focus between cell science, materials engineering and reconstructive surgery to address complex tissue deficits of the hand.

A key observation from this study is the concentration of research productivity in countries and institutions with established biomedical research infrastructures and strong international collaboration networks. Such collaborative models are illustrative of the multidisciplinary nature of MSC-oriented regenerative research, which often necessitates the confluence of technical expertise from diverse fields including orthopedics, cell biology, and biomedical engineering. This supports previous bibliometric analyses of regenerative medicine, identifying characteristics of countries that dominate research output in this area as those with strong funding and translational platforms.<sup>18,19</sup> As such, this analysis of collaboration networks highlights the role international scientific partnerships play in advancing regenerative medicine research.

Keyword and thematic analyses further identified common features of dominant themes in the field, including scaffold fabrication, biomaterial development, tendon regeneration, cartilage repair and growth factor-mediated signaling pathways. These themes mirror the key principles of tissue engineering, wherein MSCs are combined with biomaterials and/or bioactive molecules to form regenerative microenvironments for driving tissue repair. The profile of tendon and cartilage regeneration is especially pertinent in the challenge of hand reconstruction since these tissues comprise limited intrinsic healing potential often hampered by traumatic insult.<sup>11,20</sup> Together, these findings highlight the shifting research paradigm away from fundamental stem cell biology toward integrated regenerative approaches designed to restore both structure and function.

The results of this bibliometric analysis have several significant implications for scientific research and clinical practice. The focus on biomaterial scaffolds and tissue engineering strategies indicates that, in the following years, research for regenerative medicine will mainly be about improving MSCs interactions when exposed to engineered biomaterials. Biomimetic scaffold design and three-dimensional microenvironment engineering have made substantial progress in enhancing stem cell differentiation, survival, and integration of the grafts with target tissues.<sup>1</sup> Further investigation in this field could pave the way for better regenerative treatments capable of

reestablishing the intricate musculoskeletal architecture of the hand.

Beyond experimental research, the growing translational focus of MSC-based studies indicates promising clinical potential for use in reconstructive surgery. MSC therapy has been shown in preclinical models to increase collagen formation, accelerate angiogenesis, reduce inflammatory response and improve tendon healing parameters.<sup>4,20</sup> These biological effects may eventually enhance functional recovery after severe injuries to the hand. On the other hand, while there exist promising experimental and clinical evidence for MSCs applications, more studies are needed to demonstrate the safety, efficacy and long-term outcomes of MSC-based regenerative therapies. Thus, the findings of this bibliometric analysis underscore the clinical translation from bench to bedside which ought to be addressed by high quality clinical trials.

Future bibliometric studies may explore additional analytical techniques and data sources, providing broader insights on MSC regenerative medicine. Combining multiple bibliographic databases, for example, might give a better overall picture regarding global research output and lead to fewer database-related biases. Utilizing advanced bibliometric techniques such as co-citation analysis, citation burst detection, and thematic evolution mapping could provide additional insights into the intellectual structure and nascent knowledge domains of regenerative medicine research.<sup>13</sup> These analyses may assist researchers in tracking the topics that are growing quickly, as well as in finding niches for a potential interdisciplinary workforce.

From a scientific point of view, there are some promising fields of research which may lead the future development of MSC-based regenerative therapies. There has been a growing interest in recent years in cell-free strategies with MSC-derived EVs and exosomes proposed as major actors in tissue regeneration. These biological products are capable of emulating many regenerative effects seen with stem cells but may diminish the risks observed during direct cell transplantation.<sup>21</sup> Furthermore, innovations in biomaterials, gene-editing technologies, and personalized regenerative medicine will promote the therapeutic potential of MSC-mediated therapies targeting hand injuries of the musculoskeletal system. Ongoing collaboration between basic scientists, biomedical engineers and clinicians will thus be critical to translating these emerging technologies into successful regenerative therapies.

## CONCLUSION

In summary, this review offers a comprehensive understanding into the scientific landscape, research trends and novel areas of MSC-based tissue engineering. Researchers may use the results to discover any knowledge gaps, plan future investigations and aid ongoing developments of regenerative therapies for hand reconstruction

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