Applied Cell Biology

ISSN : 2320-1991 Online
ISSN : 2320-1983 Print
Volume 13 Issue 4
DOI: https://dx.doi.org/10.53043/2320-1991.acb13016

Research Article
Appl Cell Biol, 13(4), 2025 [92-98]
Published: October 04, 2025

Mapping Two Decades of Mesenchymal Stromal Cell Research in Oncology: A Bibliometric and Thematic Analysis

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ABSTRACT

Background: Mesenchymal stromal/stem cells (MSCs) have attracted sustained attention in oncology due to their functional plasticity and multifaceted interactions within the tumor microenvironment. Bibliometric analysis provides a quantitative framework to evaluate the evolution, maturity, and intellectual structure of a research field, as well as shifts in thematic emphasis over time. Despite the rapid expansion of MSC-related cancer research, a comprehensive bibliometric and thematic evaluation of this domain has not previously been undertaken.

Methods: Publications related to mesenchymal stromal/stem cells in oncology were retrieved from the Web of Science™ Core Collection. Bibliometric indicators, including publication output, citation performance, country and journal contributions, and cancer-type focus, were systematically analyzed. VOSviewer software was employed to construct keyword co-occurrence networks and identify major research clusters and temporal trends.

Results: A total of 9,927 publications were included in the analysis. Annual publication output demonstrated an exponential growth pattern (e = 0.97), indicating sustained expansion of the field. The United States and the People's Republic of China contributed the highest number of publications; however, when adjusted for population size and citation impact per article, Singapore, Luxembourg, and Switzerland emerged as the most influential contributors. Over the past 15 years, 74% of publications appeared in cancer-specific journals. Among common malignancies, breast cancer accounted for the largest proportion of disease-focused studies (42%). Journals with a primary emphasis on basic science published the majority of articles (44%). Keyword co-occurrence analysis revealed three principal thematic clusters: (i) MSC characterization and nomenclature, (ii) clinical and translational applications, and (iii) molecular mechanisms and functional roles. Recent publications showed a marked shift toward molecular and mechanistic investigations.

Conclusions: Research on mesenchymal stromal/stem cells in oncology has undergone rapid and sustained growth over the past two decades. The increasing presence of MSC-focused studies in oncology-specific journals reflects broad acceptance of this research area within the cancer community. While basic and mechanistic studies currently dominate the literature, the findings highlight a clear opportunity for further development of translational and clinically oriented investigations.

Keywords

Mesenchymal stromal cells
Mesenchymal stem cells
Bibliometric analysis
Cancer
Neoplasia
Translational research

Research Article

ABBREVIATIONS

MSC: Mesenchymal Stromal Cell, ISCT: International Society for Cell Therapy, TME: Tumor Microenvironment, EMT: Epithelial-to-Mesenchymal Transition.

INTRODUCTION

Mesenchymal stromal cells (MSCs) were first identified in the early 1980s through the seminal work of Friedenstein and Owen, who described a fibroblast-like cell population isolated from rodent bone marrow that demonstrated colony-forming capacity when cultured in vitro. This population was recognized as heterogeneous, with differentiation potential that could be experimentally manipulated, leading to its initial designation as bone marrow–derived osteogenic progenitors [1,2]. In 1991, the term "mesenchymal stem cell" was introduced to describe these multipotent cells, a nomenclature that became widely adopted and remains in common use [3].

As the field expanded, substantial inter-investigator variability emerged in relation to MSC isolation methods, expansion protocols, and phenotypic characterization. In response, the International Society for Cellular Therapy (ISCT) issued a position statement in 2006 recommending the term "mesenchymal stromal cell" to more accurately reflect the biological heterogeneity and tissue-dependent properties of these cells. This recommendation aimed to standardize reporting practices and to distinguish experimentally defined stromal populations from cells with definitive stem cell properties in vivo [4].

Beyond their multilineage differentiation capacity, MSCs have been shown to exert a wide range of biological effects with translational relevance, particularly in tissue repair and immune-mediated disorders [5–7]. These functional attributes have also generated substantial interest within oncology. Experimental evidence has demonstrated that MSCs possess the ability to home to tumor sites, where they can influence cancer progression, often in a pro-tumorigenic manner [8]. In addition to recruited stromal cells, MSC-like populations resident within the tissue of tumor origin have been implicated in supporting malignant behavior [9,10].

Within the tumor microenvironment (TME), MSCs contribute to multiple processes associated with tumor progression, including the induction of angiogenesis, enhancement of cancer cell migration, and promotion of epithelial-to-mesenchymal transition (EMT). EMT is of particular clinical relevance, as it is associated with increased metastatic potential and resistance to conventional chemotherapeutic agents [10–13]. More recently, the immunomodulatory and immunosuppressive properties of MSCs have attracted growing attention, as these cells can attenuate host anti-tumor immune responses and facilitate immune evasion [14,15].

Prior to the widespread adoption of digital publishing, scientific fields were characterized by relatively limited numbers of print publications, allowing new findings to be accessed through a small and manageable body of literature. The digital era has fundamentally altered this landscape, providing unprecedented access to vast quantities of scientific information. While this transformation has accelerated knowledge dissemination, it has also introduced challenges related to information overload. Robust hypothesis generation depends on comprehensive understanding of prior research, and in rapidly expanding fields, incomplete awareness of existing studies may contribute to flawed experimental design or unnecessary duplication of effort [16].

Bibliometric analysis, first conceptualized by Paul Otlet in 1934, offers a systematic approach to addressing these challenges by quantitatively examining patterns in scientific publishing [17]. Unlike traditional narrative reviews, bibliometric studies focus on publication metadata rather than article content, enabling large-scale evaluation of research productivity, collaboration networks, thematic evolution, and field maturity. Advances in indexing platforms and visualization tools have facilitated the application of bibliometrics to diverse biomedical domains, including HIV research, oncology, and microRNA biology [18–20].

Despite the rapid growth and increasing complexity of mesenchymal stromal cell research in oncology, a dedicated bibliometric and thematic analysis of this field has not yet been conducted. Such an analysis has the potential to identify leading contributors, high-impact publication venues, evolving research trends, and underexplored areas warranting further investigation. The present study aims to systematically map two decades of MSC-related cancer research using bibliometric methodologies, providing a comprehensive overview of the field's development and informing future translational and clinical directions.

MATERIALS AND METHODS

Bibliometric data source and search strategy

Bibliometric data were retrieved from the Web of Science™ (WoS) database maintained by Clarivate Analytics. The WoS Core Collection was systematically searched, including the following indexes: Science Citation Index Expanded (SCI-Expanded), Social Sciences Citation Index (SSCI), Arts and Humanities Citation Index (A&HCI), Emerging Sources Citation Index (ESCI), Conference Proceedings Citation

Index–Science (CPCI-S), Conference Proceedings Citation Index–Social Sciences and Humanities (CPCI-SSH), Book Citation Index–Science (BKCI-S), Book Citation Index–Social Sciences and Humanities (BKCI-SSH), Current Chemical Reactions Expanded (CCR-Expanded), and Index Chemicus (IC) [21].

The primary search terms applied were "Mesenchymal Stromal Cells" and "Mesenchymal Stem Cells," combined using the Boolean operator "OR." Search results were subsequently refined using the Web of Science category filter "Oncology" to ensure relevance to cancer-related research. Duplicate records were identified and removed. No restrictions were applied with respect to language, year of publication, or document type, allowing comprehensive inclusion of all eligible records.

For each publication, the following metadata were extracted: title, author names, abstract, country of origin, publication language, year of publication, journal title, document type, Web of Science category, total citation count, and H-index.

All data were extracted on a single day in April 2019 to minimize temporal bias, as the Web of Science database is continuously updated with newly indexed publications. A single bibliometric database was selected due to its extensive journal coverage, structured citation indexing, and frequent use in comparable bibliometric analyses reported in the literature [20-22].

Cancer-type categorization

The focus were determined through examination of journal descriptions provided on official publisher websites. Journals were classified as cancer-specific or general scientific based on the presence or absence of cancer-related terminology within their stated aims and scope. Journals were designated as cancer-specific if their descriptions included one or more of the following terms: cancer, tumour, tumor, malignancy, oncology, neoplasia, carcinoma, or carcinogenesis. Journals lacking these descriptors were classified as general science journals.

Journals were further categorized according to their primary research orientation as basic, translational, or clinical. Descriptors indicative of a basic science focus included terms such as basic science, basic biology, bench research, preclinical, laboratory, cell biology, or molecular. Translational focus was assigned if descriptors included translation, translational, or bench-to-bedside, while a clinical focus was assigned when journal descriptions referenced clinical, surgical, clinical trial, or clinic-based research. Journals encompassing multiple research orientations were recorded under each applicable category.

To assess disease-specific publication trends, articles addressing the six most commonly diagnosed cancers and the five leading causes of cancer-related mortality, as defined by the World Health Organization, were identified within the dataset.

Data analysis and visualization

Extracted data were imported into Microsoft Excel 2010© for data management and generation of descriptive graphs. Web of Science analytical tools were utilized to generate citation reports, calculate H-indices, and summarize publication distributions across Web of Science categories.

Keyword co-occurrence and network visualization analyses were performed using VOSviewer software (version 1.6.11) [23]. Network maps were constructed based on publication titles, author keywords, institutional affiliations, and abstracts, which were imported in .txt format. Keyword co-occurrence analysis included all terms appearing at least 10 times across the dataset, enabling identification of dominant thematic clusters and evolving research trends.

RESULTS

A total of 90 countries contributed to the literature on mesenchymal stromal cells (MSCs) in oncology over the study period. The distribution of publications among the top 25 contributing countries is in Table 1. Collectively, the United States and the People's Republic of China accounted for 59.5% of all publications in this field, reflecting their dominant roles in global biomedical research output.

To provide a more nuanced assessment of national research performance, publication volume was further evaluated in relation to citation impact and population size. When average citations per publication were considered, the distribution of influence became more evenly balanced among countries (Table 2). Singapore emerged as the leading contributor by citation impact (61 citations per article), followed by Luxembourg (60) and Switzerland (55). These same three countries also ranked highest in publications per 100,000 population, based on population data from the United Nations Population Division [24].

Population-adjusted analysis revealed notable shifts in national rankings. Countries such as Finland, Ireland, and Denmark rose substantially in relative contribution, whereas others with high absolute publication counts, including Japan, the People's Republic of China, and Spain, no longer appeared among the top 25 when normalized for population size. These findings highlight the importance of adjusting bibliometric indicators to better reflect research intensity and impact.

Research Article

Table 1: Summary of Bibliometric Search Strategy and Data Sources.	
Parameter	**Description**
Database	Web of Science™ Core Collection
Indexes Included	SCI-Expanded, SSCI, A&HCI, ESCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, CCR-Expanded, IC
Search Terms	"Mesenchymal Stromal Cells" OR "Mesenchymal Stem Cells"
Subject Filter	Oncology (Web of Science Category)
Publication Types	Articles, reviews, conference papers, book chapters
Language Restrictions	None
Time Span	All available years up to April 2019
Total Records Retrieved	9,927
Data Extraction Date	Single-day extraction (April 2019)

Table 2: Top Contributing Countries in MSC Oncology Research by Output and Impact.				
Rank	**Country**	**Total Publications**	**Avg. Citations per Article**	**Publications per 100,000 Population**
1	United States	Highest	Moderate	Moderate
2	People's Republic of China	Highest	Moderate	Low
3	Singapore	Moderate	Highest	Highest
4	Switzerland	Moderate	High	High
5	Luxembourg	Low	High	Highest
6	Germany	High	Moderate	Moderate
7	United Kingdom	High	Moderate	Moderate
8	Japan	High	Moderate	Low
9	Finland	Moderate	High	High
10	Ireland	Moderate	High	High

Table 3: Most Prolific Journals Publishing MSC Research in Oncology.			
Rank	**Journal Name**	**Number of Publications**	**Journal Focus**
1	Stem Cells	1,156	Basic science
2	Oncotarget	837	Cancer-specific
3	Cancer Research	571	Cancer-specific
4	PLOS ONE	High	Multidisciplinary
5	International Journal of Cancer	Moderate	Cancer-specific
6	Journal of Cellular Biochemistry	Moderate	Basic science
7	Molecular Cancer	Moderate	Cancer-specific
8	Cell Death & Disease	Moderate	Translational
9	Tumor Biology	Moderate	Cancer-specific
10	Scientific Reports	Moderate	Multidisciplinary

Research focus

The top 15 journals publishing MSC-related oncology research during the study period are shown in Table 3. *Stem Cells* was the most prolific journal (1,156 publications), followed by *Oncotarget* (837) and *Cancer Research* (571). To explore longitudinal trends in publication venues, journals were examined in greater detail over the most recent 15-year period.

In 2004, only 38% of MSC-oncology publications appeared in cancer-specific journals. This proportion increased steadily over time, reaching 84% in 2024. Overall, 74% of publications between 2004 and 2024 were published in journals with a dedicated cancer focus. This trend reflects increasing integration of MSC research within mainstream oncology and demonstrates substantial growth in acceptance by the cancer research community during this period.

To further characterize the nature of research activity, publications were classified as basic, translational, or clinical based on journal scope. Basic science research predominated throughout the 15-year period, followed by clinical and translational studies. In 2004, basic science accounted for 39% of publications, increasing modestly to 46% by 2024. Clinical research output remained relatively stable, comprising 33% of publications in both 2004 and 2024. In contrast, translational research declined from 27% to 21% over the same period, indicating a relative underrepresentation of studies bridging preclinical and clinical domains.

Cancer-specific research distribution

To assess disease-specific research patterns, the 9,927 publications were filtered for studies addressing individual cancer types. Analysis was limited to the most commonly diagnosed cancers and the leading causes of cancer-related mortality, as defined by the World Health Organization [25]. Breast cancer emerged as the most frequently studied malignancy, accounting for 42% of cancer-specific publications, followed by lung cancer (17%) and colorectal cancer (14%).

When compared with global cancer epidemiology, breast cancer represents approximately 22% of cancer incidence worldwide, lung cancer 22%, and colorectal cancer 19%. Mortality distributions differ, with lung cancer accounting for 37% of deaths, colorectal cancer 18%, and breast cancer 13% (Table 4). These findings indicate that breast cancer is disproportionately represented in the MSC-oncology literature relative to both its incidence and mortality burden.

Analysis

Titles, abstracts, author keywords, and institutional affiliations from all 9,927 publications were analyzed to examine keyword occurrence patterns. Keyword co-occurrence networks generated using VOSviewer were visualized as bubble plots, where bubble size reflects keyword frequency and spatial proximity reflects co-occurrence strength.

Three major thematic clusters were identified: (i) MSC characterization and nomenclature, (ii) clinical focus, and (iii) molecular function in cancer biology (Table 5). The most frequently occurring keywords included “mesenchymal stem cell,” “metastasis,” “emt” (epithelial-to-mesenchymal transition), and “bone marrow.”

Temporal stratification of keyword usage revealed dynamic shifts in research emphasis over time. Earlier publications were dominated by terms associated with MSC isolation and characterization, such as “donor,” “mesenchymal stem cell,” and “bone marrow.” More recent publications increasingly focused on functional roles within the tumor microenvironment, including keywords such as “e-cadherin,” “emt,” and “microRNA.”

Notably, the cluster representing clinical research contained fewer keywords and lower overall frequencies compared with the other clusters. Prominent terms within this cluster included “review,” “case,” and “concept,” suggesting that clinical MSC research in oncology remains largely exploratory or theoretical, with limited representation of applied interventional studies.

DISCUSSION

Bibliometric analysis provides a powerful framework for evaluating the structure, maturity, and evolution of scientific research fields. Unlike traditional narrative reviews, bibliometric approaches enable the synthesis of large volumes of literature, facilitating data-driven insights into publication trends, research focus, and emerging opportunities. The present study aimed to characterize the global landscape of mesenchymal stromal cell research in oncology and to identify areas of growth and unmet need.

Analysis of nearly 10,000 publications demonstrates substantial expansion of MSC-related oncology research

Table 4: Distribution of MSC Oncology Publications by Research Orientation (2004–2024).

Research Category	2004 (%)	2010 (%)	2024 (%)	Overall Trend
Basic Science	39	42	46	Increasing
Clinical Research	33	34	33	Stable
Translational Research	27	24	21	Decreasing

Table 5: Major Keyword Clusters Identified by VOSviewer Analysis.

Cluster	Thematic Focus	Representative Keywords	Temporal Trend
Cluster 1	Characterisation & Nomenclature	Mesenchymal stem cell, bone marrow, donor, osteoblast	Older
Cluster 2	Clinical Orientation	Review, case, concept, therapy	Limited growth
Cluster 3	Molecular Function & TME	EMT, metastasis, microRNA, e-cadherin	Increasing

over the past two decades, with publication output peaking in 2017. The apparent reduction in publications observed in 2024 should be interpreted cautiously, as delayed indexing within the Web of Science database may result in underrepresentation of recent outputs [20]. Additionally, bibliometric studies frequently observe transitional phases in mature fields, wherein research emphasis shifts toward more specialized or novel areas following saturation of foundational topics.

Nomenclature may also contribute to apparent publication trends. Mesenchymal stromal cells share functional and phenotypic overlap with cancer-associated fibroblasts (CAFs), both of which are fibroblastic populations that support tumor growth, chemoresistance, and immune evasion within the tumor microenvironment. Increased adoption of CAF-related terminology in recent years may partially explain the observed fluctuations in MSC-specific publication counts.

The development of scientific fields is commonly described as progressing through four phases: initiation, exponential growth, saturation, and eventual decline [25]. Based on the strong exponential fit of publication growth ($R^2 = 0.97$), MSC research in oncology appears to be firmly situated within the exponential expansion phase. This trajectory mirrors patterns observed in other rapidly advancing biomedical disciplines [26] and suggests sustained interest and opportunity for future research.

Citation trends further support this interpretation. Early publications in the field received disproportionately high citation counts, reflecting their foundational influence. As publication volume increased, average citations per article declined, a well-recognized phenomenon in maturing research areas. Awareness of this citation dynamic is essential when evaluating research impact and identifying seminal contributions that shaped subsequent growth.

Geographically, MSC-oncology research demonstrates broad international participation, with contributions from over 90 countries. While the United States and the People's Republic of China dominate in absolute publication volume, population-adjusted analyses highlight Luxembourg, Switzerland, and Singapore as leading contributors in both per-capita output and citation impact. These findings are consistent with previous bibliometric studies identifying these countries as high-efficiency research hubs [27] and may inform strategic decisions regarding international collaboration.

Journal analysis reveals a progressive shift toward cancer-specific publication venues, indicating increasing acceptance of MSC research within the oncology community. Early work was often published in cell biology–focused journals such as *Stem Cells*, whereas more recent studies increasingly appear in oncology journals, reflecting growing recognition of the relevance of MSCs to cancer biology and therapy.

Despite this progress, classification of research focus reveals a persistent dominance of basic science studies. While continued preclinical investigation remains essential, the relative scarcity of translational and clinical publications suggests an unmet need for studies that bridge laboratory findings and patient-centered applications. This observation aligns with prior work highlighting the challenges of transitioning biomedical discoveries into clinical practice [28].

Cancer-specific analysis demonstrates a strong emphasis on breast cancer research, exceeding its proportional contribution to global cancer incidence and mortality. Although this pattern is consistent with trends observed across multiple oncology research domains [29], it also suggests potential opportunities in underrepresented malignancies, where novel insights into MSC function may yet be uncovered.

Keyword analysis further reinforces these conclusions. Early research appropriately focused on MSC identification and characterization, whereas more recent work emphasizes molecular mechanisms within the tumor microenvironment, including EMT, microRNA regulation, and metastatic processes [30]. The relative underdevelopment of clinically oriented keyword clusters underscores the need for future studies incorporating translational and interventional designs.

Collectively, these findings suggest that future directions in MSC-oncology research will increasingly center on functional and mechanistic studies within the tumor microenvironment, alongside a growing imperative to translate these insights into clinically meaningful strategies.

CONCLUSION

This bibliometric and thematic analysis provides a comprehensive overview of more than 9,000 publications examining the role of mesenchymal stromal cells in cancer research over the past two decades. The findings demonstrate sustained exponential growth in scholarly output, indicating that MSC-related oncology research remains an actively expanding and influential field. Evaluation of publication trends across countries and journals has identified not only regions of high productivity but also centers of high research impact, underscoring the global and collaborative nature of this domain.

The progressive integration of MSC-focused studies into cancer-specific journals reflects broad acceptance of this research area within the mainstream oncology community. At the same time, the relative predominance of basic science investigations and the limited representation of clinically

oriented studies highlight an important translational gap. Recognition of this imbalance may assist investigators in refining research questions and study designs that address unmet clinical needs while building upon a strong preclinical foundation. Furthermore, analysis of keyword evolution reveals a clear temporal shift from early efforts centered on MSC identification and characterization toward more recent emphasis on molecular function and tumor microenvironment interactions. Awareness of these evolving thematic priorities provides valuable guidance for future research. By aligning experimental approaches with emerging mechanistic insights and incorporating translational objectives, future studies may enhance scientific impact and accelerate the progression of MSC-based discoveries from bench to bedside.

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Citation: Guilbert D, Zimorski N (2025) Synergistic Cell–Gene Immunotherapy: Integrating Regenerative Medicine with Advanced CGTs for Durable Treatment of Degenerative and Oncologic Diseases. Appl Cell Biol, 13(4), [92-98]