Development Patterns and Research Hotspots in Synovial Membrane Mesenchymal Stem Cells and Synovial Fluid Mesenchymal Stem Cells

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Abstract

Synovial membrane mesenchymal stem cells (SM-MSCs), a type of tissue-specific stem cells, are involved in forming synovial joints in embryos and the maintenance and repair of joint tissue in adults. Mesenchymal stem cells (MSCs) produced from synovial fluid (SF-MSCs) may have therapeutic properties with a higher capacity for cartilage proliferation than other MSC types.The research domains of SM-MSCs and SF-MSCs, however, have not been subjected to bibliometric analysis.This study aimed to visualize and analyze their research areas and trends using a bibliometric approach. Most studies on SM-MSCs and SF-MSCs are focused on basic research, but as SM-MSCs play important roles in chondrogenesis, osteogenesis, myogenesis, and tendon formation, they may have therapeutic potential for cartilage and tissue repair linked to diseases. The current study is the first to thoroughly introduce the development patterns and hotspots in this field of study.

1. Introduction

Pluripotent stem cells derived from the mesoderm are called mesenchymal stem cells (MSCs), and mainly exist in the connective tissue and interstitial organs[1].In 1991, inducible cells from bone marrow were identified for the first time by Friedenstein et al.[2] and named MSC. Characteristic of stem cells, they possess self-renewal and exhibit multidirectional differentiation, and can differentiate into bone, cartilage, muscle, or tendon, thus providing a source of cells for the clinical treatment of trauma.They have a strong immune regulatory function and vascular regulatory characteristics and participate in tissue repair by proliferating and regenerating through paracrine mechanisms[3].

De Bari et al. isolated MSCs from the human synovium in 2001 and documented their capacity for self-renewal and differentiation. They were named “synovial membrane-derived MSCs” (SM-MSCs)[4]. In 2004, MSCs were extracted by researchers from synovial fluid (SF-MSCs). SM-MSCs and SF-MSCs have high proliferative capacity and differentiation potential, joint specificity, and can form cartilage and repair tissue[2, 5]. Compared with MSCs from other sources such as adipose tissues, SM-MSCs and SF-MSCs show considerable superiority in chondrogenesis, osteogenesis, myogenesis, and tendogenesis. They are easy to obtain and have wide clinical application prospects[6]. Researchers have begun experimentation with SM-MSCs and SF-MSCs for treating diseases, including osteoarthritis(OA)[7] and rheumatoid arthritis[8], with important breakthroughs. However, few reports have directly compare SF-MSCs and SM-MSCs immediately after their acquisition and during culture. In-depth studies on SM-MSCs and SF-MSCs can determine their therapeutic roles in disease development and prognosis and provide new ideas for managing clinical diseases.

Bibliometric tools are often used for visual analysis literature and are used in various disciplines of medicine, such as rheumatology[9]. Some scholars have reported bibliometric studies on adipose-derived MSCs.However, no study has used this method to analyze and summarize SM-MSC research.

Therefore, this study aimed to quantitatively and qualitatively analyze publications on SM-MSC and SF-MSC research using bibliometric approach over the past 22 years, and identify research hotspots and development prospects using publications.

2. Methods

2.1 Retrieval strategy

On March 12, 2023, the Web of Science Core database was searched for every piece of literature included in our study. (TS = (Synovial Mesenchymal Stem Cells) OR TS = (SM-MSCs) OR TS = (SM-MSCs) OR TS = (SM-MSCs) OR TS = (SM-MSCs) OR TS = (Synovial Fluid Mesenchymal Stem Cells) OR TS = (SFMSCs) OR TS = (SF-MSCs))was the search formula. The titles, abstracts and full texts of the articles were evaluated according to their topics, and articles that were not related to the keywords “Synovial Mesenchymal Stem Cells” and “Synovial Fluid Mesenchymal Stem Cells” were excluded (Table 1).

Table 1. Summary of data source and selection

Category	Specific Standard Requirements
Database	Web of Science core collection
Citation indexes	SSCI, SCI
Search string	(TS = (Synovial Mesenchymal Stem Cells) OR TS = (SMSC) OR TS = (SM-MSCs) OR TS = (Synovial Fluid Mesenchymal Stem Cells) OR TS = (SFMSC) OR TS = (SF-MSCs))
Searching period	January 2001 to December 2022
Language	English
Document types	“Articles” and “reviews”
Exclusion criteria	Meeting Abstracts, Proceeding Paper, Editorial material, Book Chapters, Early Access, Correction, Letter, and Documents not related to Synovial Mesenchymal Stem Cells and Synovial Fluid Mesenchymal Stem Cells
Result	438 documents

2.2 Statistical Analysis

Graphs were visualized using VOSviewer, CiteSpace, Scimago Graphica, and Microsoft Office software.VOSviewer is a visual analysis program that extracts important parameters from large amounts of data and constructs cooperative or co-occurring relationships between different objects.CiteSpace is a visual citation analysis software that is used to perform a number of bibliometric and network analyses[18].Scimago Graphica can be adapted to VOSviewer for the visualisation of maps , obtaining various forms of graphs. Trends in annual postings are also analysed and visualised using Microsoft Office 2019.

3. Results

3.1 Literature publication trend

The number of articles published over time serves as an indicator of the evolving research trends in this field.A few relevant publications appeared in Stage I, addressing the initial exploration stages of research. The general increased trend in Stage II article counts suggests developing attention to this topic, and a possible breakthrough in the study of SM-MSCs and SF-MSCs. Despite variable numbers of Stage III articles, the annual number of publications generally showed an increasing trend and peaked in 2019 and 2021 (Fig.1).

3.2 Domain

In the domain dimension, superimposed map analysis was performed on the fields involved in SM-MSC- and SF-MSC-related publications. As shown in Figure 1, 438 papers were distributed in 227 different fields. The five colored clusters represent different domain clusters. The red clusters represent Biology and Medicine, green represent Psychology and Social Sciences, blue represent Chemistry and Physics, yellow represent Ecology and Environment, and purple represent Engineering and Mathematics. Thus, many scholars studied SM-MSCs clustered in Biology and Medicine, including Cell and Tissue Engineering, Biochemistry and Molecular Biology, and Medical Laboratory Technology domains. We detected cooperation across different fields, although there were exceptions; for example, little cooperation was detected between SMSC research and Anthropology.

3.3 Distribution of countries and institutions

Researchers from Asia, North America, and Europe have published the majority of the articles (Fig.2a). China and Japan are at the top in terms of the number of papers published, accounting for one-half of all published articles (Table 2). The 438 articles on SM-MSCs and SF-MSCs were published by researchers from 39 countries(Fig.2b).It is evident that most nations actively cooperate with one another, and institutions in industrialized countries have a combined output of publications significantly higher than that of emerging nations, with the exception of China.

The top five institutions in terms of publications are mainly located in Asia. Tokyo Medical & Dental University was the most published institution and the institution with the most cooperation. The number of publications and the relationship between the cooperation networks of each institution are shown in Fig.2c. The closest cooperation was between Tokyo Medical & Dental University and Southern University of Science and Technology.

Table 2: The publications of the top five countries and institutions

Rank	Country	Counts (% of 4338)	Citations	Institution	Counts (%)	Citations
1	China (Asia)	128 (29.2%)	3296	Tokyo Medical & Dental University (Japan)	59 (13.5%)	2622
2	Japan (Asia)	102 (23.3%)	3964	University of Calgary (Canada)	31 (7.1%)	1142
3	USA (North America)	68 (15.5%)	1720	Osaka University (Japan)	25 (5.7%)	944
4	Canada (Europe)	40 (9.1%)	1535	Sun Yat Sen University (China)	20 (4.6%)	453
5	South Korea (Europe)	28 (6.4%)	603	University of Leeds (United Kingdom)	14 (3.2%)	1100

3.4 Analysis of journals and co-cited journals

179 academic journals published the articles, with Stem Cell Research & Therapy publishing most of them. Biomaterials, one of the top 10 journals, has the highest impact factor (IF = 15.304).Osteoarthritis and Cartilage was the most cited journal,Arthritis & Rheumatology had the greatest impact factor of any journal(Table 3). There was a positive common citation relationship across the journals (Fig.3a b).

The distribution of relationships between journals is depicted via a double map overlay of journals. The orange and green paths in Figure 3c are the main citation–cited relationships. The orange path denotes that literature from the journals Molecules, Biology, and Immunology regularly references literature from Molecules, Biology, and Genetics.

Table 3. Top 10 journals and co-cited journals

Rank	Journal	Count (%)	IF (2022)	JCR	Co-cited Journal	Citation	IF (2022)	JCR
1	Stem Cell Research & Therapy	25 (5.71%)	8.079	Q1	Arthritis & Rheumatology	1070	15.483	Q1
2	Stem Cell International	18 (4.1%)	5.131	Q2	Osteoarthritis And Cartilage	854	7.507	Q1
3	Journal Of Osteoarthritis Research	16 (3.6%)	3.102	Q1	Biomaterials	471	15.304	Q1
4	Osteoarthritis And Cartilage	14 (3.2%)	7.507	Q1	Journal of Orthopaedic Research	462	3.102	Q1
5	Science reports	14 (3.2%)	4.996	Q2	Stem Cell	439	5.845	Q1
6	Tissue Engineering Part A	11 (2.5%)	4.080	Q2	Arthritis Research & Therapy	353	5.606	Q1
7	American Journal of Sports Medicine	10 (2.3%)	7.010	Q1	American Journal of Sports Medicine	340	7.010	Q1
8	Arthritis Research & Therapy	10 (2.3%)	5.606	Q1	Stem Cell Research & Therapy	337	8.079	Q1
9	Plos One	10 (2.3%)	3.752	Q2	Journal of Bone and Joint Surgery American	327	8.043	Q1
10	Biomaterials	10 (2.3%)	15.304	Q1	Plos One	321	4.080	Q2

*IF: Impar Factor; JCR, Journal Citation Reports.

3.5 Co-Cited Authors

Authors cited in many papers are considered co-cited authors. Although Cosimo De Bari has published very few articles, De Bari et al. introduced SMSC in the history of academic research and are cited by a wide range of researchers, with Cosimo De Bari being the most cited author(Table 4). But when it comes to the quantity of publications, co-authorship, and co-citations, Ichiro Sekiya came out on top, making him the most significant author in the field of SM-MSCs and SF-MSCs. As shown in Fig.4, cooperation between different co-cited authors was common.

Table 4. Top five authors and co-cited authors

Rank	Co-cited Author	Documents	Citation
1	Cosimo De Bari	3	622
2	Ichiro Sekiya	61	241
3	Yusuke Sakaguchi	5	197
4	Elena A Jones	1	136
5	Hideyuki Koga	46	127

3.6 Analysis of references and co-cited references

Cluster analysis of the literature using CiteSpace showed that the largest cluster was "cartilage formation," followed by "synovial fluid" and "intra-articular injection" (Figure 5a). According to the timeline axis, the focus of the study gradually changed from "cartilage formation" to "synovial fluid "and "extracellular vesicles" (Fig.5b).

Widely cited references are known as co-cited references. As shown in Table 5, half of the top 10 co-cited references for SM-MSC research were published in the journal Arthritis & Rheumatology. There was a positive citation relationship across the literature. "Comparison of human stem cells derived from various mesenchymal tissues: superiority of synovium as a cell source" had the most nodes and represented most references.

Table 5. Top ten co-cited references

Rank	Co-Cited Reference	Year	Journal	Citations
1	Comparison of human stem cells derived from various mesenchymal tissues: superiority of synovium as a cell source	2005	Arthritis & Rheumatology	185
2	Multipotent mesenchymal stem cells from adult human synovial membrane	2001	Arthritis & Rheumatology	165
3	Minimal criteria for defining multipotent mesenchymal stromal cells. The International Society for Cellular Therapy position statement	2006	Cytotherapy	127
4	Multilineage potential of adult human mesenchymal stem cells	1999	Science	99
5	Comparison of rat mesenchymal stem cells derived from bone marrow, synovium, periosteum, adipose tissue, and muscle	2007	Cell and Tissue Research	75
6	Synovial fluid-derived mesenchymal stem cells increase after intra-articular ligament injury in humans	2008	Rheumatology	72
7	Enumeration and phenotypic characterization of synovial fluid multipotential mesenchymal progenitor cells in inflammatory and degenerative arthritis	2004	Arthritis & Rheumatology	69
8	Higher chondrogenic potential of fibrous synovium- and adipose synovium-derived cells compared with subcutaneous fat-derived cells: distinguishing properties of mesenchymal stem cells in humans	2006	Arthritis & Rheumatology	68
9	Human mesenchymal stem cells in synovial fluid increase in the knee with degenerated cartilage and osteoarthritis	2012	Journal of Orthopaedic Research	66
10	Synovial fluid mesenchymal stem cells in health and early osteoarthritis: detection and functional evaluation at the single-cell level	2008	Arthritis & Rheumatology	64

3.7 Keyword analysis

Through keyword analysis,it can be found that "osteoarthritis" is the main related disease in the study of SMSC and SF-MSC, and "articular cartilage" is the key position in the study(Table 6).The main keywords of the red cluster comprise mesenchymal stem cells, differentiation, stromal cells, and others.(Fig.6a). Moreover, according to the keywords marked with different colors in Fig.6b, the yellow keywords, such as extracellular vesicles and intra-articular injection, appeared later. Taking intra-articular injection as an example, studies have shown that intra-articular injections of SM-MSCs and SF-MSCs are often used to treat joint diseases.

Table 6. Top five keywords

Rank	Keywords	Counts
1	mesenchymal stem cells	179
2	osteoarthritis	148
3	stromal cells	106
4	differentiation	105
5	bone-marrow	98

3.8 Burstiness detection

Burst detection examines the issues raised by numerous academics and shows that the article has been often referenced over time by experts in the same subject. “Comparison of human stem cells derived from various mesenchymal tissues: superiority of synovium as a cell source” was the article with the strongest citation burst, which broke out between 2006 and 2010 (Fig.7a). The strongest burstiness word was “extracellular vesicle,” which broke out between 2021 and 2022 (Fig.7b). Reference years of the top 10 were evenly distributed, representing the steady progress of SM-MSC research. The top 10 burstiness words were rare from 2015 to 2017, which could be why the annual publication volume of related literature did not show a significant increase from 2015 to 2017.

4. Discussion

General information

The volume, growth, and decline of publications may provide insights into the direction of future development in each field of study. The annual number of publications in Phase III was much higher than that in Phase II. Overall, there was an increase in publications on SM-MSCs in the past 20 years, indicating SM-MSCs to be an important and popular research topic. This is a positive development for the future clinical treatment of joint diseases.

There are five major categories of publications related to SM-MSCs and SF-MSCs, among which, the basic medicine category is mainly applicable to SM-MSCs. Among the 438 articles included in the study, the number of articles related to basic research far exceeded the number of articles related to clinical efficacy. In basic research articles, a wide variety of animal species were used in the experiments, including mice,rats, horses, rabbits, and pigs[10, 11].Clinical experiments also included the efficacy studies of SM-MSCs in the treatment of knee joints, ankle joint, and hip joints[12, 13], and various factors affecting the efficacy, such as steroids, platelet plasma (PRP) infiltratio, and naproxen[14, 15].However, since the clinical application of SM-MSCs is still quite limited, the sample size was small, and the clinical basis was insufficient. Therefore, future research should focus more on clinical studies.

From a graphic examination of the nations and distribution of institutions, institutions in industrialized countries have a combined output of publications significantly higher than that of emerging nations, with the exception of China. As the largest growing nation in the world, as well as the one with the greatest output of publications and degree of collaboration, China should increase its research cooperation with developed countries while jointly promoting the development of this field to enhance the results and influence of research.

The journal with the greatest number of citations and articles on SMSC was Osteoarthritis and Cartilage. The main research areas of SMSC and SF-MSC-related articles were the relationship between SMSC and SF-MSC levels and OA, OA treatment via signal pathway, the mechanism and mode of use of SM-MSCs and SF-MSC, and the description of methods to enhance the effects and differentiation of SM-MSCs. The literature promoted cross-fusion of clinical treatment of OA and basic SMSC and SF-MSC-related research results. Biomaterials (IF = 15.304) had the highest IF among the journals.Its main research areas included exosome-mediated delivery of kartogenin for stem cell therapie, functional biomaterial for in vivo cartilage regeneratio, and tissue-engineered cartilage In the double map overlay of SM-MSC- and SF-MSC-related journals (Fig.3C), the basic medicine category related to SM-MSCs and SF-MSCs is widely used and often cited by other disciplines.

Among the top 10 articles cited, “Comparison of human stem cells derived from various mesenchymal tissues: superiority of synovium as a cell source” was the most cited publication. To identify human MSCs, the International Society for Cellular Therapy's Mesenchymal and Tissue Stem Cell Committee suggested a set of minimal requirements: MSC surface markers, in vitro growth characteristics, and three differentiation capacities[16]. Cosimo De Bari et al. first reported that human pluripotent stem cells could be isolated from knee joint MSCs and the development of cell therapy for postnatal bone tissue repair was expected thereafter[4]. Yusuke Sakaguchi and Hideya Yoshimura et al. investigated the yield, expansion, and multipotential properties of MSCs from different tissue sources and found that the most proliferative and cartilage-forming capacity was shown by synovial-derived cells[17], and they may also be a source of bone marrow MSCs[11].

In the study of SM-MSCs in healthy and diseased states, Murphy J Mary et al. found that MSCs stimulate the regeneration of meniscus tissue, delay the progressive destruction common in the OA model, and play a definite role in treating OA[18]. Patients with OA and degenerative cartilage had more MSCs in their synovial fluid, according to research by Elena A. Jones and Ichiro Sekiya et al.[19]. Catabolism of chondrocytes was stronger than anabolism in such patients, causing articular cartilage damage[20, 21]. Toshiyuki Morito et al. reported that SF-MSC numbers increased after intra-articular ligament injury[22]. Moreover, fibrous synovial and adipose synovial-derived cells have higher chondrogenic potential than subcutaneous adipose-derived cells[23] This provides a direction for further studies on whether intra-articular injection of SM-MSCs could inhibit arthritis progression.

Hot spots and frontiers

Differentiation of SM-MSCs and SF-MSCs

SM-MSCs and SF-MSCs can expand in vitro and undergo multidirectional differentiation. Cell subpopulations differ in their ability to differentiate cartilage; for example, the CD73(+) CD39(+) cell subpopulation has higher levels of Sox9 and Runx2 and more pronounced cartilage osteogenic potency compared to the CD73(+) CD39(-) cell subpopulation[24]. The environment in which the cells are placed and the external stimuli affect the direction of cell differentiation.Controlling the chondrogenic differentiation of transplanted MSCs in the joint remains challenging. IL-1β can hinder cartilage differentiation in SF-MSCs, and upregulation of IL-6 and activation of the NF-κB pathway further promote this biological behavior[25]. SM-MSCs were cultured in specific media, and the cells aggregated to form spheroids for further differentiation to chondrocytes[26]. Corresponding mechanical stimulation also increased the cellular expression of osteogenic markers (ALP and Cbfa1) and chondrogenic markers (Sox9 and Col2a1). In studies of scaffold compositions that promote cellular chondrogenesis/osteogenesis, the PEG-CSC-TGF β1 scaffold promoted enhanced chondrogenic differentiation of SM-MSCs, and osteoblast markers were induced to increase by the PEG-PDMS-BMP2 scaffold. Additionally, SM-MSC differentiated cells changed from chondrocytes to hypertrophic chondrocytes to osteoblast-like cells as a result of the stepwise switch from PEG-CSC-TGF-1 to PEG-PDMS-BMP2 scaffolds. The differentiation potential of SF-MSCs toward meniscal fibrochondrocytes increased after the addition of exogenous growth factors, such as insulin-like growth factor 1 and transforming growth factor beta-3 during inoculation and culture on meniscal-derived decellularized matrix scaffolds.

Extracellular vesicles of SM-MSCs and SF-MSCs

Stem cell drugs have strong clinical potential, but there are unknown risks, such as chromosome mutation, immunosuppression, and capillary occlusio. Xu Ke et al. found that small extracellular vesicles (EVs) derived from MSCs could mimic the role of MSCs while reducing the risk of adverse events[27]. EVs are membrane-derived cell structures that range in size from 50 to 200 nm and contain proteins and miRNAs. EVs are delivered from primary cells to target cells for intercellular communication and are involved in various physiological and pathological cell processes[28]. Owing to the paracrine action of EVs, which transport specific chemicals (massive amounts of DNA, RNA, proteins, and lipids from MSCs) to the recipient cells, MSC-based therapy for cartilage regeneration is effective[29]. Duan Ao et al. studied the EVs of human SM-MSCs pretreated with LPS and found that compared to PBS and EVs, LPS-pre-EVs may increase chondrocyte migration and proliferation while reducing apoptosis in these cells and improve their ability to treat OA[30]. Moreover, compared to treatment with MSCs, MSC-derived EV therapies are safer because they contain fewer membrane-bound proteins; hence, they cannot form tumors directly, reducing the possibility of side effects[31]. Joint development and homeostasis are regulated by cell-derived EVs in the synovial fluid, and SM-MSC- and SF-MSC-derived EVs may be a hot spot for future research.

Role of SM-MSCs and SF-MSCs in arthritis

OA, a degenerative disease characterized by cartilage injury, the contributory factors include ag, joint injury, and femoral acetabular impact shape[32]. One study showed that the number of SF-MSCs increased with cartilage degeneration and the severity of osteoarthritic disease compared to healthy controls[19].During OA progression, CD44 expression gradually increases[33]. The development of hip OA may be linked to widespread immunological mobilization driven by SM-MSCs that are CD44/CD105 double positive[34] and articular cartilage CD44 expression levels and SF-MSC CD44 expression levels correlated with OA joint

severity[35]. SM-MSCs are crucial for the early preservation of bone joints. Tao Shicong et al. have studied the extracellular vesicles of human SM-MSCs with high expression of miR-140-5p and found them to activate YAP through signal pathways to enhance the proliferation and migration of chondrocytes, successfully preventing OA in rats[36]. SM-MSCs may also improve OA by reducing chondrocyte reactive oxygen species (ROS) levels and inhibiting inflammatory responses during OA disease progression[37, 38] (Fig.8). A comparison of SF-MSCs with SM-MSCs in in vitro and in vivo investigations revealed that SF-MSCs have non-inferior chondrocytic differentiation and articular cartilage regeneration capacity. In vitro, SF-MSCs have a lower proliferation capability than SM-MSCs. Traditional methods for collecting SM-MSCs include incision of synovial tissue or intra-articular injection of digestive factors[39]. Tissue resection can cause joint trauma, and similarly, intra-articular injection of digestive factors can damage SM-MSCs, whereas SF-MSCs can be obtained by arthrocentesis, which is less invasive and more widely used in outpatient settings than the previous two methods. Therefore, SF-MSCs can be an alternative to SM-MSCs[40]. Studies on SF-MSCs for clinical availability may increase in future, benefiting patients with autologous transplants.

Further, SM-MSCs are crucial in various joint conditions. T cell activation and proliferation can be induced by SM-MSCs in the inflammatory environment caused by RA, leading to abnormalities in the immune system and persistence of inflammation. Arthritis leads to joint injury, inhibits the value-added differentiation potential of SM-MSCs, and affects their immunomodulatory ability. The remarkable cartilage differentiation capability of SM-MSCs has opened a new area of study for the treatment of bone and joint ailments with stem cells and regenerative medicine. In contrast, SF-MSCs have been relatively neglected by researchers. Yet, compared to other MSC sources, including adipose tissue and bone marrow, they possess a greater ability for cartilage growth.SF-MSCs are easily extracted from patients with temporomandibular joint (TMJ) disease and are a promising research direction for TMJ cartilage repair[25, 41].

SM-MSCs and SF-MSCs show clear superiority in chondrogenesis, osteogenesis, myogenesis, and tendinogenesis, and their capacity to treat illnesses offers significant potential for repairing cartilage and tissue. For the regeneration of bone and cartilage in OA and RA, the differentiation capability of SM-MSCs and SF-MSCs is extremely important; SM-MSC and SF-MSC-derived EVs can significantly promote chondrocyte proliferation and migration, which has good prospects for clinical applications. As SF-MSCs are very similar to synovial fibroblasts, distinguishing them after isolation is difficult. SF-MSCs and synovial fibroblasts are indistinguishable based on cell shape, cell surface markers, differentiation capacity, and immunomodulatory features. Current research data are insufficient to determine whether SM-MSCs, SF-MSCs, and synovial fibroblasts all pertain to the same cell type; more research is necessary to establish this[42].

5. Conclusion

Our findings indicated an annual increase in the volume of SMSC-related research over the study period. Researchers from various countries and institutions are becoming increasingly enthusiastic about SMSC research, and cooperation between multiple countries and institutions has been increasing. Visualization analysis provided a clear documentation of the action texture, research hotspots, and development trends across various fields. Earlier research focused on basic science, studying subjects such as OA, EVs, and

differentiation as short-term research hotspots. The analysis of the keywords and references may be used as a resource for researchers to advance the studies on SM-MSCs and SF-MSCs. In the future, not only basic but also clinical research is expected to develop rapidly.

Abbreviations

SM-MSCs: Synovial mesenchymal stem cells; SF-MSCs:Synovial fluid-derived mesenchymal stem cells ;OA: Osteoarthritis; MSCs: Mesenchymal stem cells; HO: Hip osteoarthritis; TGF- β: Transforming growth factor-β; EVs: Cell- derived extracellular vesicles; RA: Rheumatoid arthritis.

Declarations

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Conflict of interest

The authors declare no competing interests.

Ethical approval

This manuscript does not involve human participants or animals. Thus, ethical approval is not required.

Informed consent

This manuscript does not involve human participants or animals. Thus, Informed consent is not required.

Author Contributions

XQ and WS performed and wrote the manuscript; NQ, LJX, JJQ, and WL collected the references and designed the table; XQ and LJX drew the figures; GJF modified the manuscript. All authors contributed to the article and approved the submitted version. XQ and WS have contributed equally to this work and share first authorship.

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Figures

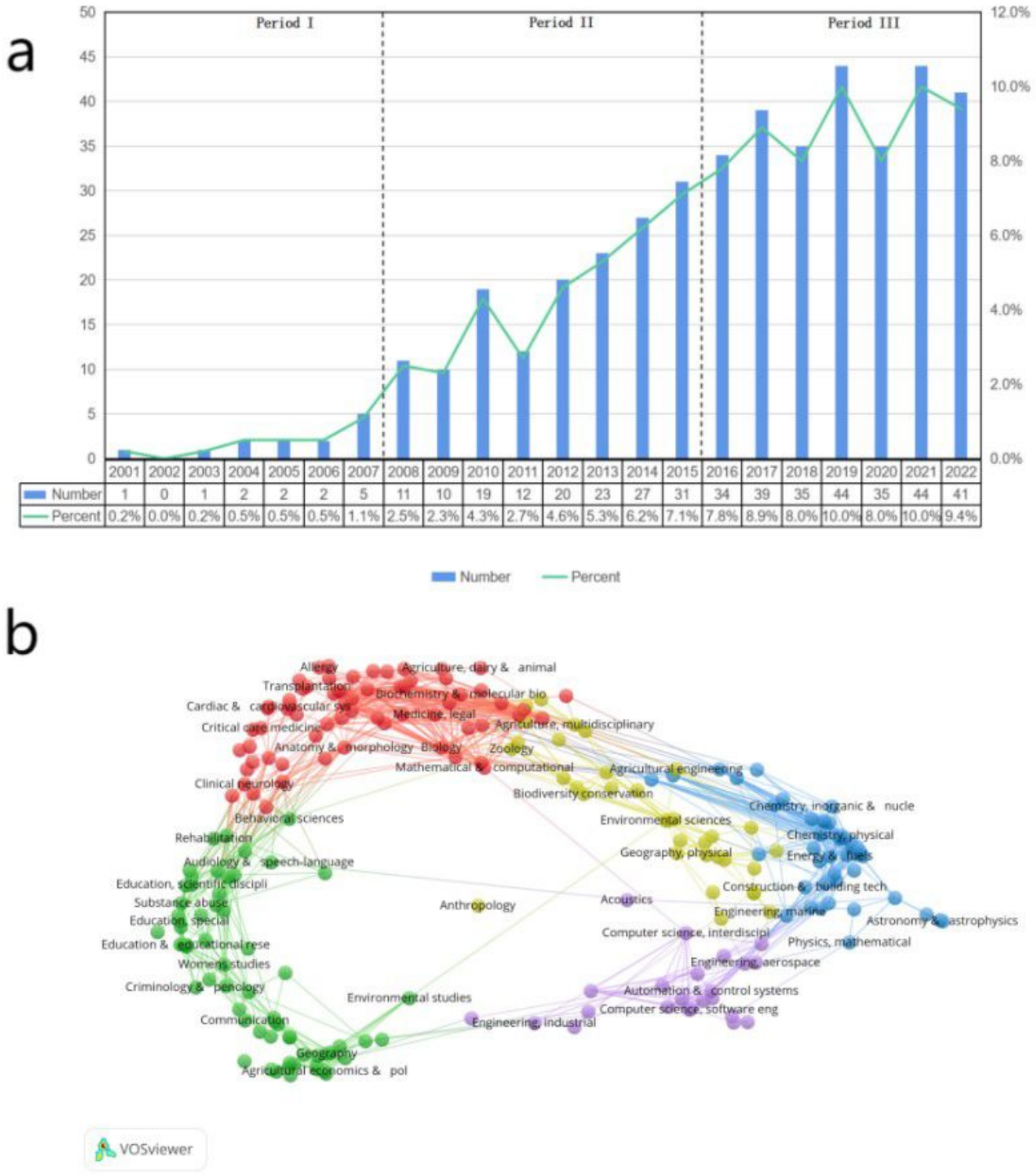

Figure 1

(a) The annual number of publications; (b) Domain Analysis

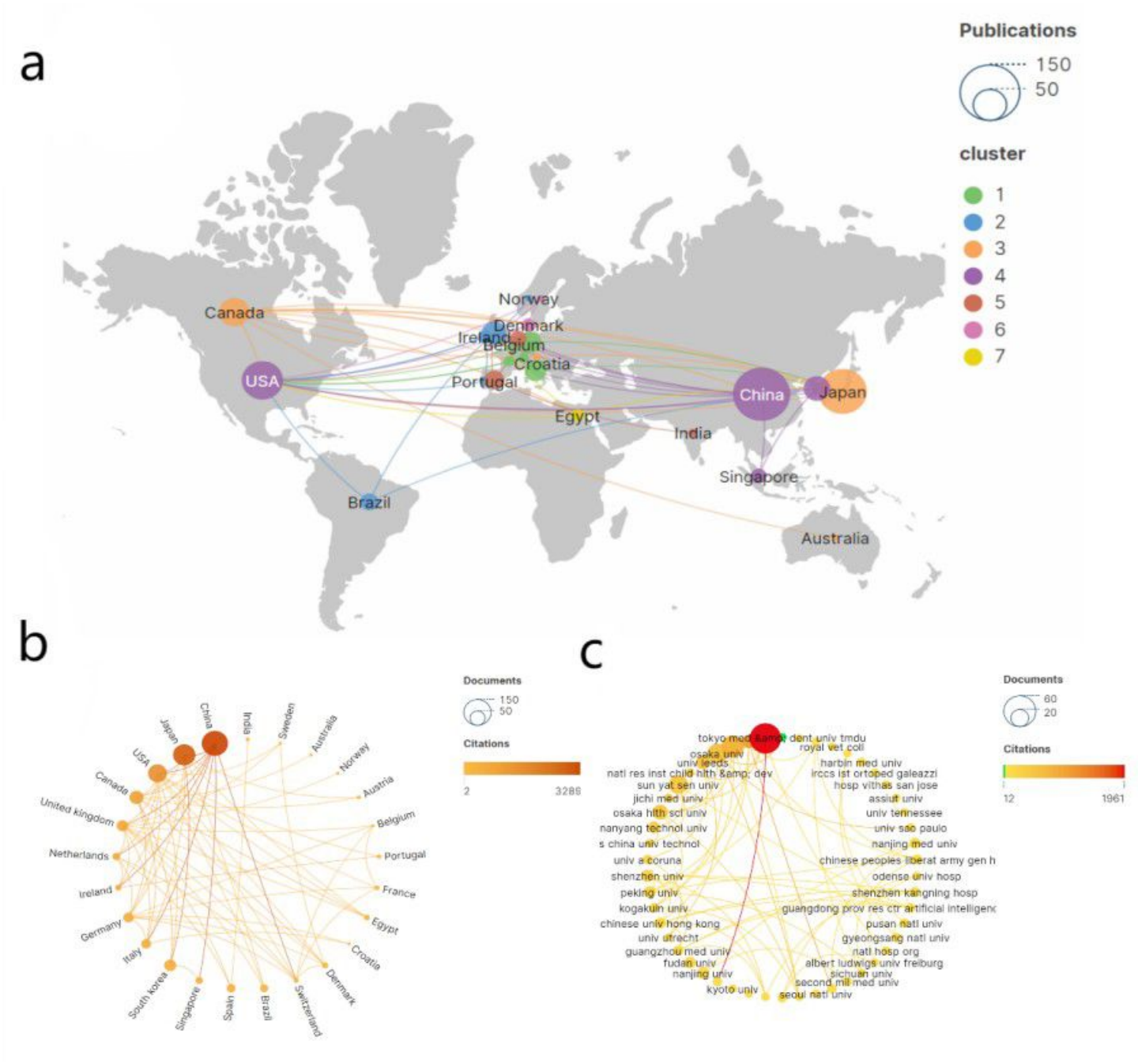

Figure 2

(a) Geographical distribution of countries with publications;(b,c) Total number of publications produced by each nation and each institution

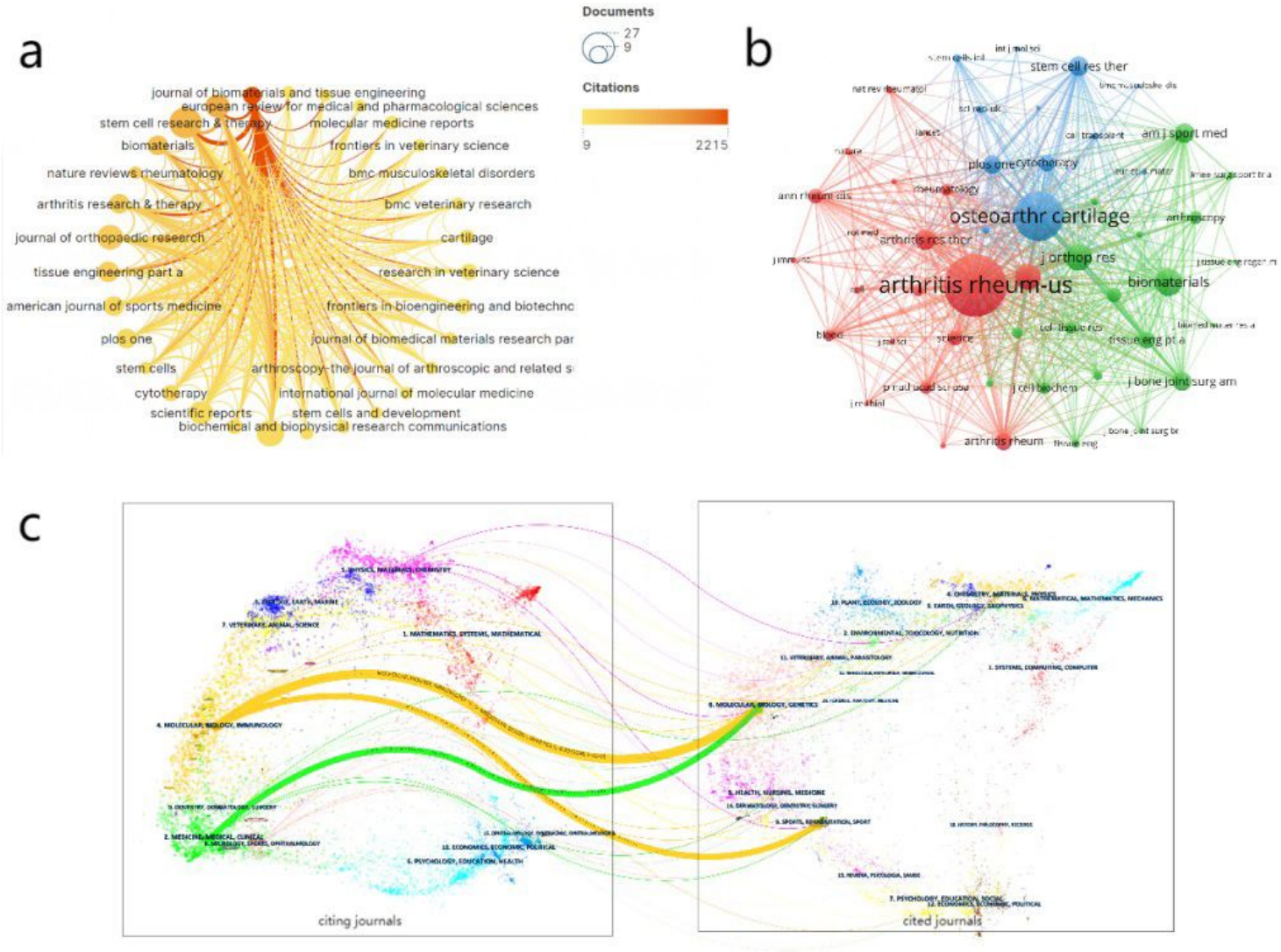

Figure 3

(a) Visualization analysis of journals; (b) Network map of journal co-citation analysis; (c) Dual-map overlay of journals

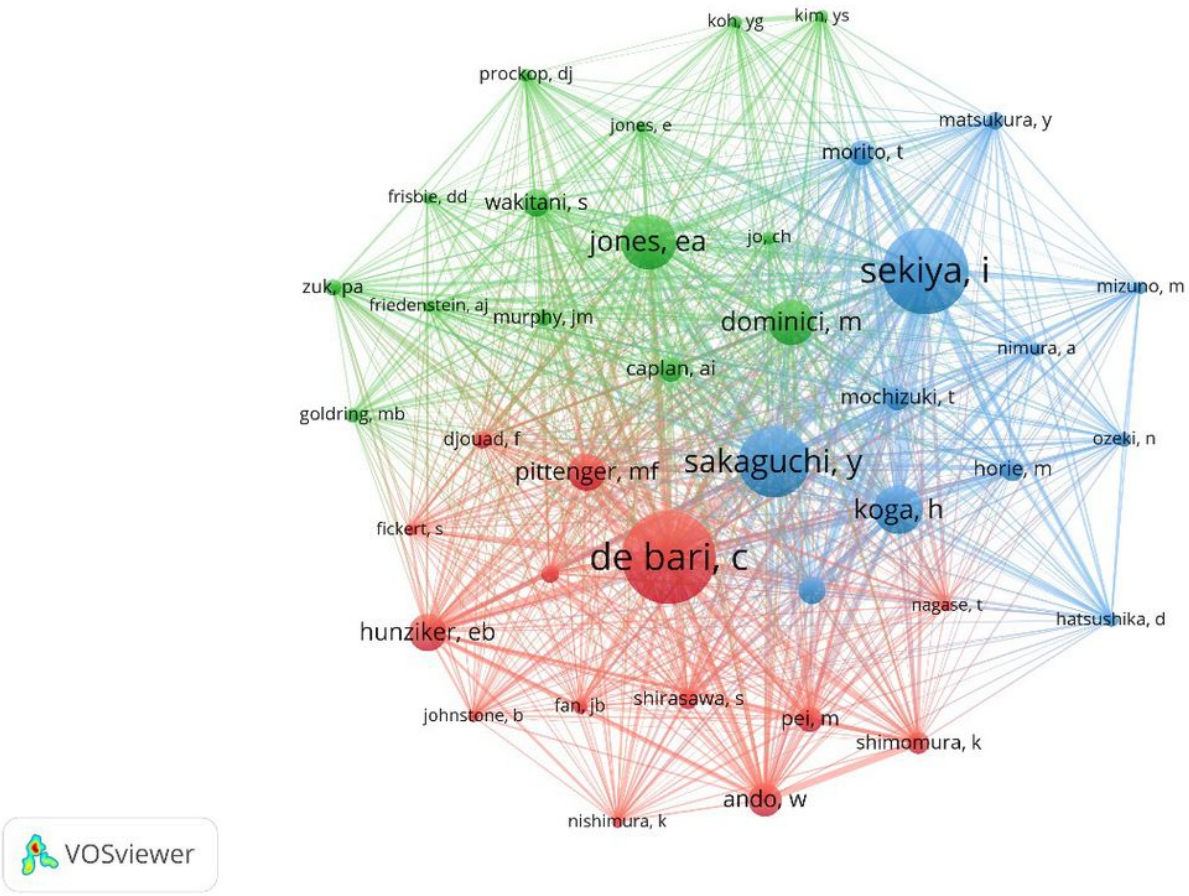

Figure 4

Network map of journal co-cited authors

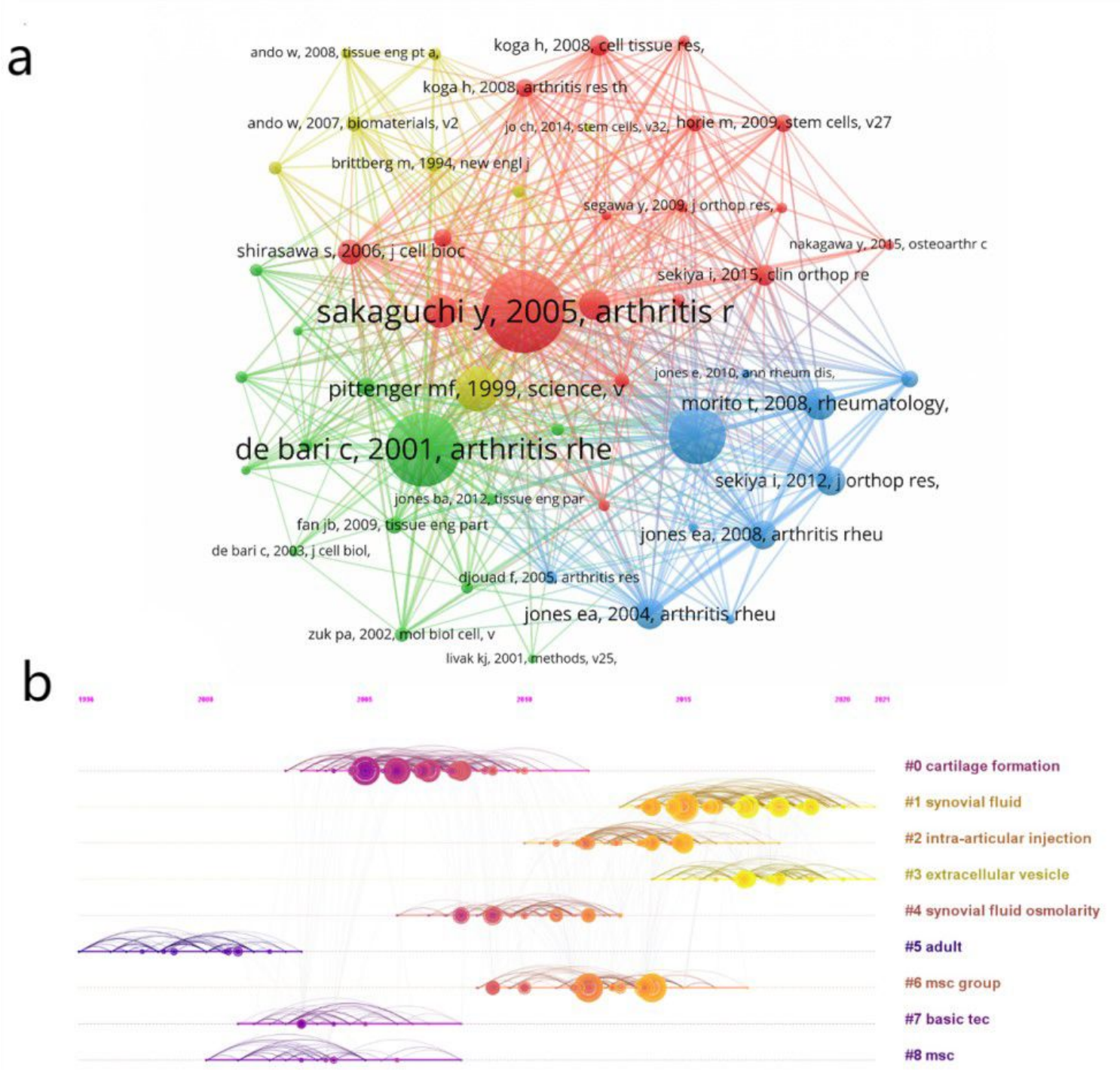

Figure 5

(a) Network map of reference analysis; (b) Timeline map of reference analysis

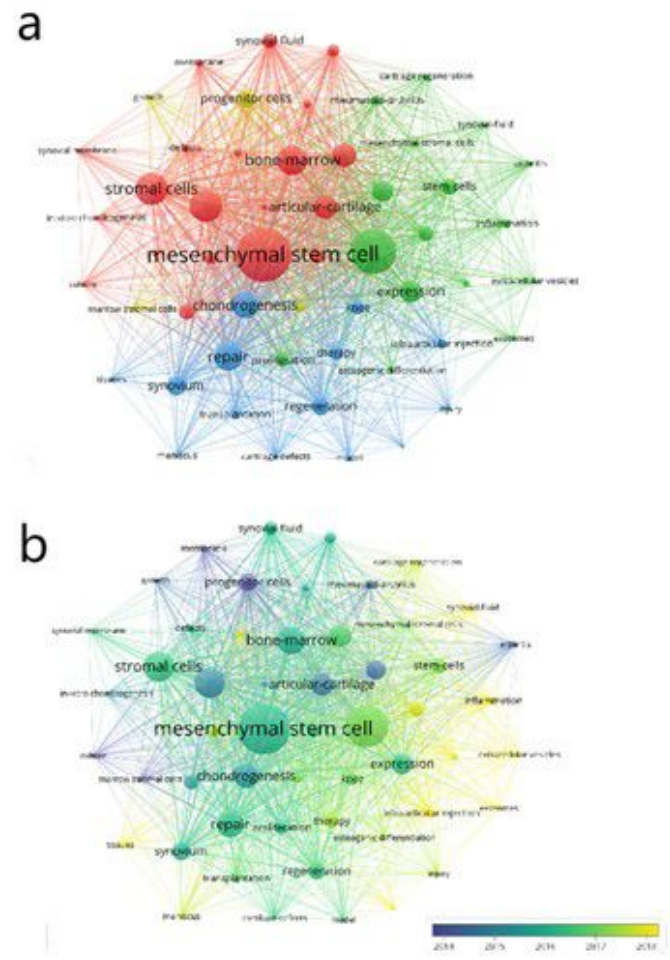

Figure 6

(a) Keyword cluster analysis; (b) Distribution of average time for keywords

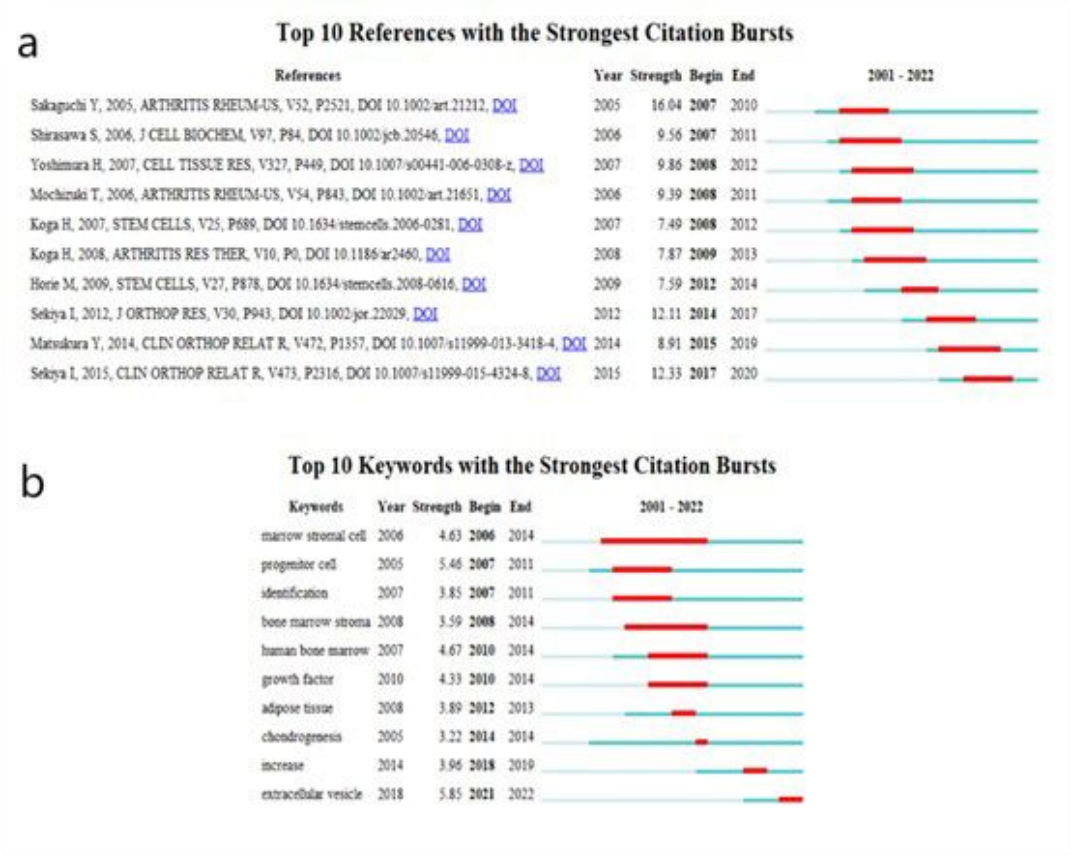

Figure 7

(a) Top ten references with the strongest citation bursts; (b) Top ten keywords with the strongest citation burst

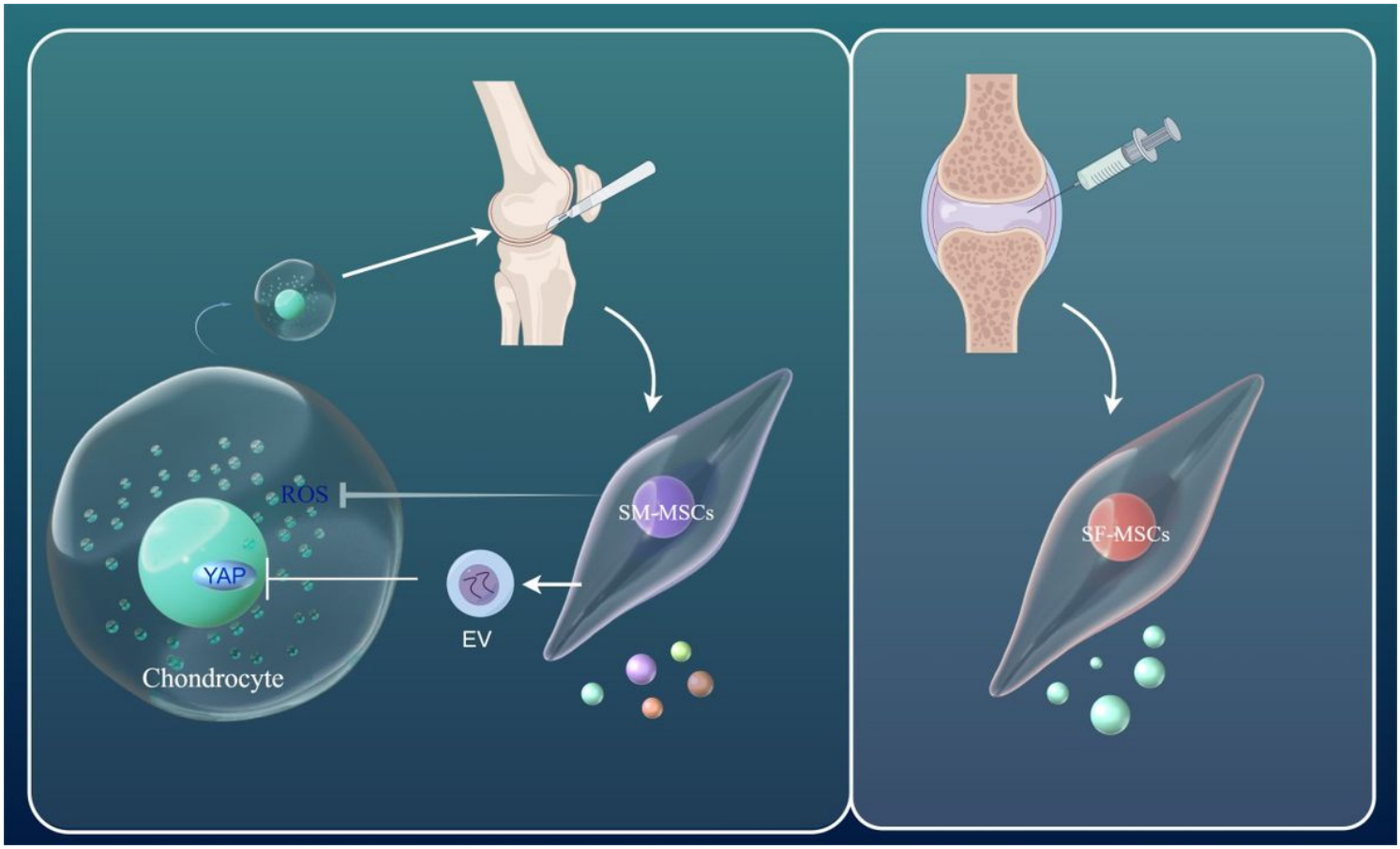

Figure 8

Research on SM MSCs and SF MSCs in joints (diagram by Figdraw)