Bone and Arthrosurgery Science, 2024, Volume 2, Issue 6
http://ojs.bbwpublisher.com/index.php/BAS
Online ISSN: 2981-8222

Current Research Trends and Advances in Osteoarthritis: A Bibliometric Study

Zewei Dang[1,2], Yuqiang Zhang[1,2], Ya Li[1,2], Yupeng He[1,2], Wei Wang[1,2]*

[1]Department of Orthopedics, First Affiliated Hospital of Jinzhou Medical University, Jinzhou 121000, Liaoning Province, China
[2]Orthopedics Institute of Jinzhou Medical University, Jinzhou 121000, Liaoning Province, China

***Corresponding author:** Wei Wang, jydgys@126.com

Abstract: *Background:* With the aging of the population and the rise in obesity and injury rates, the prevalence of osteoarthritis (OA) is increasing annually. Therefore, it is necessary to study experimental OA models. *Methods:* From January 1, 2000 to November 25, 2023, articles on the selection of experimental OA models from the Web of Science Core Collection (WOSCC) were collected. CiteSpace was used to analyze countries or regions, institutions, authors, bursting keywords, and references. Co-authorship, co-journal, and keyword co-occurrence visual analyses were performed using VOSviewer. *Results:* An analysis of 3,206 articles found that the annual volume of articles showed a rapid growth trend. The United States leads in terms of number of publications (1,039), total citations (29,844), h-index (77), and intermediary centrality (0.24), showing the journal with the most articles on Osteoarthritis and Cartilage. The emerging keywords stem cell, cartilage repair, and oxidative stress from 2019 to 2023 reflect the current study hotspots. *Conclusion:* This study comprehensively summarizes the research progress of OA model selection and evaluation criteria using bibliometric analysis, and provides a valuable reference for further establishing OA standard models, evaluation criteria, and researchers in this field.

Keywords: Osteoarthritis; Animal model; Standard model; Model preparation; Bibliometrics; VOSviewer

Online publication: January 8, 2025

1. Introduction

Osteoarthritis (OA) is a common degenerative joint disease. These lesions often involve joint cartilage, subchondral bone, ligaments, joint capsule, and synovium. The main clinical manifestations include pain, morning stiffness, joint crepitus, and end-stage disease, which can lead to loss of joint function and severely affect the quality of life [1]. The etiology of OA is complex and multifactorial and includes factors such as trauma, infection, developmental abnormalities of the joint, malalignment, and genetics. The mechanisms involved are complex and involve mechanical, inflammatory, and metabolic pathways [2]. The mutual influence between tissue destruction and repair disrupts the original homeostasis, making it a dynamic pathological process rather than a simple description of degeneration or mechanical wear [3].

Animal models of OA are a class of models that simulate the development of human OA in order to improve our understanding and treatment. The establishment of OA animal models provides a more intuitive study of OA pathogenesis and staging under controllable conditions, which is conducive to exploring the onset and progression of the disease [4]. As a technical tool, animal models of OA aim to provide a theoretical basis and experimental guidance for OA research. Different animal models have their own advantages and disadvantages, and selecting an appropriate animal model and modeling method is essential to ensure the smooth progress of experiments. It is worth noting that there is currently no consensus model for OA that fully reflects the human disease [5].

Several options are available for animal species and methods for OA animal experiments. Experimental animals include mice, rabbits, dogs, sheep, and horses, with various modeling methods [6]. Therefore, it is necessary to analyze the current status of OA model selection. This study adopts bibliometric analysis to categorize and evaluate the methods of model preparation from a macro perspective and summarizes the evaluation criteria of the models. By retrieving relevant studies from the Web of Science database, visual analysis was conducted on the included literature, along with an analysis of current research hotspots based on indicators such as citation frequency, h-index, and intermediary centrality. This study aims to provide guidance for the selection and reference of OA animal model preparation and offer insights into the establishment of future standard OA models.

2. Methodology

Web of Science was chosen as the main database for this study because it comprehensively covers more than 10 academic journals and is frequently used by researchers. Compared to other databases such as Scopus, Medline, and PubMed, Web of Science provides the most comprehensive and reliable bibliometric analysis [7]. Data retrieval was conducted on November 25, 2023, in the WOSCC using a subject retrieval strategy with search terms including "osteoarthritis, animal model, standard model, and model preparation," spanning 2000 to 2023. The inclusion criteria were "article" literature type; exclusion criteria were "meeting abstract, letter, editorial, etc." For ease of further analysis of the literature content, only articles written in English were included.

CiteSpace and VOSviewer software were used for visual analysis. The search results and complete records of cited references were exported in text format, and the CiteSpace 6.2R6 software was used to remove duplicate records. Since the first relevant literature in the search results was published in 2008, the time span in the software was set from 2008 to 2023, with a time slice interval of 2 years. Due to the large volume of literature and a significant number of keywords, the threshold for keyword analysis was set at "top 50 nodes per slice," and the threshold for countries or regions, institutions, and authors was set at g-index, K=15. The g-index is based on the ranking of citation counts. For a researcher's top g papers, each paper should receive at least g^2 citations, and the (g+1) paper should not receive more than $(g+1)^2$ citations [8]. Total citation frequency represents the number of times the published paper has been cited and is one of the internationally recognized standards for measuring the quality of published literature [9]. H-index refers to the number n, where a scholar has n papers that have been cited at least n times each, making the h-index n. It is an important indicator for measuring the influence of scholars [10]. Intermediate centrality is used to measure the importance of nodes in the visualization map, ≥ 0.1 is defined as a key indicator. The higher the intermediate centrality, the more important the node is in the field [11]. Keywords burst increases rapidly over a short period, reflecting changes in the research hotspots in a certain field [12]. VOSviewer

1.6.20 software was used to conduct author co-citation, journal co-citation, and reference co-citation (see the Results section for details on software settings), and a visualization map was drawn.

Information on annual publication, subject distribution, country/institution distribution, journal distribution, author, keywords, etc. was analyzed and visualized to analyze the research status, hotspots, and trends in this field.

3. Results

A total of 3,777 studies were retrieved using the subject words "osteoarthritis, animal model, standard model, and model preparation," and 3,206 studies were retrieved after excluding the non-reviewed literature. As for the annual number of publications selected by the experimental model of osteoarthritis (**Figure 1**), the number of published studies in this field has shown an increasing trend year by year. The total citation frequency of these studies was 71,323, the average citation frequency of each article was 22.25 times, the total citation frequency after citation was 65,497, and the h-index was 102. In 2008, American scholars Li *et al.* [13] published a related study in the Journal of Medicinal Chemistry in which an OA model of MMP-13 transgenic mice was obtained through transgenic construction technology. This technique provides a valuable model for the study and treatment of OA. From 2009 to 2023, 3,776 papers were published, showing an overall trend of rapid growth, with an average annual number of 269.7, suggesting that OA model selection and treatment have received global attention from scholars.

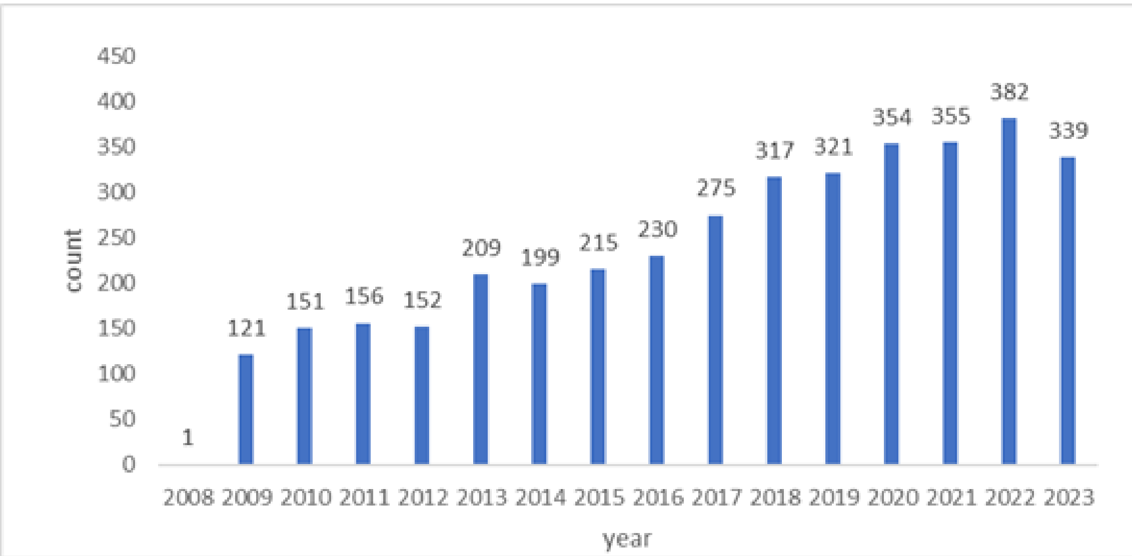

Figure 1. Trend chart of annual publication volume

The CiteSpace 6.2R6 software was used to analyze the distribution of countries or regions and generate a visual map (**Figure 2A**). There are 82 nodes in the visual map, representing 3,206 articles published by 82 countries, and 82 connecting lines, representing the number of occurrences of any two countries in the same literature, indicating the cooperative relationship between these two countries. As can be seen from the figure, cooperation among countries is mainly centered on the United States, Italy, the United Kingdom, Saudi Arabia, and other countries, while cooperation between China and other countries is not very close. The United States has published the most papers in this field, with a total of 1,039 papers (32.4%), 29,844 citations, and an h-index of 77, followed by China (602 papers), the United Kingdom (247 papers), Canada (242 papers), Germany (204 papers), and Japan (173 papers) (**Figure 2B**). The United States has a much higher number of papers than other countries. This indicates that it is in a leading position in this field. In terms of intermediary centrality, the United States ranks first with Italy at 0.24, reflecting the relatively high research influence of the United States in this field and the frequency of foreign cooperation, whereas China's intermediary centrality is only 0.13, indicating a gap with the United States in this field of research (**Figure 2C**).

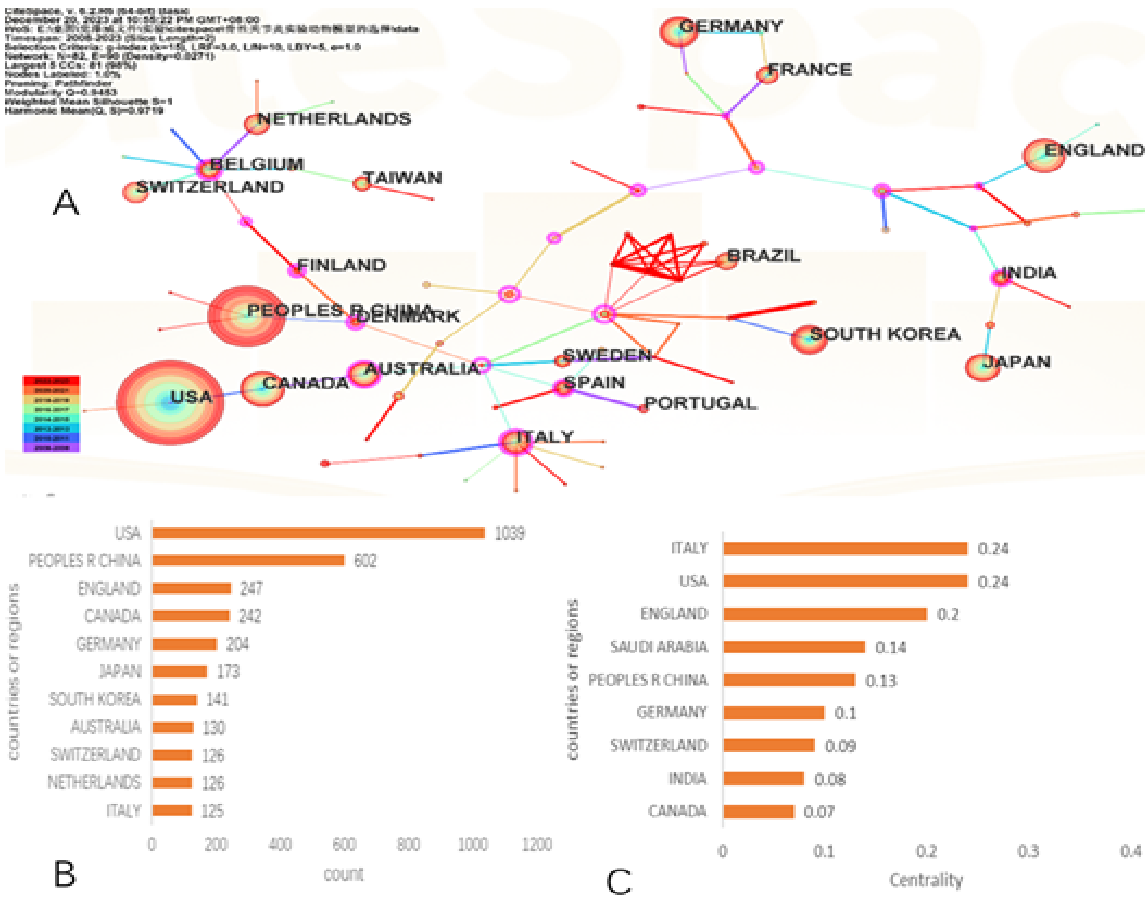

Figure 2. Country/region analysis. (A) Visualization of country or regional cooperation; (B) Number of published papers in countries/regions (Top 10); (C) Top 10 intermediary centrality in countries/regions studied

The CiteSpace 6.2R6 software was used to analyze the distribution of research institutions and generate a visual map (**Figure 3A**). There were 256 nodes in the visual map, representing 3,206 papers published by 256 institutions. In terms of the number of published papers issued by institutions, Harvard University has 101 papers in total, ranking first with a centrality of 0.47. The top three institutions with the highest number of publications are all from the United States, and among the top five central institutions, only the University of Oxford in the United Kingdom is not from the United States. These data show that most studies in the field of OA treatment are from American institutions. Among the top 10 institutions in China, only Shanghai Jiao Tong University ranked sixth, with 48 articles (**Figure 3B**). Tianjin University and Huazhong University of Science and Technology ranked 11th and 12th in the rankings of intermediary centrality (**Figure 3C**), indicating that these two institutions have close cooperation with other institutions and should strengthen cooperation with domestic and foreign OA research institutions and continue to make efforts to expand the influence of Chinese research institutions or universities in this field. In general, China's research in this field needs to be strengthened through cooperation with domestic and foreign research institutions and universities to enhance China's influence in this field.

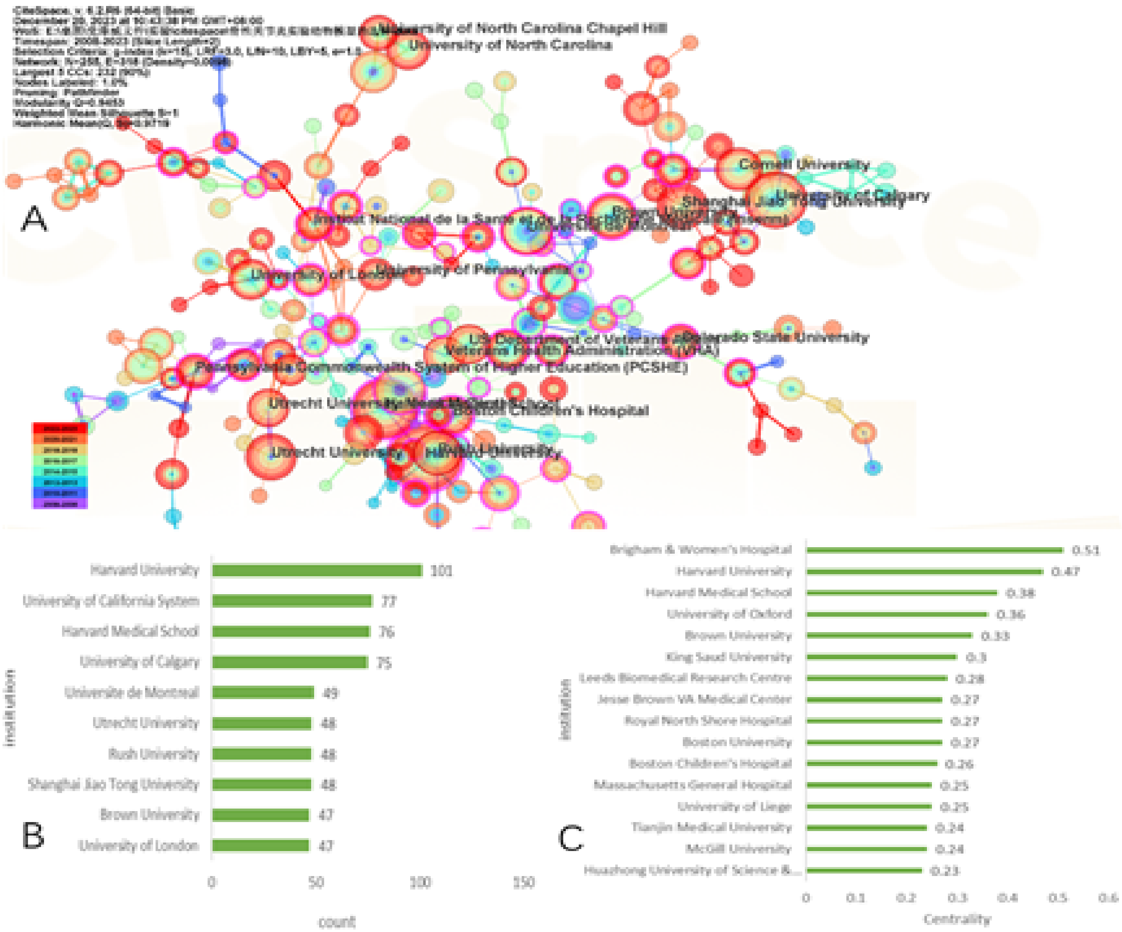

Figure 3. Distribution of research institutions. (A) Visualization of institutional cooperation; (B) Number of published documents of institutions (Top 10); (C) Value of intermediary centrality of institutions (Top 12)

The CiteSpace 6.2R6 software was used to analyze the distribution of authors and generate a visual graph (**Figure 4A**). The analysis shows that Braden C. Fleming, an American scholar, had the highest number of published papers. Fleming joined Brown University in 2003 and has been involved in orthopedics, where his research projects include the development of experimental models of anterior cruciate ligament injury and osteoarthritis progression, repair, and reconstruction studies. At present, the total number of citations is 4,502, and the h-index is 39, which indicates that he is a very influential researcher in this field. This was followed by Melbourne scholar Walter Herzog (24 articles), German scholar Henning Madry (23 articles), Canadian scholar David A. Hart (23 articles), and Columbia scholar James L. Cook (21 articles). In this field, a few Chinese scholars have ranked at the top. As reflected in the distribution of countries and institutions before, although the number of published papers by these authors is relatively large, their intermediary centrality of less than 0.01 reflects the lack of close cooperation among them. From the h-index, the German scholar Henning Madry ranked first, with 45, who has been engaged in OA research committed to articular cartilage and subchondral bone injury repair. Followed by Dutch scholar Floris P. J. G. Lafeber (44), American scholar Braden C. Fleming (39), Melbourne scholar Walter Herzog (37), Canadian scholar David A. Hart (37), and Columbia scholar James L. Cook (37) *et* *al.*, the h-index of Chinese scholars is relatively low. Judging from the total number of citations, they were German scholar Henning Madry (6,702 times), Dutch scholar Floris P. J. G. Lafeber (6,210 times), Melbourne scholar Walter Herzog (5,693 times), Columbia scholar James L. Cook (5,201 times), and American scholar Braden C. Fleming (4,502 times) (**Figure 4B**), the above data show that scholars with greater influence in this field are in the forefront in the number of publications, h-index, and total cited frequency.

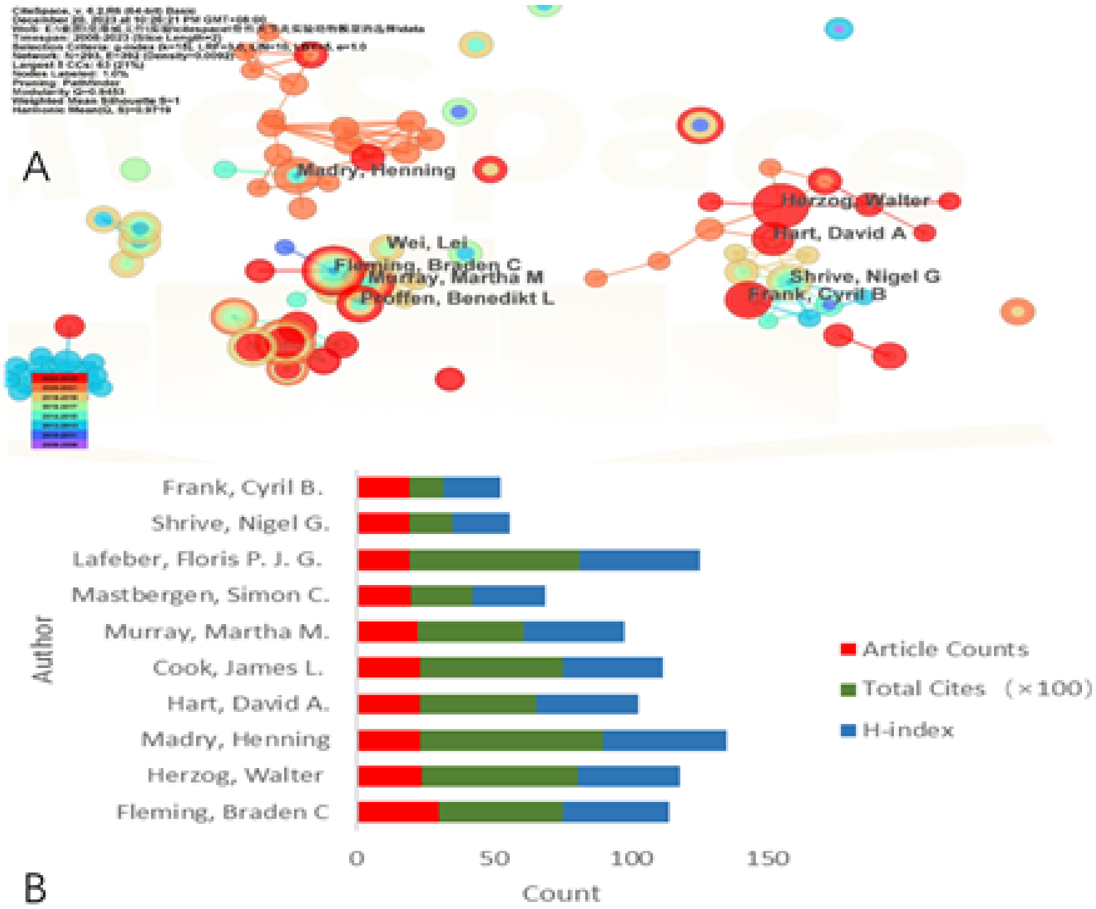

Figure 4. Distribution of authors. (A) Visualization of author distribution cooperation; (B) Number of published papers, total cites, and h-index (Top 10)

Due to the large number of studies and authors included, the minimum number of citations was set to 75, and a total of 87 literatures with 55,980 authors were included in the analysis. VOSviewer was used to analyze the co-citation intensity, correlation, and visualization map of eight references that met the threshold. Through the cluster analysis of the authors in the literature by VOSviewer, a total of five clusters were obtained, which are red, green, blue, yellow, and purple, with red representing the first cluster. There are 20 scholars in total, with DJ Hunter, DT Felson, and W Zhang at the center. Green represents the second cluster, with 20 scholars centered on SE Bove scholars. Blue represents the third cluster, consisting of 19 scholars, centered on MB Goldring, Koh Pritzker, and RF Loeser. Yellow represents the fourth cluster, with HJ Mankin and DD Frisbie as the center. Purple represents the fifth cluster, centered on SS Glasson scholars (**Figure 5A**).

Due to the large number of studies and journals included, the minimum number of citations was set to 150, and 142 out of 10,814 journals were finally included in the analysis. Co-citation analysis, correlation analysis, and visualization map analysis of 111 journals meeting the threshold were carried out using VOSviewer. Four clusters were obtained through the co-cluster analysis of periodicals by VOSviewer: red, green, blue, and yellow. Red indicates the first cluster, 75 journals mainly received literature on arthritis and articular chondrocyte osteoarthritis. Green represents the second cluster, a total of 30 journals, mainly receiving literature on osteoarthritis-related clinical trials. Blue represents the third cluster, a total of 24 journals, mainly receiving the research direction of stem cells and biomaterials for OA. Yellow represents the fourth cluster, a total of 13 journals, mainly receiving articles on osteoarthritis bone injury repair research direction (**Figure 5B**). As an authoritative journal in the field of osteoarthritis, Osteoarthritic Cartilage ranked first, with a total of 10,451 citations. This journal is the official journal of the International Society for Osteoarthritis Research. The focus areas include osteoarthritis, cartilage repair, orthopedics, and molecular biology. Histological evaluation criteria have been proposed for different animals in OA models. This was followed by Arthritis Rheum-US, J Orthop Res, and other periodicals (**Table 1**)

Table 1. Statistics of the frequency of co-citations of periodicals (Top 10)

Co-cited journal	Count	Year
Osteoarthr Cartilage	10451	1993
Arthritis Rheum-US	3824	1958
J Orthop Res	2796	1983
Ann Rheum Dis	2708	1939
J Bone Joint Surg Am	2318	1948
Arthritis Res Ther	2265	1999
Am J Sport Med	2191	1976
Clin Orthop Relat R	1976	2008
Arthritis Rheum	1829	1993
PAIN	1798	1975

The minimum number of citations was set to 30 due to the large number of references. Finally, 125 of the 86,562 citations were included in the analysis. The VOSviewer software was used to analyze the co-citation intensity, correlation, and visualization of the 125 citations that met the threshold. Through VOSviewer cluster analysis of reference citations, a total of four clusters were obtained: red, green, blue, and yellow. Red represents the first cluster with a total of 43 studies and green represents the second cluster with a total of 31 studies. Blue represents the third cluster with 26 articles and yellow represents the fourth cluster with a total of 25 articles (**Figure 5C**).

The top 10 cited references were mainly engaged in research on osteoarthritis modeling methods and evaluation criteria in rats and mice (**Table 2**). Among them, 2 and 5 established osteoarthritis models using ACLT and DMM, respectively. Among them, 3, 6, and 9 were osteoarthritis models constructed by the chemical method of sodium iodoacetate (MIA). Among these, 1, 4, 7, and 10 are the characteristics of the principles and criteria for the pathological evaluation of OA. Only one article 8 mentioned the effect of pro-inflammatory factors on the pathophysiology of OA.

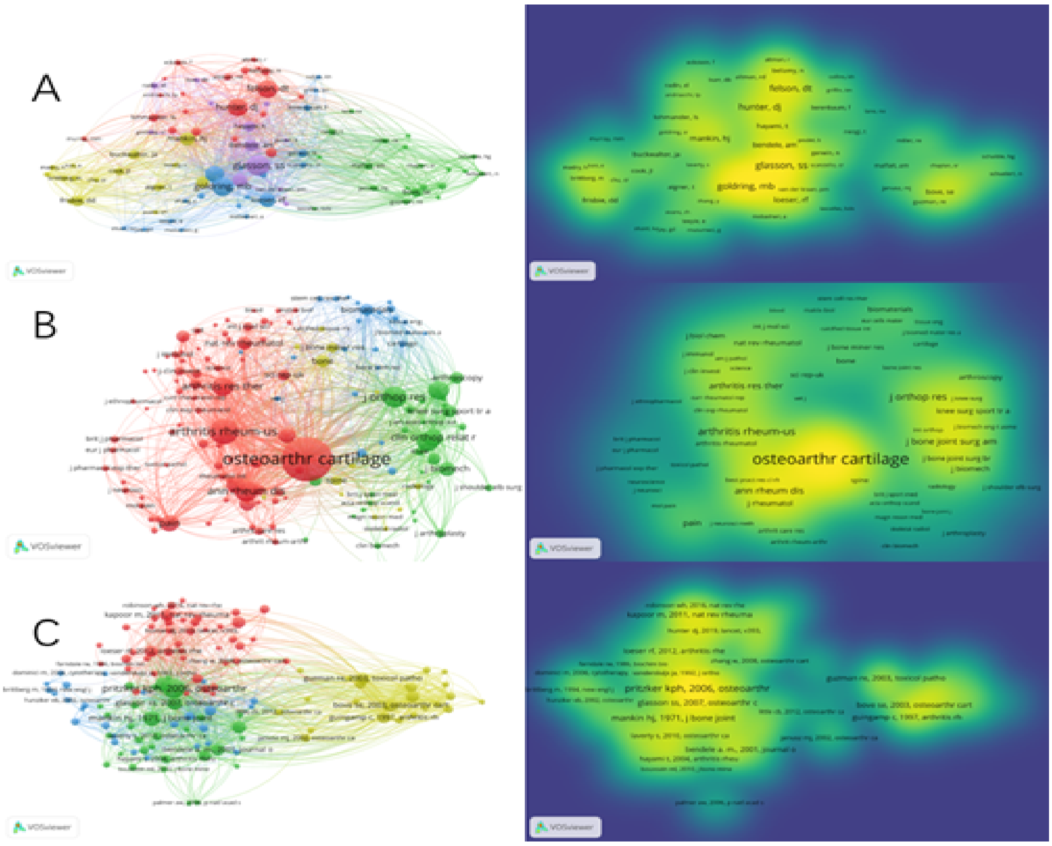

Figure 5. Cluster analysis. (A) Visual map of author co-citation analysis; (B) Visual map of journal co-citation; (C) Visual map analysis of reference co-citation

Table 2. Statistics of co-cited frequencies of references (Top 10)

Number	Co-cited references	Count
1	KPH Pritzker [14]	281
2	HJ Mankin [15]	191
3	SS Glasson [16]	162
4	SS Glasson [17]	147
5	SE Bove [18]	139
6	N Gerwin [19]	130
7	Mohit Kapoor [20]	130
8	Roberto E. Guzman [21]	123
9	JH Kellgren JS Lawrence [22]	123
10	Janet Fernihough [23]	118

The CiteSpace 6.2R6 software was used to analyze the distribution of keyword usage and generate a visualization map of keyword co-occurrence (**Figure 6A**). Keywords are important information points highlighting the article and summarizing its overall research content. Through co-occurrence analysis of all keywords in the article, the findings mainly focus on osteoarthritis, articular cartilage, knee osteoarthritis, models, animal models, and other keywords that are closely related to each other. The most frequently cited keyword was osteoarthritis, which was consistent with our research theme. Simultaneously, the LLR algorithm was used to perform cluster analysis on all keywords and draw a visual map. Twelve clusters were identified (**Figure 6B**). The cluster numbers were labeled from small to large as follows: #0 knee joint, #1 hyaluronic acid, #2 gene expression, #3 animal model, #4 regeneration, #5 rheumatoid arthritis, #6 *in vitro*, #7 knee joint osteoarthritis, #8 morbidity, #9 histopathology, #10 activation phase, #11 mesenchymal stem cells, and #12 chronic pain. Each label is related to another and does not exist independently. The corresponding color of the label indicates the time at which it first appears. The redder the label, the closer it is to the present, and the purple it is, the farther it is from the present.

Keyword emergence refers to a significant increase in the frequency of occurrence in the short term, which reflects the research direction in this field. Based on the above keyword cluster analysis, the development trend of the selection of experimental model methods for osteoarthritis is discussed using the emergence word analysis function, and a visualization map of emergence keywords is drawn. The red line on the right corresponds to the duration of the keywords, and the research direction in this field can be divided into three stages according to the emergence intensity and duration of the keywords. The first stage: Between 2009–2014, the main research direction is focused on the formation factors of osteoarthritis and the evaluation criteria for the establishment of related models; the second stage: From 2015 to 2018, the main research direction focuses on the establishment of osteoarthritis classification model and intra-articular injection therapy; the third stage: From 2019 to 2023, there are three keywords in this stage, namely "Stem cell," "Cartilage repair," and "Oxidative stress." The research mainly focuses on stem cells, oxidative stress, and cartilage damage repair in osteoarthritis in related experimental models, and cell transplantation therapy and its mechanism of action (**Figure 6C**).

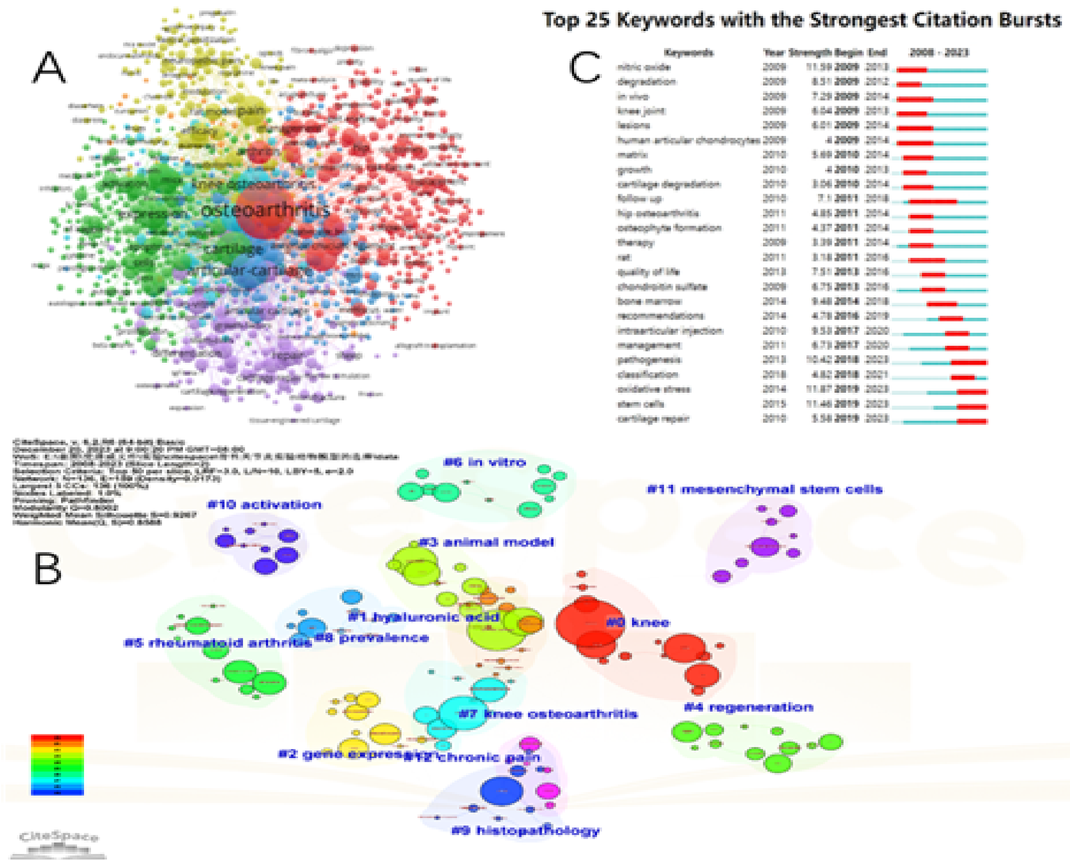

Figure 6. Distribution of keywords. (A) Visual analysis diagram of keyword co-occurrence; (B) Keyword clustering visualization analysis diagram; (C) Keyword emergence map

4. Discussion

The results of this study summarized the construction of different animal simulation models of human osteoarthritis, compared the advantages and disadvantages of different animals, different modeling methods, and application scope, and laid a theoretical foundation for the preclinical treatment of OA. By using CiteSpace and VOSviewer tools to evaluate the selection of OA experimental models, this study aimed to evaluate the number of publications by year, participation of different countries/regions, contribution of relevant institutions, role of individual authors, cited references, published journals, and keywords. In addition, combined with citation frequency, intermediate centrality, and h-index, this study aimed to conduct a comprehensive analysis of papers published since 2000, revealing the development trajectory, research trends, and core issues in the field of OA. This approach allows for a more comprehensive understanding of the driving factors behind the selection of OA experimental models, identification of leading voices and major institutions within the field, and discovery of the evolution of research topics and keywords. After 2008, the number of published papers in the United States and China ranked first and second respectively, with a total of 1,641 papers, accounting for 51.19% of the number of published papers in the world, indicating that China and the United States have made significant contributions in this field, which may also be related to the higher incidence of OA in China and the United States. The analysis results of the authors and research institutions show that scholars and universities in developed countries in Europe and the United States are in the leading position in this field. Although the number of papers published by Chinese scholars is relatively high, the cited frequency, intermediary centrality, and h-index of Chinese scholars are far lower than that of developed countries, indicating that China's research in this field is not in-depth enough. Cooperation with domestic and foreign scholars and research institutions should be strengthened, enhancing China's influence and competitiveness in this field. For journals, researchers should pay more attention to the professional journals of OA and the International Stem Cell Society (OARSI) to obtain more standard modeling methods and model evaluation criteria proposed by OARSI. This study not only focuses on quantitative indicators such as publication volume and citations, but also aims to deepen the understanding of what is of interest and how it has changed over time, thus providing a valuable perspective on the progress and future direction of OA research. The use of visual analysis tools such as CiteSpace and VOSviewer allows researchers to visualize research in the field, effectively revealing the collaboration network, knowledge base, and trends within the subject area. Such research can not only strengthen the academic community's understanding of the OA research field, but also promote scientific exploration and knowledge innovation in this field.

A higher co-citation frequency indicates that a literature has been studied earlier and has more influence in this field. Therefore, analyzing the literature can help us understand the current research hotspots. This study lists the top 10 frequently cited references. Next, important core references are expounded. Article published by JH Kallgren and JS Lawrence [22] in 1957 mainly explains the difference between the radiological examination of osteoarthritis patients and normal knee joints. HJ Parkin *et al.* [15] published an article in 1976, which mainly talked about the biochemical and metabolic abnormalities of hip cartilage in patients with osteoarthritis, and compared the histological and metabolic indexes between patients with osteoarthritis and normal knee joints. A study published by AM Mocco *et al.* [24] in 2015 mainly explained that the animal model of OA can be roughly divided into spontaneity and inductance. Spontaneity is mainly a model of the natural occurrence and genetic formation of the disease, and inductance occurs mainly through surgical operation or intra-articular injection of chemicals. Current methods of surgical induction models include partial or total meniscectomy, medial meniscal instability, meniscal laceration, anterior cruciate ligament (ACL) or posterior cruciate ligament transection, medial or lateral collateral ligament transection, osteotomy, trans articular impingement, and intraarticular osteochondroblastic [25,26]. Each model relies on a combination of joint instability, changes in joint mechanics (i.e. changes in weight-bearing or joint consistency), and inflammation to induce OA. Currently, chemical-induced disease models include sodium iodoacetate (MIA), papain, collagenase, carrageenan, and Frankenstein adjuvants. These models are mainly used to study OA pain behavior, and their effectiveness as clinical OA models remains highly controversial [27]. BJ Hern *et al.* [28] published a paper in 2009 that mainly evaluated the respective advantages and disadvantages of OA models in rats, mice, guinea pigs, rabbits, dogs, sheep, and horses. The advantages of small animal model are large number, economic price, short growth cycle, easy to feed, is the preferred animal model for many researchers, but its cartilage is particularly thin, relatively light weight, compared with human tissue structure and joint stress is quite difficult, limiting some research. N Gerwin *et al.* [19] proposed the Mankin scoring system in OARSI to evaluate rat OA models. SS Glasson *et al.* [16] proposed a "semi-quantitative scoring system" in OARSI that was applied to construct OA models in unstable, enzymatic, transgenic, and spontaneous ways in mice. VB Kraus *et al.* [29] proposed in OARSI to evaluate guinea pig OA models at macro and micro levels to help standardize guinea pig OA models, and therefore proposed OARSI-HISTOGP—A Histochemical-Histological Scoring System and related biological markers of joint fluid were used for evaluation. S Leaverty *et al.* [30] proposed the evaluation index of the rabbit ACLT model in OARSI, because the model made by anterior cruciate ligament transection (ACLT) in which rabbits lose joint stability is a repeatable and effective OA model. These above systems are simple to apply, do not require special equipment, and the score difference is small for novices and experts, used as common methods for evaluating OA models. The advantages of OA models for large animals such as dogs, sheep, and horses are that they are similar to the anatomical structure of humans, can achieve primary and secondary OA models, and have more diversified evaluation methods, but the cost is high, the growth cycle is long and slow, and there are related ethical issues that cannot be studied on a large scale. CW Merwraith [31], JL Coker [32], CB Litt [33], and other scholars evaluated large animal models with OARSI's modified Mankin scoring system and semi-quantitative histological evaluation of OA. OA models for animals such as pigs, cattle, zebrafish, and non-primates have not yet been published with histological evaluation criteria for these species, but the Mankin and OARSI (Pritzker) scoring system has been reported in some recent studies [34], in addition to being evaluated against a number of other specific research protocols. All of the above indicate that different animals with OA adopt different modeling methods and evaluation indicators. It is suggested to strengthen the exploration of the application of OA models in different animals and the differences in the results. This involves not only evaluating and comparing the effectiveness and accuracy of existing models but also the development of specific evaluation metrics required for disease-specific models. Through a more detailed and systematic comparative analysis, the potential limitations and advantages of the current OA model for simulating disease processes and treatment effects can be revealed to guide the improvement and innovation of future models. In addition, strengthening interdisciplinary cooperation in the field of OA and applying the latest research results in biology, computer science, statistics, and other fields to the development and optimization of OA models is expected to advance research on personalized treatment strategies. This comprehensive research method is not only conducive to improving the accuracy and efficiency of treatment research but also provides new ideas and tools for realizing precision medicine and improving the treatment effect of patients.

The analysis of the keywords not only revealed the oxidative stress induction, stem cell therapy, and cartilage repair methods as the research hotspots in the past five years (2019–2023), but also pointed out the new direction and focus of current scientific exploration. These aspects are further discussed below. Oxidative stress refers to the imbalance between oxidants and antioxidants that occurs in organisms when affected by stress factors. High levels of free radicals, reactive oxygen species (ROS), or reactive nitrogen species (RNS) are produced, and/or the organism's ability to fight oxidation is reduced, triggering a cascade of pathological changes that destroys the original stable state of oxidation and reduction in living organisms. In the case of OA, oxidative stress leads to local joint pathological changes and synovial inflammation, which interfere with the normal synthesis and metabolism of chondrocytes and lead to the breakdown of cartilage, which is a key factor in the development of osteoarthritis [35].

Therefore, it can protect cartilage by eliminating free radicals and anti-oxidation, thus delaying the development of OA. The pathological changes induced by oxidative stress not only occur in the development of osteoarthritis but are also a common link in the formation and progression of many diseases, such as cardiovascular and cerebrovascular diseases, neurodegenerative diseases, and some types of cancer. Therefore, an in-depth exploration of the mechanism of oxidative stress is of great significance for the early diagnosis, treatment, and prevention of diseases. Stem cells have become the "seed players" in OA treatment because of their pluripotency, immune regulation, and paracrine mechanisms. Stem cells have the ability to transform into osteoblasts, chondrocytes, and fat cells. In addition to their differentiation potential, these cells also produce and release numerous physiological regulatory substances involved in side effects, such as growth hormones, immunomodulators, and chemo-guiding molecules, which promote cartilage nutrition and delay the progression of OA by activating associated cell proliferation and angiogenesis pathways [36]. Further exploration in this area will likely include a more in-depth analysis of the mechanisms of stem cell paracrine action and how to improve the therapeutic outcomes of osteoarthritis by regulating the expression and release of these bioactive factors. Research may focus on further elucidation of the specific roles and regulatory mechanisms of growth factors, cytokines, and chemokines secreted by stem cells in cartilage repair and regeneration, as well as the development of new strategies or therapies, such as gene editing or nanotechnology, to enhance the positive effects of these regulators to more effectively delay or reverse the pathological progression of osteoarthritis. In addition, exploring the differences and specificities of different types of stem cells (such as mesenchymal stem cells, embryonic stem cells, etc.) in paracrine mechanisms may reveal new therapeutic targets and pathways, and provide a broader vision and possibility for the treatment of osteoarthritis and other degenerative diseases. In short, in terms of oxidative stress induction, future studies may further explore the regulatory mechanisms of specific signaling pathways, and in the field of stem cell therapy, the challenge is how to ensure the long-term effect of therapy and patient safety, with a focus on optimizing the biological activity and durable stability of the material. In short, the emergence of these keywords not only reflects current research hotspots, but also points out the direction for future research.

5. Conclusion

This paper summarized the literature related to arthritis OA over the past 20 years, including the number of publications, countries/regions, institutions, authors, journals, etc., analyzed the current research hotspots and trends, and predicted future research trends. This interdisciplinary research method, combined with advanced knowledge and technology in multiple fields such as cell biology, molecular biology, and materials science, is expected to bring revolutionary progress to the clinical application of stem cell therapy. Cartilage injury and degenerative joint disease are some of the main factors affecting human health and quality of life. Traditional treatment methods often fail to achieve the ideal effect, and in the past five years, the development of cartilage tissue technology has provided new hope for patients. Researchers are developing a variety of novel biomaterials, growth factors, and stem cell technologies to promote the regeneration and repair of damaged cartilage. For example, the application of 3D bioprinting technology enables the preparation of customized cartilage components, showing higher accuracy and better compatibility compared to traditional methods. These research advances not only mark the rapid development of science and technology in these subdivisions, but also shed light on possible directions for future research.

Funding

(1) School-Enterprise Cooperation Fund of Jinzhou Medical University (2020002)
(2) Innovation and the First Affiliated Hospital of Jinzhou Medical University (FSHX202403)
(3) Guiding Science and Technology Program of Jinzhou City (JZ2023B090)

Disclosure statement

The authors declare no conflict of interest.

Author contributions

Conceptual design: Zewei Dang, Wei Wang
Data collection and analysis: Yuqiang Zhang, Ya Li
Software visual analysis: Yupeng He
Writing: Zewei Dang
Project guidance, revision, and review: Wei Wang

References

[1] Martel-Pelletier J, Barr AJ, Cicuttini FM, et al., 2016, Osteoarthritis. Nature Reviews. Disease Primers, (2): 16072.
[2] Glyn-Jones S, Palmer AJR, Agricola R, et al., 2015, Osteoarthritis. Lancet (London, England), 386(9991): 376–387.
[3] Hunter DJ, Bierma-Zeinstra S, 2019, Osteoarthritis. Lancet (London, England), 393(10182): 1745–1759.
[4] Rai MF, Brophy RH, Sandell LJ, 2019, Osteoarthritis Following Meniscus and Ligament Injury: Insights from Translational Studies and Animal Models. Current Opinion in Rheumatology, 31(1): 70–79.
[5] Cope PJ, Ourradi K, Li Y, et al., 2019, Models of Osteoarthritis: The Good, the Bad and the Promising. Osteoarthritis and Cartilage, 27(2): 230–239.
[6] Brandt JS, Hadaya O, Schuster M, et al., 2019, A Bibliometric Analysis of Top-Cited Journal Articles in Obstetrics and Gynecology. JAMA Network Open, 2(12): e1918007.
[7] Anatolitou A, Mavrogenis AF, Sideri KI, et al., 2023, Comparison of Allogeneic Mesenchymal Stem Cells Therapeutic Potentials in Rabbits' cartilage defects: Macroscopic and Histological Outcomes. Research in Veterinary Science, 162: 104948.
[8] Wu YY, Li CC, Lin X, et al., 2023, Global Publication Trends and Research Trends of Necroptosis Application in Tumor: A Bibliometric Analysis. Frontiers in Pharmacology, 14: 1112484.
[9] Zhou J, Li J, Zhang J, et al., 2022, The Relationship Between Endorsing Reporting Guidelines or Trial Registration

and the Impact Factor or Total Citations in Surgical Journals. PeerJ, 10: e12837.

[10] Favre J, Germond T, Clavert P, et al., 2020, Want a Better H-Index? All You Need to Know About Copyright and Open Access. Orthopaedics & Traumatology, Surgery & Research: OTSR, 106(8): 1475–1480.

[11] Zhang Y, Shao C, He S, et al., 2020, Resilience Centrality in Complex Networks. Physical Review E, 101(2–1): 022304.

[12] Jiang S, Liu Y, Zheng H, et al., 2023, Evolutionary Patterns and Research Frontiers in Neoadjuvant Immunotherapy: A Bibliometric Analysis. International Journal of Surgery (London, England), 109(9): 2774–2783.

[13] Li JJ, Nahra J, Johnson AR, et al., 2008, Quinazolinones and Pyrido[3,4-d]pyrimidin-4-ones as Orally Active and Specific Matrix Metalloproteinase-13 Inhibitors for the Treatment of Osteoarthritis. Journal of Medicinal Chemistry, 51(4): 835–841.

[14] Pritzker KPH, Gay S, Jimenez SA, et al., 2006, Osteoarthritis Cartilage Histopathology: Grading and Staging. Osteoarthritis and Cartilage, 14(1): 13–29.

[15] Mankin HJ, Dorfman H, Lippiello L, et al., 1971, Biochemical and Metabolic Abnormalities in Articular Cartilage from Osteoarthritic Human Hips. II. Correlation of Morphology with Biochemical and Metabolic Data. The Journal of Bone and Joint Surgery. American Volume, 53(3): 523–537.

[16] Glasson SS, Chambers MG, Van Den Berg WB, et al., 2010, The OARSI Histopathology Initiative—Recommendations for Histological Assessments of Osteoarthritis in the Mouse. Osteoarthritis and Cartilage, 18 Suppl 3: S17–23.

[17] Glasson SS, Blanchet TJ, Morris EA, 2007, The Surgical Destabilization of the Medial Meniscus (DMM) Model of Osteoarthritis in the 129/SVEV Mouse. Osteoarthritis and Cartilage, 15(9): 1061–1069.

[18] Bove SE, Calcaterra SL, Brooker RM, et al., 2003, Weight Bearing as a Measure of Disease Progression and Efficacy of Anti-Inflammatory Compounds in a Model of Monosodium Iodoacetate-Induced Osteoarthritis. Osteoarthritis and Cartilage, 11(11): 821–830.

[19] Gerwin N, Bendele AM, Glasson S, et al., 2010, The OARSI Histopathology Initiative—Recommendations for Histological Assessments of Osteoarthritis in the Rat. Osteoarthritis and Cartilage, 18 Suppl 3: S24–34.

[20] Kapoor M, Martel-Pelletier J, Lajeunesse D, et al., 2011, Role of Proinflammatory Cytokines in the Pathophysiology of Osteoarthritis. Nature Reviews. Rheumatology, 7(1): 33–42.

[21] Guzman RE, Evans MG, Bove S, et al., 2003, Mono-Iodoacetate-Induced Histologic Changes in Subchondral Bone and Articular Cartilage of Rat Femorotibial Joints: An Animal Model of Osteoarthritis. Toxicologic Pathology, 31(6): 619–624.

[22] Kellgren JH, Lawrence JS, 1957, Radiological Assessment of Osteo-Arthrosis. Annals of the Rheumatic Diseases, 16(4): 494–502.

[23] Fernihough J, Gentry C, Malcangio M, et al., 2004, Pain Related Behaviour in Two Models of Osteoarthritis in the Rat Knee. Pain, 112(1–2): 83–93.

[24] McCoy AM, 2015, Animal Models of Osteoarthritis: Comparisons and Key Considerations. Veterinary Pathology, 52(5): 803–818.

[25] Lampropoulou-Adamidou K, Lelovas P, Karadimas EV, et al., 2014, Useful Animal Models for the Research of Osteoarthritis. European Journal of Orthopaedic Surgery & Traumatology: Orthopedie Traumatologie, 24(3): 263–271.

[26] Little CB, Zaki S, 2012, What Constitutes an "Animal Model of Osteoarthritis"—The Need for Consensus? Osteoarthritis and Cartilage, 20(4): 261–267.

[27] Teeple E, Jay GD, Elsaid KA, et al., 2013, Animal Models of Osteoarthritis: Challenges of Model Selection and Analysis. The AAPS Journal, 15(2): 438–446.

[28] Ahern BJ, Parvizi J, Boston R, et al., 2009, Preclinical Animal Models in Single Site Cartilage Defect Testing: A Systematic Review. Osteoarthritis and Cartilage, 17(6): 705–713.

[29] Kraus VB, Huebner JL, DeGroot J, et al., 2010, The OARSI Histopathology Initiative—Recommendations for Histological Assessments of Osteoarthritis in the Guinea Pig. Osteoarthritis and Cartilage, 18 Suppl 3(Suppl 3): S35–52.

[30] Laverty S, Girard CA, Williams JM, et al., 2010, The OARSI Histopathology Initiative—Recommendations for Histological Assessments of Osteoarthritis in the Rabbit. Osteoarthritis and Cartilage, 18 Suppl 3: S53–65.

[31] McIlwraith CW, Frisbie DD, Kawcak CE, et al., 2010, The OARSI Histopathology Initiative—Recommendations for Histological Assessments of Osteoarthritis in the Horse. Osteoarthritis and Cartilage, 18 Suppl 3: S93–105.

[32] Cook JL, Kuroki K, Visco D, et al., 2010, The OARSI Histopathology Initiative—Recommendations for Histological Assessments of Osteoarthritis in the Dog. Osteoarthritis and Cartilage, 18 Suppl 3: S66–79.

[33] Little CB, Smith MM, Cake MA, et al., 2010, The OARSI Histopathology Initiative—Recommendations for Histological Assessments of Osteoarthritis in Sheep and Goats. Osteoarthritis and Cartilage, 18 Suppl 3: S80–92.

[34] Hargrave-Thomas EJ, Thambyah A, McGlashan SR, et al., 2013, The Bovine Patella as a Model of Early Osteoarthritis. Journal of Anatomy, 223(6): 651–664.

[35] Mizuno G, Munetsuna E, Yamada H, et al., 2021, Maternal Fructose Consumption Downregulates Hippocampal Catalase Expression via DNA Methylation in Rat Offspring. Nutrition Research (New York, N.Y.), 92: 40–48.

[36] Copp G, Robb KP, Viswanathan S, 2023, Culture-Expanded Mesenchymal Stromal Cell Therapy: Does It Work in Knee Osteoarthritis? A Pathway to Clinical Success. Cellular and Molecular Immunology, 20(6): 626–650.