Drug Design, Development and Therapy

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Bibliometric Analysis of Exosome Research in Spinal Cord Injury (2000–May 2024). Trends, Collaborations, and Emerging Insights

Zhihua Wang[1,*], Hangchuan Bi[1,*], Denghui Li[1], Wan Zhang[1], Chao Wang[1], Jianyi Yang[2], Xianglin Shen[1], Rongji Yan[1], Fei He[3], Hao Duan[4]

[1]Trauma Center, The First Affiliated Hospital of Kunming Medical University, Kunming, 650032, People's Republic of China; [2]Department of Orthopedics, Kunming Guandu District People's Hospital, Kunming, 650200, People's Republic of China; [3]Kunming Medical University Affiliated Qujing Hospital, Qujing, 655000, People's Republic of China; [4]Department of Sports Medicine, The First Affiliated Hospital of Kunming Medical University, Kunming, 650032, People's Republic of China

*These authors contributed equally to this work

Correspondence: Fei He; Hao Duan, Email drhefei@126.com; kmu.dh@hotmail.com

Purpose: Exosomes have emerged as promising therapeutic agents for spinal cord injury (SCI). The present study was conducted to provide a systematic bibliometric analysis of research trends related to SCI and exosomes.

Patients and Methods: Publications on exosomes in SCI were identified from the Web of Science Core Collection using specific search criteria. VOSviewer, CiteSpace, and R-based Bibliometrix were employed to visualize collaboration networks and research hotspots.

Results: The analysis included 281 publications across 66 countries. The publication numbers were consistently trending upwards, with the United States and China being two of the top producing countries. The top three articles were cited 539, 300, and 254 times, respectively. The analyzed publications were from 153 journals, and the *Journal of Neurotrauma, Journal of Nanobiotechnology*, and *Stem Cell Research & Therapy* had the highest total link strength in co-occurrence networks. *Stem Cell Research & Therapy, Journal of Nanobiotechnology*, and *Molecular Neurobiology* were the top journals in coupling networks. Fan Jin, Cai Weihua and Cao Yong were the most prolific and highly cited authors. Keywords analysis revealed emerging research hotspots including microglia modulation, engineered exosomes, extracellular vesicles, and targeted delivery systems.

Conclusion: The findings underscore the accelerated exploitation and promise of exosomes as a novel treatment for SCI with significant translational potential through emerging hotspots such as microglia modulation and engineered exosome platforms. The insights gained from this study are important and may be essential for the advancement of exosome-based treatments by researchers and clinicians in the field of spinal cord injury.

Keywords: bibliometrics, spinal cord injury, exosome, extracellular vesicles, targeted delivery systems, therapy

Introduction

Spinal cord injury (SCI), is an extremely strong neurologic deficit that causes the complete or partial loss of motoric power sensations and autonomic functions beneath the level of lesion.[1] SCI has a complex pathophysiology that involves primary mechanical damage followed by secondary injury cascades including inflammation, oxidative stress, and apoptosis associated with progressive tissue degeneration culminating in functional failure.[2,3] Even with advances in acute care and rehabilitation, effective therapies resulting in extensive neurological recovery following SCIs are absent.[4,5] Recent research identified targeting these secondary injury processes for neuroprotection and repair following SCI. One of the models under investigation is intercellular communication that promotes both injury and healing. Among these, extracellular vesicles and more specifically exosomes attracted increasing attention for their pivotal roles in cellular crosstalk following SCI.[6–8]

Received: 11 March 2025
Accepted: 16 July 2025
Published: 8 August 2025

Exosomes, defined as small extracellular vesicles (approximately 30–150 nm), have been identified to be essential in intercellular communication and are able to carry biologically active proteins, lipids, and nucleic acids from one cell type into another.[9,10] Mechanistically, exosomes facilitate SCI recovery through multiple pathways. They deliver anti-inflammatory microRNAs (such as miR-124 and miR-133b) that modulate microglial polarization from pro-inflammatory M1 to anti-inflammatory M2 phenotype, transfer growth factors and cytokines that promote neural stem cell proliferation and differentiation, and carry proteins involved in axonal guidance and synaptic plasticity restoration.[11] The cargo composition of therapeutic exosomes typically includes neuroprotective proteins (BDNF, VEGF), regenerative microRNAs, and anti-apoptotic factors that collectively target key signaling pathways including PI3K/Akt, Wnt/β-catenin, and MAPK cascades.[12,13] Exosomes derived from mesenchymal stem cell (MSCs) are a novel type of transport medium for direct delivery, there is mounting evidence supports that contributing to the neuroprotective and regeneration manner of exogenous exosomal preparation against SCI.[14,15] These mechanisms comprise the reduction of inflammation, cell death, and previous vessel formation as well an increase in axon growth through activation of endogenous repair processes.[16–18] Compared to alternative therapeutic approaches such as direct stem cell transplantation or biomaterial scaffolds, exosome-based therapies offer distinct advantages including reduced immunogenicity, ability to cross the blood-spinal cord barrier, and lower risk of tumorigenesis while maintaining the regenerative potential of parent cells.[19,20] Recently, research on exosomes as a treatment for SCI has attracted much attention. In animal models of SCI, exosome-based treatments robustly improve functional recovery in a variety of preclinical studies.[21] Recently, advances in exosome engineering and the development of new methods for delivery have generated a great potential to improve the therapeutic effects by using exosomes.[22–24] However, a global analysis of the existing works and trends in this quickly changing area is still lacking.

Bibliometric analysis has gained substantial importance as a tool to quantitatively evaluate the productivity and impact of science in any area.[25,26] Unlike traditional narrative reviews that may be subject to selection bias, bibliometric analysis provides objective, data-driven insights into research trends, collaboration patterns, and knowledge evolution through statistical analysis of publication metadata. This approach is particularly valuable for rapidly evolving fields like exosome research, where comprehensive manual review becomes increasingly challenging due to exponential growth in publications.[27,28] By scrutinizing publication trends, citation networks and research hotspots, bibliometric analysis can provide valuable insights into the development of a certain research field.[29,30] These analyses provide researchers with information on gaps in knowledge and areas where additional research is most needed.[31,32] The timeframe of 2000–2024 was selected to capture the complete evolution of exosome research in SCI, beginning from early foundational studies on extracellular vesicles around 2000 and extending through recent advances in exosome engineering and targeted delivery systems. This period encompasses key technological milestones including improved exosome isolation techniques (ultracentrifugation, size-exclusion chromatography), advanced characterization methods (nanoparticle tracking analysis, cryo-electron microscopy), and the emergence of exosome modification strategies for enhanced therapeutic efficacy.[33,34] There are a few bibliometric studies that have investigated exosome-associated areas, revealing the characteristics of research trends and collaboration in this field. The first is that in the wider exosome literature Wei et al (2024)[35] was a full bibliometric evaluation of exosomes based drug delivery all through 2013 to 2020 showing the surprising evolution in this field and development for therapeutic applications. Another study by Zhuo et al (2023),[36] however, data from a bibliometric perspective has highlighted the novelty of exosomes in cerebral diseases for neurodegenerative processes and brain trauma. But, unfortunately there has not been a full in-depth bibliometrics article that applies on the merger topic with spinal cord injury and exosome yet. While Web of Science Core Collection provides comprehensive coverage of high-impact journals and standardized citation tracking essential for bibliometric analysis, we acknowledge limitations including potential exclusion of relevant non-English publications and regional journals not indexed in this database. However, WoS remains the gold standard for bibliometric studies due to its rigorous quality control and comprehensive citation network.[37] To address this, the objective of this study is to provide a comprehensive bibliometric review on SCI and exosome related publications.

Materials and Methods

Search Strategies and Data Collection

We conducted a comprehensive literature search spanning 2000 to 2024 using the Web of Science Core Collection (WoSCC) database. Search formula. (TS=(spinal cord injury OR spinal cord injuries)) AND TS=(exosome OR exosomes OR exosomal OR exosomic)).[27,38] To minimize selection bias, researchers conducted the literature screening process following predefined inclusion criteria. (1) studies investigating exosomes in the context of spinal cord injury; (2) original research articles with primary data; (3) English language publications; and (4) articles published between January 2000 and May 2024. Exclusion criteria. (1) duplicate records; (2) reviews; (3) editorial material; (4) letter; (5) meeting abstract; (6) non-english publication. The data was collected in text format as "Full Records and References". Extracted information provided from each publication included the number of publications and citations, titles, author names, institutions, countries/regions, keywords, and details about the journals. A total of 281 eligible publications were analyzed in the present study. The flowchart of data screening is shown in Figure 1. In the initial database search, a total of 315 records were identified as potentially relevant. The titles and abstracts of 303 records that remained following the removal of 12 duplicates were scrutinized. This initial screen yielded 283 articles for full-text review. Only the 281 articles that met all inclusion criteria were included in this final analysis of bibliometrics following a substantial assessment process.

Statistical Analysis

The analysis and visualization of various research components, such as countries, institutions, authors and co-cited authors, journals and co-cited journals, co-cited references, and keywords, were conducted using VOSviewer (V.1.6.20), CiteSpace (V.6.3.R1), and an online bibliometric tool. Furthermore, CiteSpace was utilized to examine dual-map overlays, cluster co-cited references, and identify citation bursts and keyword burst citations. VOSviewer was used in this study to analyze the co-occurrence network of keywords in all the documents. Using the online analysis platform available, we visualized cooperative network relationships among countries and regions.

The size of each node in the data visualization maps is proportional to the frequency with which the corresponding research component appears. These nodes are interconnected to show how research components co-occur, with the thickness of the connections representing the frequency of such co-occurrences.[39] We employed total publications, total citations, average citations, the H-index, g-index and m-index to gauge the influence of research elements. The H-index serves as a key measure for evaluating the academic contributions of researchers and has the potential to predict their future scientific accomplishments.[40] The g-index was proposed as an enhancement of the H-index by Leo Egghe and it gives more weight to highly cited articles.[41] This is defined as the maximal number g of a specific publications with at least g highly cited articles, for which on average every article receives more than G citations. The m-index is a variation of the H-index that considers the number of years over which papers are published. It is calculated by dividing the H-index by the number of years since the researcher's first publication, allowing for fairer comparisons between researchers at different career stages.[42] The Journal Citation Report (JCR) Quartile rankings of 2024 ranks journals into four quartiles based on their Impact Factor within the subject categories where it is included. Journal quartile is based on the rank of specific journal in its field. Q1 represents the top 25% of journals in a field, Q2 the next 25%, and so on. By using these metrics, one can gain insights into both the collective and specific impacts of research elements.[39,43]

Results

An Overview of Publications in Research of Spinal Cord Injury and Exosomes

We identified 281 relevant articles by our search efforts. The investigation uncovered 1,792 authors from 1,006 institutions in 66 countries had contributed to these publications. These articles were published in 153 journals, and a total of 11,131 references have been cited (Figure 2A).

Publication Trends

Altogether these publications show an increasing trend from 2000 to 2024 for the period of every year as shown in Figure 2B. The data displays almost exponential growth, although with a slow start as prior to 2013 there were fewer

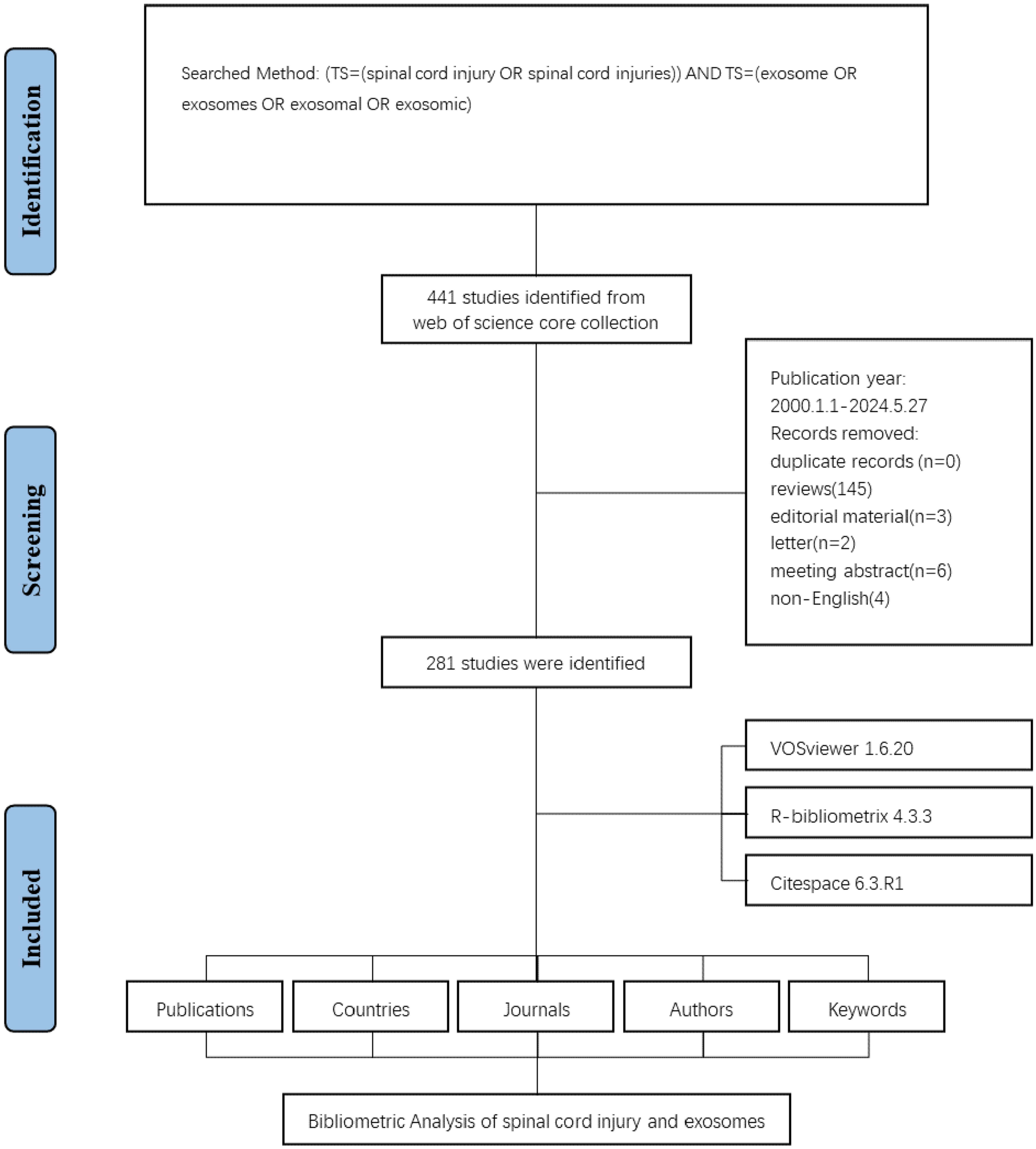

Figure 1 Flowchart for selecting papers.

than five publications reported per year. A turning point took place on 2013, when the most cited article in our analysis appeared. Between 2013 and 2015, that number increased gradually from around five to ten per year. Starting in 2015, the number of research articles doubled from just 10 papers published to a total output of twenty-two publications. This rapid growth trend continued until the field reached a new equilibrium with respect to 30–40 publications per year in 2017–2020. The research activity increased exceedingly in 2021, over fifty publications and similar numbers are also present in the year of 2022. The high point is attributed to the increased recognition of exosomes as extracellular vesicles,

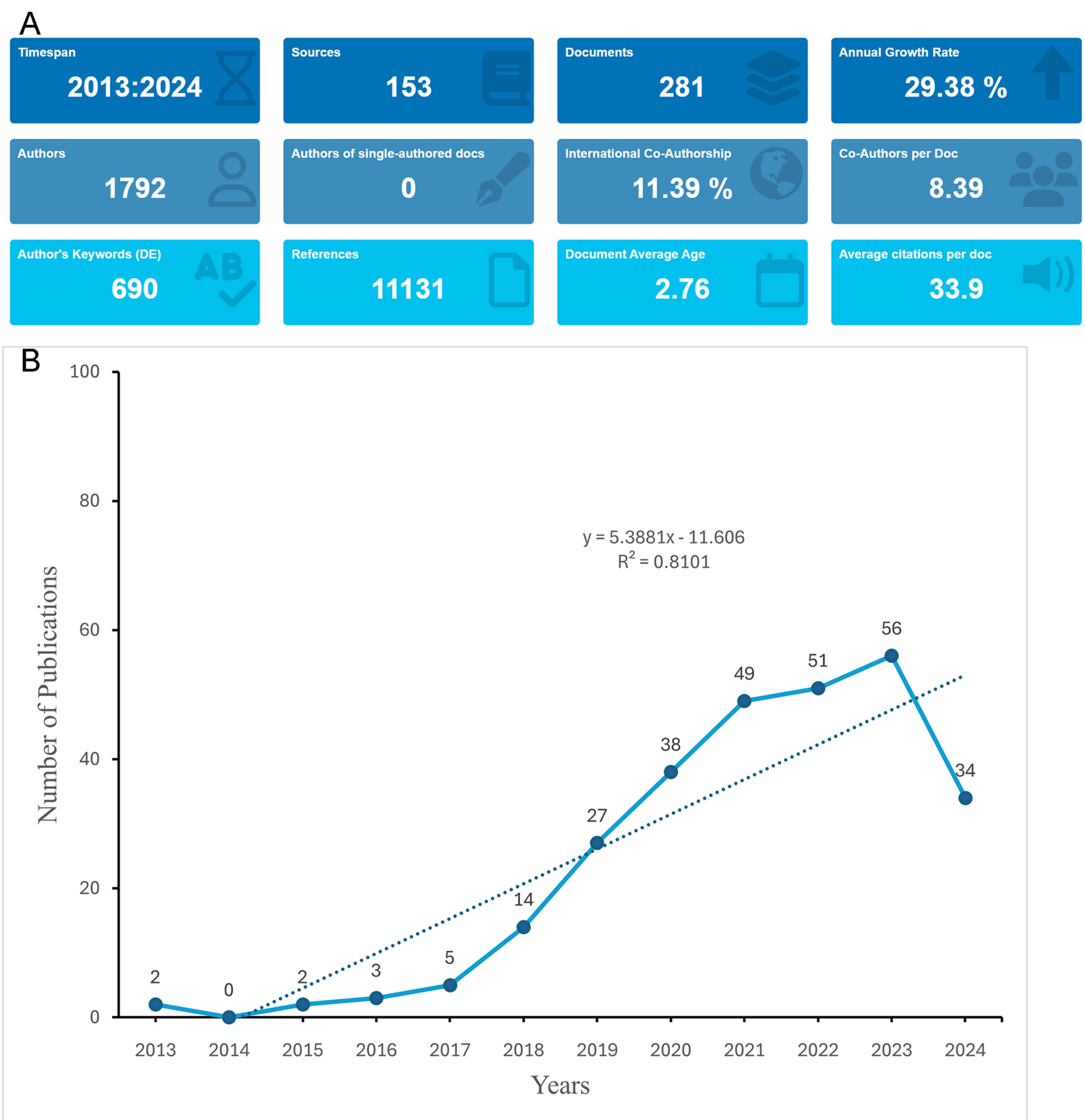

Figure 2 An overview of publications in research of spinal cord injury and exosomes. (**A**) Information on the data generated by the WoSCC database for exosomes in spinal cord injury; (**B**) The annual papers used exosomes for SCI from 2013 to 2024.

vehicles for drugs and treatment in spinal cord injury and advanced isolation techniques involving characters of exosome. Interestingly, some of the data for 2023 and early 2024 suggest a small decrease in publications if attributable to indexing delays rather than real reduced research output.

Citation Analysis

Citation analysis identified the key articles within this dataset and revealed that top 3 papers[44–46] have been cited on average of 539, 300, and 254 times, respectively. It reflects how they have been very important to the scientific community because of their extensive citations and those are key insights into exosome involvement in SCI and its promising role as a therapeutic approach.

Analysis of Journals

The fact that 281 papers have been published in 153 different journals, the breadth of interest in this topic spans various scientific disciplines. Table 1 is presenting top twenty journals as per H-index, it shows how important these publication sources are in this domain. *Stem Cell Research & Therapy* is the most forthcoming journal with an H-index of 9 and *Journal of Nanobiotechnology* takes second place with an H-index equal to 8. This suggests that these journals are very prolific in terms of publishing papers, and contribute significantly to the fields as per citations. Surprisingly *Stem Cell Research & Therapy* has an H-index of 97 (the highest) but still a lower impact factor of 7.5 as compared to journals listed below. *ACS Nano* is distinguished as it has an impact factor of 17.1, illustrating substantial reach among different scientific areas. The Journal Citation Reports (JCR2024) Quartile rankings also indicate that most of the journals are in Q1, belonging to the highest 25% in their fields.

Co-occurrence networks of journals are presented in Figure 3A, which describes the association between various publication venues. We analyzed a total of 54 journals, each represented at least twice. *Journal of Neurotrauma* (68), *Journal of Nanobiotechnology* (52), and *Stem Cell Research & Therapy* (48) had the highest total link strength in these networks. Figure 3B illustrate the coupling of journals as networks that provide a new insight into their associations. This analysis consisted of 54 journals, with at least 2 couples in each journal. *Stem Cell Research & Therapy* (1,614), *Journal of Nanobiotechnology* (1,517), and *Molecular Neurobiology* (1,440) topped challenging journals with the total link strength in both networks.

Table 1 Bibliometric Indicators of High-Impact Journals

Journal	H_Index	IF 2024	JCR_Quartile 2024	PY_Start	TP	TP_Rank	TC	TC_Rank
Stem Cell Research & Therapy	9	7.5	Q1	2018	12	2	293	2
Journal of Nanobiotechnology	8	10.2	Q1	2020	12	1	NA	>50
Molecular Neurobiology	6	5.1	Q2	2020	11	3	163	13
Neurochemical Research	5	4.4	Q2	2020	6	4	68	49
Acs Nano	4	17.1	Q1	2019	4	8	102	27
Acta Biomaterialia	4	9.7	Q1	2020	4	9	67	50
Frontiers in Cellular Neuroscience	4	5.3	Q1	2013	5	5	99	29
Journal of Neuroinflammation	4	9.3	Q1	2020	4	15	254	4
Journal of Neurotrauma	4	4.2	Q2	2017	5	6	467	1
Neuroscience Letters	4	2.5	Q3	2019	5	7	72	47
Biomedicine & Pharmacotherapy	3	7.5	Q1	2019	4	10	NA	>50
Frontiers in Bioengineering and Biotechnology	3	5.7	Q3	2022	3	21	NA	>50
Frontiers in Neuroscience	3	4.3	Q2	2018	4	11	108	26
Journal of Cellular Physiology	3	5.6	Q2	2019	3	24	NA	>50
Journal of Molecular Neuroscience	3	3.1	Q3	2020	4	14	NA	>50
Journal of Neuroscience	3	5.3	Q1	2015	3	25	276	3
Nano Letters	3	10.8	Q3	2018	3	26	NA	>50
Neural Regeneration Research	3	6.1	Q2	2022	4	16	159	14
Oxidative Medicine and Cellular Longevity	3	7.31	NA	2020	3	27	NA	>50
Plos One	3	3.7	Q3	2015	3	28	198	7

Notes: H_index. The h-index of the journal, which measures both the productivity and citation impact of the publications. IF. Impact Factor, indicating the average number of citations to recent articles published in the journal. JCR_Quartile. The quartile ranking of the journal in the Journal Citation Reports, indicating the journal's ranking relative to others in the same field (Q1. top 25%, Q2. 25%-50%, Q3. 50%-75%, Q4. bottom 25%). PY_start. Publication Year Start, indicating the year the journal started publication

Abbreviations: TP, Total Publications; TP_rank, Rank of Total Publications; TC, Total Citations; TC_rank, Rank of Total Citations; Average Citations, The average number of citations per publication.

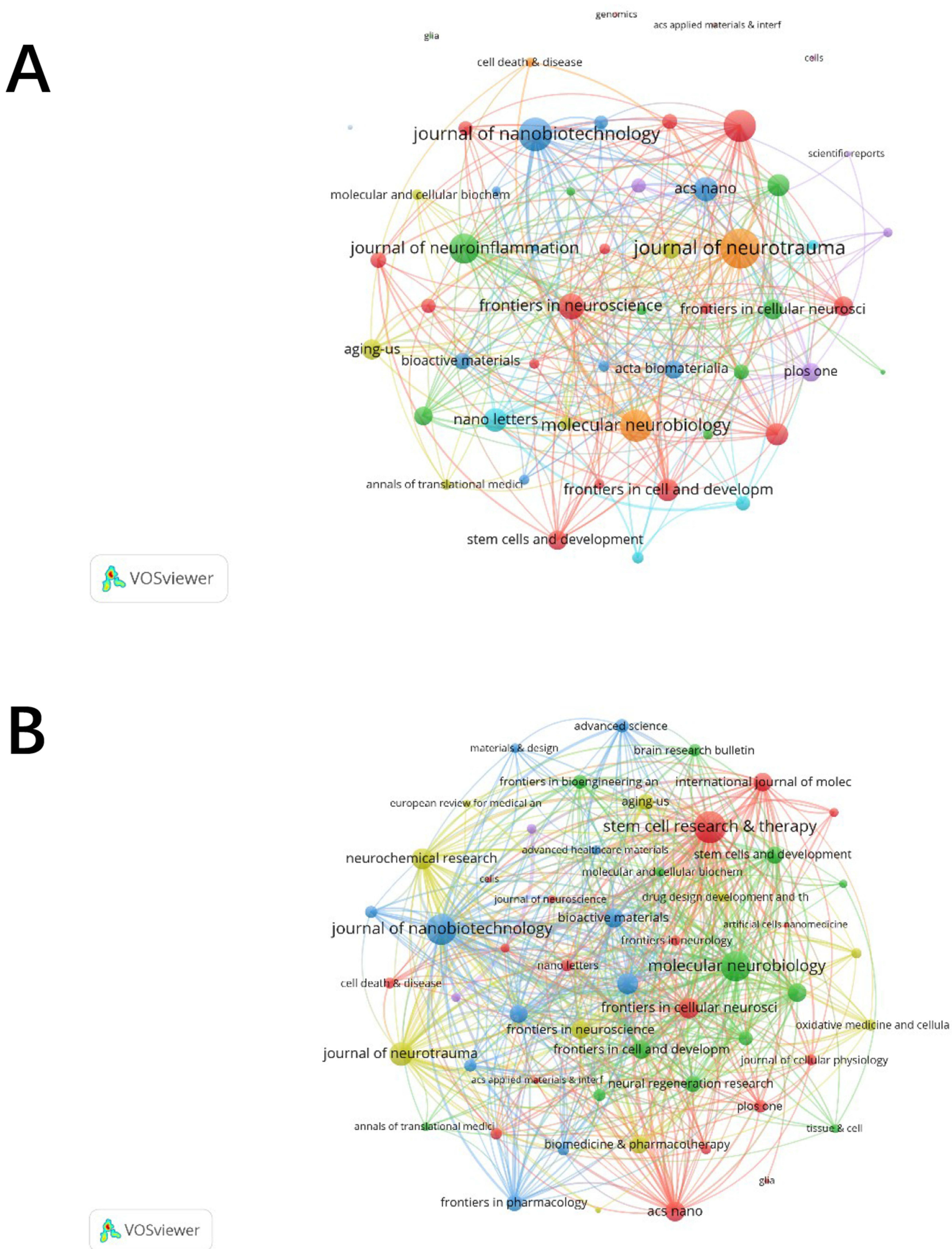

Figure 3 Visualization of journals analysis. (**A**) Co-occurrence Networks; (**B**) Coupling Networks. Journal Link Strength in co-occurrence networks measures the frequency with which two journals are cited together within the same articles or references. Journal Link Strength in coupling networks assesses the extent to which journals are linked based on the common references cited in their articles.

Analysis of Countries

A total of 66 countries/regions have published research in this field, which demonstrates the worldwide attention paid to spinal cord injury and exosome studies. Table 2 shows classification of top country wise publication and citation indices. The country with the largest number of articles was China (217; 77.2% of all publications). This was followed in the United States (6.4% of total articles) and then Iran (4.6%). Research coming from the US garnered 91.3 citations per paper, a huge lead over global average volumes across all countries. A number of countries with small publication volumes had high average citation rates that indicate their work is very influential despite its relatively low volume. For example, the average citation rate for Austria was 78.2 per paper (the second highest), but there were only four publications from there.

As shown in Figure S1, the publications of corresponding authors from different countries are distributed, and as expected, Chinese groups occupy a large proportion. Moreover, given that research trends have become more global in nature and large quantity of studies were published from China compared to other countries there is a need for future works investigating the geographic distribution of this field's efforts and resources at worldwide level. Figure S2 also contains a network visualization of international collaborations, which highlights that among the 29 countries with at least two articles involved in a collaboration, China has been engaged in most (n = 16). The USA is next in line with 12 collaborations, followed by Austria on third place at seven. This network demonstrates the level of international collaboration in this area.

Analysis of Authors

We found that 1,792 authors have contributed to publications on spinal cord injury and exosome research, reflecting broad scientific engagement with the topic. Table 3 provides a comprehensive overview of the publication and citation profiles for the top 20 most impactful authors, based on different bibliometric metrics. The leading authors in terms of citations are Fan Jin and Cai Weihua, with 953 and 946 citations, respectively. Both started their publications in this field

Table 2 Publication and Citation Profiles of Leading Countries

Country	Articles	Freq	MCP_Ratio	TP	TP_Rank	TC	TC_Rank	Average Citations
China	217	0.772	0.055	784	1	6474	1	29.8
Usa	18	0.064	0.222	73	2	1644	2	91.3
Iran	13	0.046	0.231	69	3	154	6	11.8
Japan	6	0.021	0.000	23	5	67	9	11.2
Austria	4	0.014	0.750	32	4	313	3	78.2
Russia	4	0.014	0.250	21	6	12	13	3
Korea	3	0.011	0.333	15	7	203	5	67.7
United Kingdom	3	0.011	0.333	5	14	130	7	43.3
Spain	2	0.007	0.000	9	9	125	8	62.5
Australia	1	0.004	1.000	1	27	3	16	3
Brazil	1	0.004	1.000	7	10	2	17	2
Canada	1	0.004	0.000	5	12	10	15	10
Egypt	1	0.004	0.000	2	22	0	18	0
France	1	0.004	1.000	2	24	27	12	27
Germany	1	0.004	1.000	9	8	34	11	34
India	1	0.004	1.000	4	15	0	19	0
Israel	1	0.004	1.000	6	11	254	4	254
Portugal	1	0.004	1.000	5	13	11	14	11
Saudi Arabia	1	0.004	0.000	4	16	0	20	0
Switzerland	1	0.004	0.000	4	17	62	10	62

Notes: Articles. Publications of Corresponding Authors only.
Abbreviations: Freq, Frequence of Total Publications; MCP_Ratio, Proportion of Multiple Country Publications; TP, Total Publications; TP_rank, Rank of Total Publications; TC, Total Citations; TC_rank, Rank of Total Citations; Average Citations, The average number of citations per publication.

Table 3 Publication and Citation Profiles of High-Impact Authors

Authors	H_Index	g-Index	m-Index	PY_Start	TP	TP_Frac	TP_Rank	TC	TC_Rank
Fan Jin	10	11	1.67	2019	11	0.95	5	953	1
Cai Weihua	9	11	1.50	2019	11	0.84	4	946	2
Cao Yong	9	12	1.13	2017	12	1.45	1	550	12
Liu Wei	9	9	1.50	2019	9	0.69	8	932	3
Rong Yuluo	9	9	1.50	2019	9	0.69	9	932	3
Feng Shiqing	8	10	1.33	2019	10	0.94	6	206	26
Wang Jiaxing	8	9	1.33	2019	9	0.68	10	739	5
Yin Guoyong	8	9	1.33	2019	9	0.79	11	502	13
Hu Jianzhong	7	12	1.75	2021	12	1.27	2	218	24
Ji Chengyue	7	7	1.40	2020	7	0.52	14	658	8
Lu Hongbin	6	12	1.50	2021	12	1.21	3	210	25
Duan Chunyue	5	7	1.25	2021	7	0.68	13	88	41
Gao Jianqing	5	6	1.00	2020	6	0.81	17	341	18
Ge Xuhui	5	6	1.00	2020	6	0.41	18	632	9
Huang Jiang-hu	5	5	0.63	2017	5	0.83	26	378	15
Jiang Dongdong	5	5	0.83	2019	5	0.34	27	612	11
Li Chengjun	5	9	1.00	2020	9	0.95	7	102	36
Li Liming	5	5	1.00	2020	5	0.56	28	339	20
Lin Fei-yue	5	5	0.63	2017	5	0.83	29	378	15
Liu Yudong	5	7	1.25	2021	7	0.69	15	107	35

Notes: H_index. The h-index of the journal, which measures both the productivity and citation impact of the publications. g_index. The g-index of the journal, which gives more weight to highly cited articles. m_index. The m-index of the journal, which is the h-index divided by the number of years since the first published paper. PY_start. Publication Year Start, indicating the year the journal started publication

Abbreviations: TP, Total Publications; TP_rank, Rank of Total Publications; TC, Total Citations; TC_rank, Rank of Total Citations; Average Citations, The average number of citations per publication.

in 2019 and have quickly become prominent researchers. Cao Yong is recognized for having the highest total number of publications (12) and the earliest publication date (2017) among the top authors. This indicates a sustained and prolific contribution to the field over several years.

For the top authors, the H-index ranged from 5 to 10, with Fan Jin, Cai Weihua, and Cao Yong each attaining the highest H-index of 10, reflecting their major influence in the field. The g-index, which gives more weight to highly cited papers, provides additional insights into the impact of these authors' work. Cao Yong leads with the highest g-index of 12, followed closely by Fan Jin and Cai Weihua, both with a g-index of 11. The m-index, which measures impact relative to career length, shows interesting trends. Hu Jianzhong has the highest m-index of 1.75, suggesting a notable impact since he began publishing in 2021. The co-authorship network visualized in Figure S3 reveals collaboration patterns among 303 authors who each contributed to at least 2 articles. Cai Weihua leads with the most collaborations (120), followed by Fan Jin (110) and Lu Hongbin (104). This analysis demonstrates a closely interconnected research community, with key authors acting as central hubs in the network of collaborations. The strong collaborative links suggest a high degree of knowledge sharing and joint research efforts in the field.

Analysis of the Institutions

We identified 1,006 institutions engaged in spinal cord injury and exosome research, highlighting a wide range of institutional participation. Figure 4 displays the top 10 institutions by research output, with Central South University in China leading with 20 publications. Nanjing Medical University follows with 18 publications, and Zhejiang University ranks third with 13 publications. The dominance of Chinese institutions in the top ranks aligns with the country-level analysis, further emphasizing China's significant contribution to this research field.

Figure S4 presents a network map of institutional collaborations involving 102 institutions that published at least 2 documents. The analysis illustrates detailed collaboration dynamics, showing Central South University as the top collaborator with 29 connections. Zhejiang University is second with 23 collaborations, and the Hunan Engineering

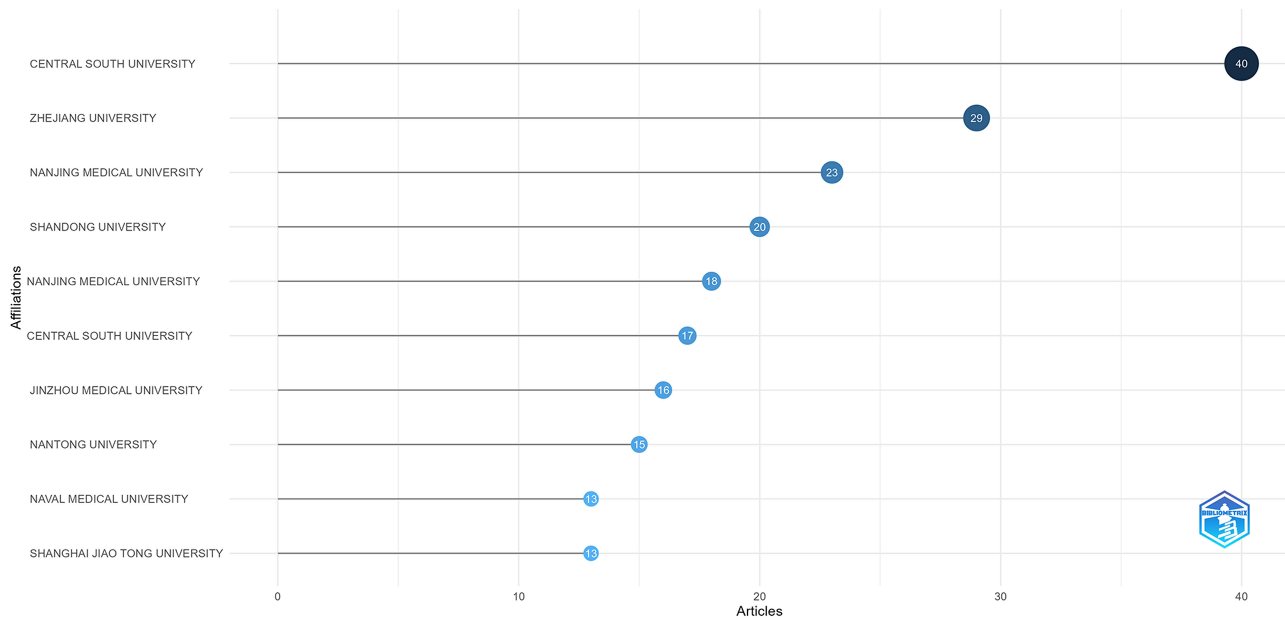

Figure 4 Top ten institutions by article count and rank (R bibliometrix).

Research Center for Sports & Health ranks third with 19. The strong collaborative networks centered around these institutions suggest that they play key roles in facilitating research partnerships and knowledge exchange in the field.

Keyword Analysis

Figure 5 provides a visual representation of the keyword co-occurrence network, with an analysis of a total of 132 keywords that occur at least 3 times. The top 5 keywords identified were. "Exosomes" (75 occurrences), "Inflammation" (55 occurrences), "Functional recovery" (49 occurrences), "Spinal-cord-injury" (48 occurrences), and "Expression" (46 occurrences). This network analysis identified numerous tight clusters, which correspond to different sub-themes in the field. A main cluster is located at the central part of its associated "exosomes", tightly connected with "mesenchymal stem cells", as well as with both of 'neuroprotection' and 'regeneration', implying heavy emphasis on research related-scientific concepts for therapeutic potentials of exosomes produced by stem cells. There is a further cluster consisting of "inflammation" and "microglia", which highlights significant attention to the neuroinflammatory aspects in SCI, particularly on how exosomes could direct these events. Furthermore, a subcluster linking "functional recovery" to both rehabilitation and plasticity indicates continued efforts in the study of functional outcome relative to current understanding of underlying mechanisms for post-spinal cord injury.

Analysis of Burst Keyword

Figure 6 displays the top-20 keywords with citation bursts from 1992 to 2024, characterizing hot points or emerging topics in research over time. Specifically, the keywords "methylprednisolone" and "neuroprotection" showed early bursts prior to 2015. In the middle period (2015–2020), elevations in mentions of terms such as "mesenchymal stem cells", "exosomes" and "microRNA" demonstrated their emergence as impactful research fields. Key words including "microglia", "neuroinflammation", "extracellular vesicles", and "biomarkers" related to topics with recent bursts post-2020. Keywords related to specific molecular mechanisms (eg, miR-126, miR-124) as well as delivery methods (eg, nanoparticles) have been more recently introduced, suggesting a shift towards the use of targeting technologies and increasingly sophisticated research methodologies for therapeutic RNA molecules at present time.

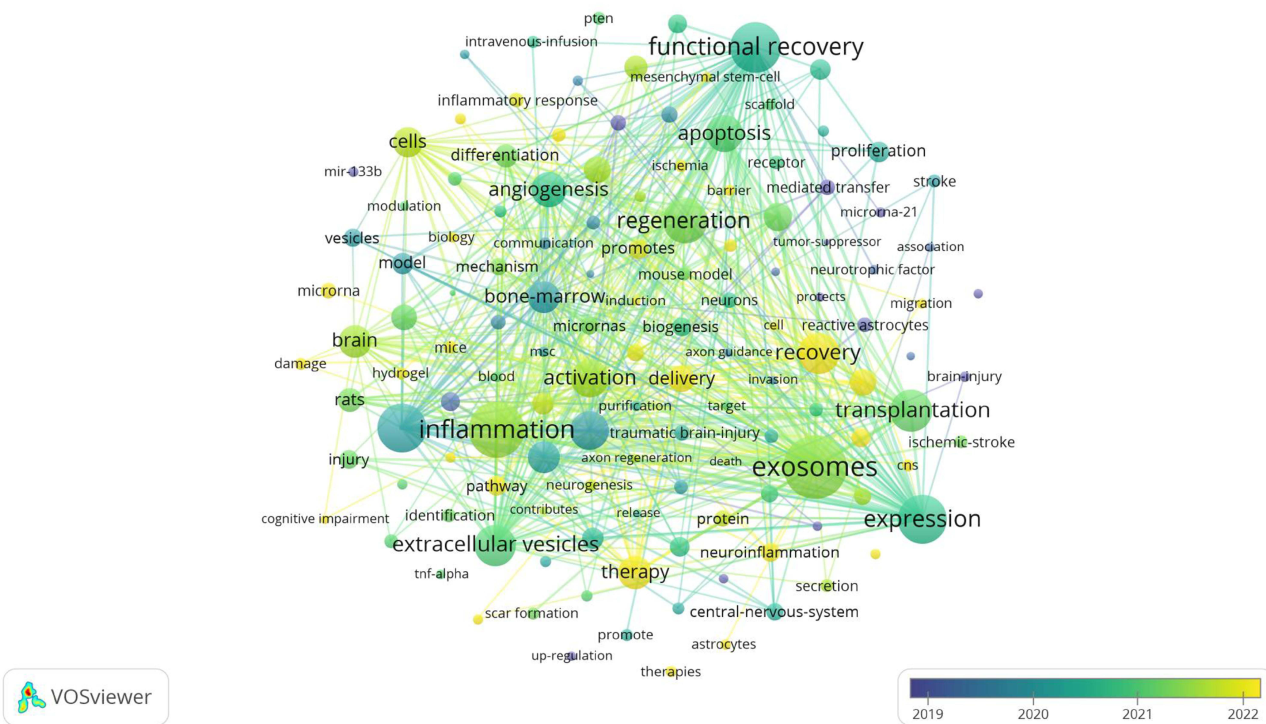

Figure 5 Visualization of Keywords analysis. This network visualization displays the co-occurrence of keywords in selected literature. Each node represents a keyword, with size indicating its frequency of occurrence. Links between nodes represent co-occurrence in the same documents, with thicker lines showing stronger associations. Colors reflect the average publication year of the articles, as indicated by the color gradient at the bottom right.

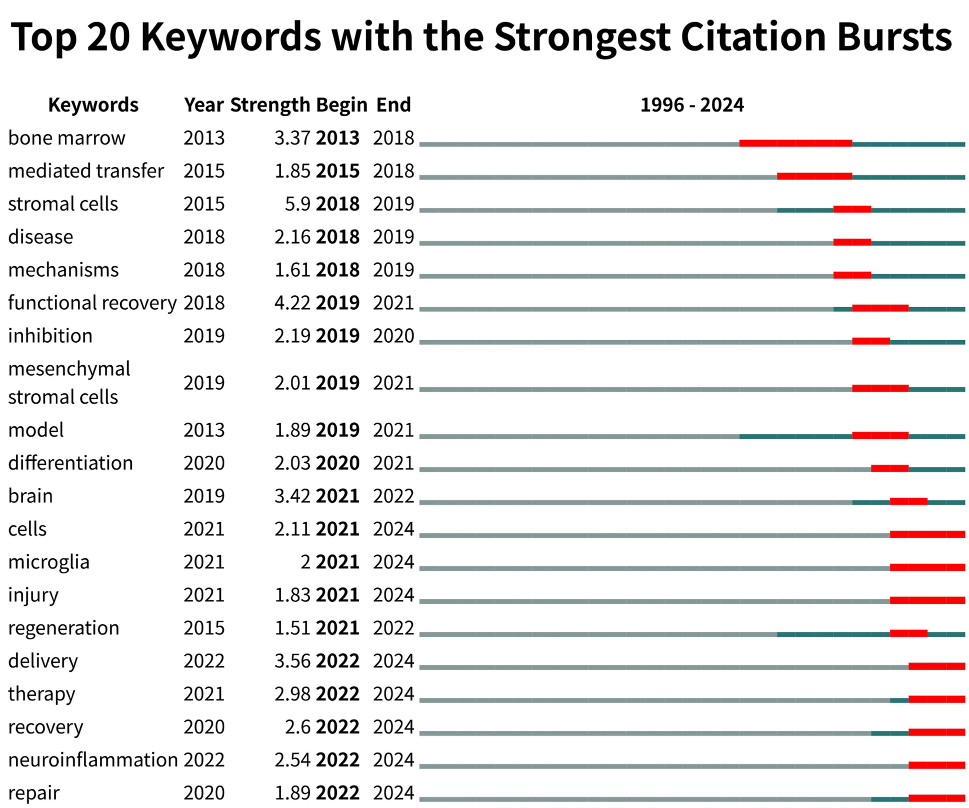

Figure 6 Top 20 Keywords with the Strongest Citation Bursts (CiteSpace).

Discussion

The bibliometric analysis presents a detailed overview of the research environment related to SCI and exosomes, illustrating the growing interest, advancements, and notable contributions in this domain. Our results indeed indicate a substantial increase in research production over time with 2015 marking as the inception year of emerging publications while peaking upon reaching the year 2022, illustrating how rapidly this field has been expanding. Regarding the global perspective, China leads in publication volume, while the United States shows high citation impact. It also names top institutions and authors conducting high-impact research with a trend toward specialized journals and theme-specific studies. Our keyword analysis further shows a shift in research themes from early, predominantly exploratory studies on a wide scale to more targeted mechanistic and translational approaches. The study underscores the increasing recognition of exosomes as promising therapeutic tools for neural repair and functional recovery post-SCI. The analysis reveals several crucial insights, challenges, and implications for future research, which are explored in the subsequent discussion.

Publication Trends and Research Growth

The considerable expansion of the number of publications since 2015 indicates increasing recognition regarding exosomes as a potential therapeutic strategy for SCI. This surge is consistent with broader trends observed in exosome research across various medical specialties, as reported by Théry et al (2018)[47] in their detailed review of extracellular vesicles. The fast increase in publications reflects that the field is currently emerging with rapid development and findings.

There are likely to be a number of factors driving this growth, not least the increasing technology skills that are available for exosome isolation, characterization, and analytical techniques. Facilitated by technologies like nanoparticle tracking analysis and high-resolution flow cytometry, our capacity to explore exosomes on a much deeper level has improved massively.[48] Exosome-based therapies have seen an increase in the number of studies that are being conducted due to their therapeutic benefits which has led researchers towards significant funding on this front. The finding likely highlights a broader trend in growing financial support for SCI-targeting regenerative medicine solutions.[49]

At the same time, neuroscientists are working within this rapidly developing interdisciplinary area to develop novel approaches by combining ideas or technology from stem cell biology and nanotechnology. This led to a cycle of ongoing discovery, in which early preclinical studies demonstrating the potential efficacy and feasibility of exosomes for neural repair and regeneration has inspired further investigation.[50]

The apparent collapse of publications for 2023 and early 2024 is most likely a consequence of the indexing timetable, not an actual fall in research output. This is a common occurrence in bibliometric studies and underscores the importance of being aware to these timing effects when interpreting new trends.

Geographical Distribution and International Collaboration

One of the main takeaways from this analysis is that Chinese institutions lead in publication, accounting for 217 out of a total if 281 publications. This trend is consistent with a broader increase in China's research productivity and impact in biomedical fields over the past decade.[51]

Government investment in scientific research is the main reason for China's future direction, especially those with potential therapeutics. Its leadership is also due to the large and increasing number of practicing scientists in advanced biomedical research. Meanwhile, efforts to advance research in areas such as regenerative medicine and neuroscience have facilitated the rise of specialized facilities for both basic science and clinical applications.

The institutional analysis further reinforces China's dominance in this research area. Among the top 10 most productive institutions, 8 are from China, with Central South University leading with 20 publications, followed by Nanjing Medical University with 18, and Zhejiang University with 13. This concentration of research output in Chinese institutions aligns with the country-level analysis and highlights the significant investments made by these institutions in SCI and exosome research. The institutional collaboration network reveals interesting patterns. Central South University, besides being the top producer of publications, also leads in collaborations with 29 connections. Zhejiang University and the Hunan Engineering Research Center for Sports & Health follow with 23 and 19 collaborations, respectively. This extensive collaborative network among Chinese institutions suggests a strong national research ecosystem in this field.

Although China leads in the number of publications, the United States achieves greater impact with the highest citations per paper. This means US researchers are publishing fewer papers, but their work is making a bigger impact. This discrepancy in number of publications compared to influence is also apparent within other biomedical research domains reinforcing the importance of a multi-dimensional assessment approach toward scientific contributions.[52]

International collaboration, especially with our Chinese as well European and US partners having strong networks is an encouraging sign. These partnerships foster knowledge transfer, sharing of resources and development of actionable protocols that are essential for a progress to be realized. However, there is some space for involving researchers from more diverse regions, particularly the Global South.

Influential Journals and Research Dissemination

Insights from the analysis of influential journals reveal the multidisciplinary approach of SCI and exosome research. The leading journals, including *Stem Cell Research & Therapy, Journal of Nanobiotechnology* and *ACS Nano*, reflect the convergence of stem cell biology, nanotechnology, and materials science. The high impact factors and JCR quartile rankings of these journals indicate that research on SCI and exosomes is being published in esteemed, high-quality venues, suggesting the field's increasing recognition and credibility among the broader scientific community.

The patterns in research dissemination revealed by the journal co-occurrence and coupling networks are quite interesting. The strong connections between neuroscience-focused journals and interdisciplinary publications showcase the field's blend of fundamental neuroscience and applied biotechnology. Additionally, the prominence of open-access journals such as *Stem Cell Research & Therapy* in these networks indicates a movement towards more accessible research dissemination, enabling quicker knowledge transfer and a wider impact.

Nonetheless, the concentration of publications within a handful of journals raises the issue of needing more specialized publication venues for exosome research in neurology. Establishing these dedicated journals could enable more thorough discussions and quicker dissemination of niche-specific findings.

Key Contributors and Collaboration Patterns

Looking at those top authors and institutions is a window into the movers and shakers of that field. Researchers such as Fan Jin and Cai Weihua have been among the fastest-rising in terms of citation counts, indicating that there is clearly a great deal going on here for newcomers to make significant progress. Fan Jin and Cai Weihua, both from The First Affiliated Hospital of Nanjing Medical University in China, have emerged as rapid shining stars after 2019. They represent the major body of research work on exosomes application in SCI treatment. In particular, investigation of exosomal microRNAs in control inflammation and functional recovery post-SCI is relatively novel but have been strongly implicated by their unit. For example, their 2020 study published in Journal of Nanobiotechnology revealed an exosomal miR-124-3p could regulate microglial polarization and contribute a new therapeutic means to SCI.[11]

Interestingly, this co-authorship analysis also highlights the high-degree of collaboration within numerous key authors and institutions which is a promising feature in the field. These collaborations enable sharing resources and expertise to tackle the complex problems in SCI, exosome research, etc. They can also encourage more powerful, wider studies able to offer better quality of evidence for potential therapeutics and induce the construction of uniform protocols as well a best practices which is substantial hurdle in exosome research.[53]

This concentration of research influence among a small group of authors and institutions underscores the call for more inclusion, in order to ensure diversity within this field. Encouraging and enabling increased participation by researchers across backgrounds as well as institutions would allow for new perspectives and novel methods to be brought into the field.

Research Themes and Emerging Trends

In our bibliometric analysis of exosomes in spinal cord injury research, the major keywords were organized into five distinct clusters, each representing specific research themes and frontier developments in this rapidly evolving field.

Cluster 1 (22 Items): Fundamental Mechanisms and Therapeutic Pathways

This cluster encompasses the core biological processes underlying exosome-mediated spinal cord repair, including angiogenesis, axon regeneration, blood-brain barrier modulation, and central nervous system communication. The research in this cluster focuses on understanding how exosomes facilitate neural repair through multiple mechanisms. Exosomes derived from mesenchymal stem cells have been shown to promote angiogenesis and axonal regeneration by delivering specific microRNAs and proteins to injured neural tissues.[54] Recent studies have demonstrated that exosomal cargo, particularly microRNA-133b and microRNA-124, plays crucial roles in promoting neuroplasticity and functional recovery after spinal cord injury.[55] The modulation of the blood–brain barrier represents another critical mechanism, where exosomes can enhance barrier permeability to facilitate therapeutic molecule delivery while simultaneously protecting neural tissues from secondary injury.[56] Furthermore, extracellular vesicles serve as important mediators of intercellular communication within the central nervous system, coordinating complex repair processes involving multiple cell types including neurons, microglia, and astrocytes.[57]

Cluster 2 (18 Items): Cellular Mechanisms and Inflammatory Responses

This cluster represents research focused on the cellular and molecular mechanisms of exosome action, particularly regarding inflammation modulation, autophagy regulation, and cellular damage control. The inflammatory response following spinal cord injury is a double-edged sword, initially providing protective effects but potentially causing secondary damage if prolonged.[58] Exosomes have emerged as powerful modulators of neuroinflammation, capable of shifting microglial polarization from pro-inflammatory M1 to anti-inflammatory M2 phenotypes.[59] Recent breakthrough studies have shown that exosomal microRNA-216a-5p from hypoxic preconditioned mesenchymal stem cells can effectively repair traumatic spinal cord injury by modulating microglial M1/M2 polarization, leading to reduced inflammation and improved functional outcomes.[60] Additionally, exosomes regulate autophagy mechanisms, which are essential for clearing damaged cellular components and maintaining cellular homeostasis following spinal cord injury. The barrier function of exosomes also extends to protecting cells from oxidative stress and excitotoxicity, two major contributors to secondary injury cascades.[61] Understanding these intricate cellular mechanisms is crucial for optimizing exosome-based therapeutic strategies.

Cluster 3 (18 Items): Therapeutic Applications and Drug Delivery Systems

This cluster represents the translational aspects of exosome research, focusing on their application as therapeutic agents and novel drug delivery vehicles. Exosomes possess unique advantages as drug carriers due to their natural biocompatibility, ability to cross biological barriers, and inherent targeting capabilities.[62] Recent studies have demonstrated the successful use of engineered exosomes for delivering therapeutic molecules directly to injured spinal cord tissues. For instance, intranasal delivery of mesenchymal stem cell-derived exosomes loaded with phosphatase and tensin homolog siRNA has shown remarkable efficacy in repairing complete spinal cord injuries.[46] The field has also witnessed significant advances in exosome engineering, where researchers modify exosomal surfaces with specific targeting ligands to enhance tissue-specific delivery. Gene expression modulation through exosomal delivery represents another frontier, with studies showing successful delivery of therapeutic genes that promote neural regeneration and inhibit apoptotic pathways.[63] Furthermore, the development of standardized protocols for exosome isolation, characterization, and therapeutic application has become increasingly important for clinical translation. The ability to combine exosomes with other therapeutic approaches, such as biomaterial scaffolds and growth factors, opens new avenues for comprehensive spinal cord injury treatment strategies.

Cluster 4 (15 Items): Preclinical Models and Functional Assessment

This cluster encompasses research methodologies, experimental models, and functional evaluation approaches used in exosome-spinal cord injury research. The development of appropriate animal models is fundamental for advancing exosome-based therapies from bench to bedside.[64] Mouse models of spinal cord injury have been extensively used to evaluate exosome therapeutic efficacy, with researchers employing various injury paradigms including contusion, compression, and transection models to simulate different aspects of human spinal cord injuries. International collaborative efforts have led to the standardization of functional recovery assessments, including locomotor scoring systems such as the Basso Mouse Scale (BMS) and the Basso, Beattie, and Bresnahan (BBB) scale for rats.[65] Recent studies have emphasized the importance of long-term functional assessments, as initial improvements may not always translate to sustained recovery. Advanced imaging techniques, including diffusion tensor imaging and functional MRI, have become invaluable tools for monitoring neural regeneration and assessing the efficacy of exosome treatments in preclinical models.[66] The development of ischemic stroke models has also contributed to understanding exosome mechanisms, as similar pathophysiological processes occur in both conditions. Moreover, researchers are increasingly focusing on developing more clinically relevant models that better recapitulate the complexity of human spinal cord injuries, including chronic injury models and models that incorporate comorbidities commonly seen in patients.[67]

Cluster 5 (14 Items): Regenerative Biology and Tissue Engineering

This cluster focuses on the fundamental biological processes of neural regeneration and the integration of exosomes with tissue engineering approaches. The field has witnessed remarkable progress in understanding how exosomes promote neurogenesis, oligodendrogenesis, and axonal regeneration following spinal cord injury.[68] Recent studies have demonstrated that exosomes can stimulate the differentiation of neural stem cells into functional neurons and oligodendrocytes, thereby replacing lost cells and restoring myelin sheaths.[69] The delivery of exosomes through hydrogel scaffolds represents an innovative approach that combines the regenerative potential of exosomes with the structural support provided by biomaterials.[70] These hybrid systems can provide sustained release of exosomal cargo while creating a permissive environment for axonal growth and neural regeneration. Growth factor delivery via exosomes has shown particular promise, with studies demonstrating enhanced expression of neurotrophic factors such as brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF) following exosome treatment.[71] The concept of cognitive impairment recovery has also gained attention, as researchers recognize that spinal cord injuries can affect not only motor function but also cognitive abilities.[72] Understanding the mechanisms by which exosomes promote both structural and functional recovery is essential for developing comprehensive therapeutic strategies that address all aspects of spinal cord injury pathology.

Study Trends Shift

The temporal dynamics of keyword bursts reveal a sophisticated evolutionary trajectory in exosome-spinal cord injury research, characterized by three distinct paradigmatic phases that reflect the field's intellectual maturation and translational imperative.

Foundational Era (2013–2018). This pioneering phase was fundamentally defined by "bone marrow" research (strength = 3.37), representing not merely a focus on cellular origins, but rather the field's initial conceptual framework rooted in mesenchymal stem cell biology. This period established the revolutionary understanding that bone marrow-derived cells could generate therapeutically relevant exosomes, fundamentally challenging traditional cell replacement paradigms in neural repair.[73] The concurrent emergence of "mediated transfer" (strength = 1.85, 2015–2018) signified a mechanistic awakening—researchers began recognizing exosomes as sophisticated biological couriers rather than cellular debris, marking a conceptual revolution in intercellular communication theory that would reshape regenerative medicine approaches.

Mechanistic Enlightenment Era (2019–2021). This transformative phase witnessed an intellectual convergence around multiple breakthrough concepts. The dominance of "functional recovery" (strength = 4.22) reflected growing confidence in exosome therapeutic efficacy, while "stromal cells" (strength = 5.9, transitioning from 2018 to 2019) indicated deeper appreciation for cellular heterogeneity and therapeutic potential. The simultaneous bursts in "disease" (strength = 2.16), "mechanisms" (strength = 1.61) and "inhibition" (strength = 2.19) suggest researchers were grappling with fundamental questions of how pathological microenvironments influence exosome biogenesis and therapeutic targeting. "Mesenchymal stromal cells" (strength = 2.01) and "differentiation" (strength = 2.03) bursts indicated sophisticated understanding of how exosomal cargo could reprogram recipient cell fate, while "model" (strength = 1.89) reflected methodological maturation toward clinically relevant experimental paradigms.[74]

Precision Translation Era (2022–2024). The contemporary phase reveals unprecedented therapeutic sophistication, with "delivery" (strength = 3.56) emerging as the dominant concern, reflecting the field's recognition that therapeutic success requires bioengineering precision beyond simple exosome administration. The constellation of "therapy" (strength = 2.98), "neuroinflammation" (strength = 2.54), "recovery" (strength = 2.6), and "repair" (strength = 1.89) indicates a nuanced understanding that successful intervention requires orchestrated modulation of multiple pathophysiological processes. Notably, the sustained bursts in "cells" (strength = 2.11, extending from 2021), "microglia" (strength = 2.0), and "injury" (strength = 1.83) suggest the field's recognition that therapeutic success depends on understanding the dual nature of cellular responses—both pathological and reparative—requiring exquisitely controlled modulation rather than blanket intervention strategies.[75]

Predicted Research Hotspots for Post-2025 Era

Precision exosome engineering will dominate based on keyword evolution patterns, with delivery prominence evolving toward injury-specific targeting capabilities.[76] Combinatorial therapeutic strategies emerge from strengthening links between biomaterials, rehabilitation protocols, and exosome therapy clusters. Co-occurrence analysis shows connections between extracellular vesicles and recovery themes, suggesting integrated approaches.[77] Personalized exosome medicine progression toward patient-stratified approaches is evidenced by sustained microglia keyword bursts, indicating recognition of individualized inflammatory responses requiring tailored interventions supported by advancing omics technologies.[78]

Challenges and Future Directions

While considerable progress has been made in this area, the bibliometric analysis highlights key issues and opportunities for future research. The rapid field growth has led to a variety of approaches in exosome isolation, characterization and application that highlights the importance for standardized protocols. Further clinical research is necessary to define, validate, and ensure adherence with these standards across the field.

Although ample evidence exists for the efficacy of exosomes derived from different types of stem cells in SCI models, there are many unknown regarding how exosome function. We should examine the molecular and cellular mechanisms by which exosomes stimulate recovery or regeneration in future investigations. With the advancement of the field towards clinical implementation, resolving issues relating to large-scale manufacture of clinically compliant exosomes will be a critical requirement. Expansion of exosome production and bioengineering techniques is another promising target for improvement.[79]

Nevertheless, the delivery approaches need to be further developed for local and systematical application of exosomes in injured spinal cord recovery especially in chronic SCI.[80] Investigating new delivery structures with higher targeting ability, such as biomaterial scaffolds or reprogrammed exosomes in the light-activated region could be an exciting avenue for ensuing research. In addition, since most of the existing studies have focused on immediate results, long-term investigations still needed to determine how time-resistant exosome-mediated effects really are and if there may be any chronic safety issues.

To allow exosome-based therapies to become ultimately useful treatment strategies, the potential advantages of such a therapy in combination with other interventions including rehabilitation or electrical stimulation should be explored. The identification of exosomes as biomarkers for SCI progression and recovery could help carry out more personalized therapeutic plans. In anticipation of the clinical application, critical ethical issues, and regulatory concerns in the development of healthcare products based on exosomes should be considered.

Efforts to engage researchers from non-traditional areas would enrich the diversity of research approaches and patient populations. Furthermore, incorporation of knowledge from fields like materials science, bioengineering, and computational biology may help in advancement of novel exosome-based therapies to treat SCI.

Limitations of the Study

This bibliometric analysis provides some insights but also has several limitations. Some publications relevant to our target journals may have been missed by utilizing the Web of Science database exclusively. These could be important subjects for further studies that might include additional databases ensuring more systematic evaluation. The limitation to English-language publications likely also excluded some important contributions in other languages, given the international scope of this area of research. While the number of citations provides an indication of research impact, it does not necessarily equate to high quality or clinical relevance. That said, alternative metrics such as altmetrics could potentially reveal a publication's wider-reaching impact. Due to the time delay in indexing and updating databases, some recent articles may not be captured. In addition, since keyword analysis is reliant on the terms that have been used by authors it means not all aspects of research content are well represented.

Conclusion

This comprehensive bibliometric analysis reveals SCI-exosome research as a rapidly evolving field poised for clinical breakthrough but constrained by geographical concentration, mechanistic knowledge gaps, and translational infrastructure limitations. The study's novel contribution lies in providing the first quantitative roadmap for SCI-exosome research advancement, identifying specific bottlenecks, and strategic interventions necessary for therapeutic realization. Unlike previous bibliometric studies that provided descriptive overviews, this analysis offers predictive insights and actionable recommendations that can accelerate clinical translation and optimize research resource allocation. This study establishes bibliometric analysis as a valuable tool for translational research planning, demonstrating how sophisticated analytical approaches can transform research trend observation into strategic therapeutic development guidance.

Scope Statement

The professional section of the manuscript provides a comprehensive bibliometric analysis of the growing body of research on exosomes as a therapeutic approach for spinal cord injury (SCI). It highlights the increasing trend in publications, with a total of 281 articles authored by 1,792 researchers from 1,006 institutions across 66 countries, indicating a robust global interest in this area. The United States and China emerge as leading contributors, reflecting significant international collaboration. Key findings include the identification of the most influential journals and authors, with notable publications receiving high citation counts, which underscores the impact of this research. The analysis also reveals emerging hotspots such as microglia, extracellular vesicles, and targeted delivery systems, suggesting active areas for future exploration. Overall, the study emphasizes the potential of exosomes as a novel treatment for SCI and provides critical insights that can guide researchers and clinicians in advancing exosome-based therapies, ultimately contributing to improved outcomes for patients with spinal cord injuries.

Data Sharing Statement

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

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception (Zhihua Wang and Hangchuan Bi), study design (Zhihua Wang and Hangchuan Bi), execution (Chao Wang, Xianglin Shen and Jianyi Yang), acquisition of data (Denghui Li and Wan zhang), or analysis and interpretation (Hangchuan Bi and Rongji Yan); All authors took part in drafting, revising or critically reviewing the article; All authors gave final approval of the version to be published; All authors have agreed on the journal to which the article has been submitted; and all authors agree to be accountable for all aspects of the work.

Funding

1.The Major Science and Technology Project of Yunnan Provincial Department of Science and Technology, Yunnan Provincial Orthopedic and Sports Rehabilitation Clinical Medicine Research Center (grant NO. 202102AA310068). 2. Priority Union Foundation of Yunnan Provincial Science and Technology Department and Kunming Medical University (Grant No. 202401AY070001-353) and (Grant No. 202201AY070001-085). 3. Yunnan Clinical Center for Emergency Traumatic Diseases (Grant No. YWLCYXZX2023300075).

Disclosure

The authors declare that they have no competing interests.

References

1. Perrouin-Verbe B, Lefevre C, Kieny P, Gross R, Reiss B, Le Fort M. Spinal cord injury: a multisystem physiological impairment/dysfunction. *Revue neurologique*. 2021;177(5):594–605. doi:10.1016/j.neurol.2021.02.385
2. Anjum A, Yazid MD, Fauzi Daud M, et al. Spinal cord injury: pathophysiology, multimolecular interactions, and underlying recovery mechanisms. *Int J Mol Sci*. 2020;21(20):7533. doi:10.3390/ijms21207533
3. Hachem LD, Fehlings MG. Pathophysiology of spinal cord injury. *Neurosurg Clinics*. 2021;32(3):305–313. doi:10.1016/j.nec.2021.03.002
4. Flack JA, Sharma KD, Xie JY. Delving into the recent advancements of spinal cord injury treatment: a review of recent progress. *Neural Reg Res*. 2022;17(2):283–291. doi:10.4103/1673-5374.317961
5. Gadot R, Smith DN, Prablek M, Grochmal JK, Fuentes A, Ropper AE. Established and emerging therapies in acute spinal cord injury. *Neurospine*. 2022;19(2):283. doi:10.14245/ns.2244176.088
6. Liu W-Z, Ma Z-J, Li J-R, Kang X-W. Mesenchymal stem cell-derived exosomes: therapeutic opportunities and challenges for spinal cord injury. *Stem Cell Res Ther*. 2021;12(1):1–15. doi:10.1186/s13287-021-02153-8
7. Ren Z, Qi Y, Sun S, Tao Y, Shi R. Mesenchymal stem cell-derived exosomes: hope for spinal cord injury repair. *Stem Cells Development*. 2020;29 (23):1467–1478. doi:10.1089/scd.2020.0133
8. Feng J, Zhang Y, Zhu Z, Gu C, Waqas A, Chen L. Emerging exosomes and exosomal MiRNAs in spinal cord injury. *Front Cell Develop Biol*. 2021;9(703989). doi:10.3389/fcell.2021.703989
9. Di Bella MA. Overview and update on extracellular vesicles: considerations on exosomes and their application in modern medicine. *Biology*. 2022;11(6):804. doi:10.3390/biology11060804
10. Donoso-Quezada J, Ayala-Mar S, González-Valdez J. The role of lipids in exosome biology and intercellular communication: function, analytics and applications. *Traffic*. 2021;22(7):204–220. doi:10.1111/tra.12803
11. Jiang D, Gong F, Ge X, et al. Neuron-derived exosomes-transmitted miR-124-3p protect traumatically injured spinal cord by suppressing the activation of neurotoxic microglia and astrocytes. *J Nanobiotechnol*. 2020;18(1):1–20. doi:10.1186/s12951-020-00665-8
12. Xiao C-L, Yin W-C, Zhong Y-C, et al. The role of PI3K/Akt signalling pathway in spinal cord injury. *Biomed Pharmacother*. 2022;156:113881. doi:10.1016/j.biopha.2022.113881
13. Li K, Chen Z, Chang X, Xue R, Wang H, Guo W. Wnt signaling pathway in spinal cord injury: from mechanisms to potential applications. *Front Mol Neurosci*. 2024;17(1427054). doi:10.3389/fnmol.2024.1427054
14. Schepici G, Silvestro S, Mazzon E. Regenerative effects of exosomes-derived MSCs: an overview on spinal cord injury experimental studies. *Biomedicines*. 2023;11(1):201. doi:10.3390/biomedicines11010201
15. Cheng L-F, You C-Q, Peng C, Ren -J-J, Guo K, Liu T-L. Mesenchymal stem cell-derived exosomes as a new drug carrier for the treatment of spinal cord injury: a review. *Chin J Traumatol*. 2024;27(3):134–146. doi:10.1016/j.cjtee.2024.03.009
16. Kim G-U, Sung S-E, Kang -K-K, et al. Therapeutic potential of mesenchymal stem cells (MSCs) and MSC-derived extracellular vesicles for the treatment of spinal cord injury. *Int J Mol Sci*. 2021;22(24):13672. doi:10.3390/ijms222413672
17. Liang Z-Y, Xu X-J, Rao J, Yang Z-L, Wang C-H, Chen C-M. Mesenchymal stem cell-derived exosomal miRNAs promote M2 macrophages polarization: therapeutic opportunities for spinal cord injury. *Front Mol Neurosci*. 2022;15:926928. doi:10.3389/fnmol.2022.926928
18. Yang Z-L, Rao J, Lin F-B, et al. The role of exosomes and exosomal noncoding RNAs from different cell sources in spinal cord injury. *Front Cell Neurosci*. 2022;16(882306). doi:10.3389/fncel.2022.882306
19. Li Y, Luo W, Meng C, Shi K, Gu R, Cui S. Exosomes as promising bioactive materials in the treatment of spinal cord injury. *Stem Cell Res Ther*. 2024;15(1):335. doi:10.1186/s13287-024-03952-5
20. Elsharkasy OM, Nordin JZ, Hagey DW, et al. Extracellular vesicles as drug delivery systems: why and how? *Adv Drug Delivery Rev*. 2020;159:332–343. doi:10.1016/j.addr.2020.04.004
21. Zhang C, Deng R, Zhang G, et al. Therapeutic effect of exosomes derived from stem cells in spinal cord injury: a systematic review based on animal studies. *Front Neurol*. 2022;13:847444.
22. Ferreira D, Moreira JN, Rodrigues LR. New advances in exosome-based targeted drug delivery systems. *Crit Rev Oncol/Hematol*. 2022;172:103628. doi:10.1016/j.critrevonc.2022.103628
23. Fu S, Wang Y, Xia X, Zheng JC. Exosome engineering: current progress in cargo loading and targeted delivery. *NanoImpact*. 2020;20 (100261):100261. doi:10.1016/j.impact.2020.100261
24. Jafari D, Shajari S, Jafari R, et al. Designer exosomes: a new platform for biotechnology therapeutics. *BioDrugs*. 2020;34(5):567–586. doi:10.1007/s40259-020-00434-x
25. Kumar M, George RJ, A PS. Bibliometric analysis for medical research. *Indian J Psychological Med*. 2023;45(3):277–282. doi:10.1177/02537176221103617
26. Moral-Muñoz JA, Herrera-Viedma E, Santisteban-Espejo A, Cobo MJ. Software tools for conducting bibliometric analysis in science: an up-to-date review. *Profesional Inform*. 2020;29(1). doi:10.3145/epi.2020.ene.03
27. Ma D, Guan B, Song L, et al. A bibliometric analysis of exosomes in cardiovascular diseases from 2001 to 2021. *Frontiers in Cardiovascular Medicine*. 2021;8(734514). doi:10.3389/fcvm.2021.734514
28. Dehghanbanadaki H, Aazami H, Razi F, Nasli-Esfahani E, Norouzi P, Hashemi E. The global trend of exosome in diabetes research: a bibliometric approach. *Diabetes Metab Syndr*. 2022;16(4):102450. doi:10.1016/j.dsx.2022.102450
29. Donthu N, Kumar S, Mukherjee D, Pandey N, Lim WM. How to conduct a bibliometric analysis: an overview and guidelines. *Journal of Business Research*. 2021;133:285–296. doi:10.1016/j.jbusres.2021.04.070
30. Kokol P, Blažun Vošner H, Završnik J. Application of bibliometrics in medicine: a historical bibliometrics analysis. *Health Inf Libraries J*. 2021;38 (2):125–138. doi:10.1111/hir.12295
31. Ellegaard O, Wallin JA. The bibliometric analysis of scholarly production: how great is the impact? *Scientometrics*. 2015;105(3):1809–1831. doi:10.1007/s11192-015-1645-z
32. Agarwal A, Durairajanayagam D, Tatagari S, et al. Bibliometrics: tracking research impact by selecting the appropriate metrics. *Asian J Androl*. 2016;18(2):296–309. doi:10.4103/1008-682X.171582

33. Erdbrügger U, Lannigan J. Analytical challenges of extracellular vesicle detection: a comparison of different techniques. *Cytometry Part A*. 2016;89(2):123–134. doi:10.1002/cyto.a.22795
34. Li P, Kaslan M, Lee SH, Yao J, Gao Z. Progress in exosome isolation techniques. *Theranostics*. 2017;7(3):789. doi:10.7150/thno.18133
35. Wei B, Huang H, Cao Q, Song X, Zhang Z. Bibliometric and visualized analysis of the applications of exosomes based drug delivery. *Biomed Pharmacother*. 2024;176:116803. doi:10.1016/j.biopha.2024.116803
36. Zhuo Y, Ai K, He K, et al. Global Research Trends of Exosomes in the Central Nervous System: a Bibliometric and Visualized Analysis. *Neurospine*. 2023;20(2):507. doi:10.14245/ns.2244988.494
37. AlRyalat SAS, Malkawi LW, Momani SM. Comparing bibliometric analysis using PubMed, Scopus, and Web of Science databases. *J vis exp*. 2019;2019(152):e58494.
38. Wang Y-Z, Wu -C-C, Wang X-Q. Bibliometric study of pain after spinal cord injury. *Neural Plast*. 2021;2021(1):6634644. doi:10.1155/2021/6634644
39. Ahmad SJ, Ahmed AR, Kowalewski KF, et al. Citation classics in general medical journals: assessing the quality of evidence; a systematic review. *Gastroenterol Hepatol Bed Bench*. 2020;13(2):101.
40. Bertoli-Barsotti L, Lando T. A theoretical model of the relationship between the h-index and other simple citation indicators. *Scientometrics*. 2017;111(3):1415–1448. doi:10.1007/s11192-017-2351-9
41. Egghe L. *An Improvement of the h-Index: The g-Index*. Vol. 2006. 2006.
42. Novak D, Batko M, Zezula P. Metric index: an efficient and scalable solution for precise and approximate similarity search. *Inform Syst*. 2011;36(4):721–733. doi:10.1016/j.is.2010.10.002
43. Hirsch JE. An index to quantify an individual's scientific research output. *Proc Natl Acad Sci*. 2005;102(46):16569–16572. doi:10.1073/pnas.0507655102
44. Xin H, Li Y, Liu Z, et al. MiR-133b promotes neural plasticity and functional recovery after treatment of stroke with multipotent mesenchymal stromal cells in rats via transfer of exosome-enriched extracellular particles. *Stem Cells*. 2013;31(12):2737–2746. doi:10.1002/stem.1409
45. Liu W, Rong Y, Wang J, et al. Exosome-shuttled miR-216a-5p from hypoxic preconditioned mesenchymal stem cells repair traumatic spinal cord injury by shifting microglial M1/M2 polarization. *J Neuroinflammation*. 2020;17(1):1–22. doi:10.1186/s12974-020-1726-7
46. Guo S, Perets N, Betzer O, et al. Intranasal delivery of mesenchymal stem cell derived exosomes loaded with phosphatase and tensin homolog siRNA repairs complete spinal cord injury. *ACS nano*. 2019;13(9):10015–10028. doi:10.1021/acsnano.9b01892
47. Théry C, Witwer KW, Aikawa E, et al. Minimal information for studies of extracellular vesicles 2018 (MISEV2018): a position statement of the International Society for Extracellular Vesicles and update of the MISEV2014 guidelines. *J Extracell Vesicles*. 2018;7(1):1535750. doi:10.1080/20013078.2018.1535750
48. Witwer KW, Buzás EI, Bemis LT, et al. Standardization of sample collection, isolation and analysis methods in extracellular vesicle research. *J Extracell Vesicles*. 2013;2(1):20360. doi:10.3402/jev.v2i0.20360
49. Ahuja CS, Wilson JR, Nori S, et al. Traumatic spinal cord injury. *Nature Reviews Disease Primers*. 2017;3(1):1–21. doi:10.1038/nrdp.2017.18
50. Huang J-H, Yin X-M, Xu Y, et al. Systemic administration of exosomes released from mesenchymal stromal cells attenuates apoptosis, inflammation, and promotes angiogenesis after spinal cord injury in rats. *Journal of Neurotrauma*. 2017;34(24):3388–3396. doi:10.1089/neu.2017.5063
51. Bornmann L, Haunschild R, Mutz R. Growth rates of modern science: a latent piecewise growth curve approach to model publication numbers from established and new literature databases. *Humanit Soc Sci Commun*. 2021;8(1):1–15. doi:10.1057/s41599-021-00903-w
52. Bornmann L, Mutz R. Growth rates of modern science: a bibliometric analysis based on the number of publications and cited references. *J Assoc Informat Sci Technol*. 2015;66(11):2215–2222. doi:10.1002/asi.23329
53. Witwer KW, Soekmadji C, Hill AF, et al. Updating the MISEV minimal requirements for extracellular vesicle studies: building bridges to reproducibility. *Journal of Extracellular Vesicles*. 2017;6(1):1396823. doi:10.1080/20013078.2017.1396823
54. Hedayat M, Ahmadi M, Shoaran M, Rezaie J. Therapeutic application of mesenchymal stem cells derived exosomes in neurodegenerative diseases: a focus on non-coding RNAs cargo, drug delivery potential, perspective. *Life Sci*. 2023;320(121566):121566. doi:10.1016/j.lfs.2023.121566
55. Zhang X, Cao J, Wu J, Gao JQ. Biomaterial-based defenders boost biopharmaceuticals efficacy for spinal cord injury treatment: a review. *Adv Mater Interfaces*. 2023;10(8):2202034. doi:10.1002/admi.202202034
56. Heidarzadeh M, Gürsoy-özdemir Y, Kaya M, et al. Exosomal delivery of therapeutic modulators through the blood–brain barrier; promise and pitfalls. *Cell Biosci*. 2021;11(1):1–28. doi:10.1186/s13578-021-00650-0
57. Filannino FM, Panaro MA, Benameur T, Pizzolorusso I, Porro C. Extracellular vesicles in the central nervous system: a novel mechanism of neuronal cell communication. *Int J Mol Sci*. 2024;25(3):1629. doi:10.3390/ijms25031629
58. Singh N, Guha L, Kumar H. From hope to healing: exploring the therapeutic potential of exosomes in spinal cord injury. *Extracellular Vesicle*. 2024;3(100044):100044. doi:10.1016/j.vesic.2024.100044
59. Arabpour M, Saghazadeh A, Rezaei N. Anti-inflammatory and M2 macrophage polarization-promoting effect of mesenchymal stem cell-derived exosomes. *Int Immunopharmacol*. 2021;97:107823. doi:10.1016/j.intimp.2021.107823
60. Xue H, Ran B, Li J, Wang G, Chen B, Mao H. Bone marrow mesenchymal stem cell exosomes-derived microRNA-216a-5p on locomotor performance, neuronal injury, and microglia inflammation in spinal cord injury. *Front Cell Develop Biol*. 2023;11:1227440. doi:10.3389/fcell.2023.1227440
61. Wang X, Zhou Y, Gao Q, et al. The role of exosomal microRNAs and oxidative stress in neurodegenerative diseases. *Oxid Med Cell Longev*. 2020;2020(1):3232869. doi:10.1155/2020/3232869
62. Elliott RO, He M. Unlocking the power of exosomes for crossing biological barriers in drug delivery. *Pharmaceutics*. 2021;13(1):122. doi:10.3390/pharmaceutics13010122
63. Zeng C-W, Zhang C-L. Neuronal regeneration after injury: a new perspective on gene therapy. *Front Neurosci*. 2023;17(1181816). doi:10.3389/fnins.2023.1181816
64. Cui L, Song Y, Hou Z, Yang L, Guo S, Wang C. From bench to bedside: the research status and application opportunity of extracellular vesicles and their engineering strategies in the treatment of skin defects. *J Nanobiotechnol*. 2025;23(1):1–29. doi:10.1186/s12951-025-03461-4
65. Franz S, Hug A, Weidner N. Functional recovery in CNS disease. In: *Oxford Textbook of Neurorehabilitation*. 2020:131.

66. Tsintou M, Dalamagkas K, Moore TL, et al. The use of hydrogel-delivered extracellular vesicles in recovery of motor function in stroke: a testable experimental hypothesis for clinical translation including behavioral and neuroimaging assessment approaches. *Neural Regeneration Research*. 2021;16(4):605–613. doi:10.4103/1673-5374.295269
67. Kondiles BR, Rana S, Weiner D, et al. Lessons Learned and Recommendations from a SCOPE Spinal Cord Injury Neurorestorative Clinical Trials Update. *Neurotrauma Reports*. 2025;6(1):210–231. doi:10.1089/neur.2024.0163
68. Akbari-Gharalari N, Khodakarimi S, Nezhadshahmohammad F, Karimipour M, Ebrahimi-Kalan A, Wu J. Exosomes in neuron-glia communication: a review on neurodegeneration. *Bioimpacts*. 2024;14(5):30153. doi:10.34172/bi.2023.30153
69. Allegretta C, D'Amico E, Manuti V, Avolio C, Conese M. Mesenchymal stem cell-derived extracellular vesicles and their therapeutic use in central nervous system demyelinating disorders. *Int J Mol Sci*. 2022;23(7):3829. doi:10.3390/ijms23073829
70. Gu C, Feng J, Waqas A, et al. Technological advances of 3D scaffold-based stem cell/exosome therapy in tissues and organs. *Front Cell Develop Biol*. 2021;9(709204). doi:10.3389/fcell.2021.709204
71. Ciszowski K, Gomółka E, Gawlikowski T, Szpak D, Potoczek A, Boba M. Brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF) blood levels in patients with acute carbon monoxide poisoning-a preliminary observations. *Przeglad Lekarski*. 2016;73(8):552–559.
72. Dudley-Javoroski S, Lee J, Shields RK. Cognitive function, quality of life, and aging: relationships in individuals with and without spinal cord injury. *Physiother Theory Pract*. 2022;38(1):36–45. doi:10.1080/09593985.2020.1712755
73. Xin H, Li Y, Cui Y, Yang JJ, Zhang ZG, Chopp M. Systemic administration of exosomes released from mesenchymal stromal cells promote functional recovery and neurovascular plasticity after stroke in rats. *J Cereb Blood Flow Metab*. 2013;33(11):1711–1715. doi:10.1038/jcbfm.2013.152
74. Rasouli A, Roshangar L, Hosseini M, Pourmohammadfazel A, Nikzad S. Beyond boundaries: the therapeutic potential of exosomes in neural microenvironments in neurological disorders. *Neuroscience*. 2024;553:98–109. doi:10.1016/j.neuroscience.2024.06.031
75. Yu Q, Cai Z, Liu X, et al. Research Progress on Treating Spinal Cord Injury by Modulating the Phenotype of Microglia. *Journal of Integrative Neuroscience*. 2024;23(9):171. doi:10.31083/j.jin2309171
76. Li J, Wang Z, Wei Y, et al. Advances in Tracing Techniques: mapping the Trajectory of Mesenchymal Stem-Cell-Derived Extracellular Vesicles. *Chemi Biomed Imag*. 2025;3(3):137–168. doi:10.1021/cbmi.4c00085
77. Rondelli V, Helmy S, Passignani G, Parisse P, Di Silvestre D. Integrated strategies for a holistic view of extracellular vesicles. *ACS omega*. 2022;7(23):19058–19069. doi:10.1021/acsomega.2c01003
78. Yamamoto Y, Kanayama N, Nakayama Y, Matsushima N. Current status, issues and future prospects of personalized medicine for each disease. *Journal of Personalized Medicine*. 2022;12(3):444. doi:10.3390/jpm12030444
79. Gimona M, Pachler K, Laner-Plamberger S, Schallmoser K, Rohde E. Manufacturing of human extracellular vesicle-based therapeutics for clinical use. *Int J Mol Sci*. 2017;18(6):1190. doi:10.3390/ijms18061190
80. Mu J, Wu J, Cao J, et al. Rapid and effective treatment of traumatic spinal cord injury using stem cell derived exosomes. *Asian J Pharm Sci*. 2021;16(6):806–815. doi:10.1016/j.ajps.2021.10.002