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Knowledge mapping and research trends of stem cell in wound healing: A bibliometric analysis

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Abstract

Wound nonhealing is a common and difficult problem in clinic. Stem cells are pluripotent cells, and their undifferentiated and self-replicating characteristics have attracted much attention in the regenerative medicine-related researches. New treatment approaches might result from an understanding of the function of stem cells in wound healing. Using bibliometric techniques, this study proposed to analyse the research status, hotspots, and research trends in stem cell and wound healing. By using the Web of Science Core Collection (WoSCC), we conducted an in-depth review of publications on stem cells in wound healing from 1999 to 2023. We used scientometric analysis methods to examine annual trends, institutions, countries, journals, authors, keywords, co-occurrence references and their closed relationship, revealing present hotspots and potential future advancements in this field. We analysed 19 728 English studies and discovered a consistent rise in annual publications. The United States and China were the two countries with the most publications. The most three influential institutions in the field were Shanghai Jiao Tong University, Sun Yat-sen University, and University of Pittsburgh. *International Journal of Molecular Sciences* and *Biomaterials* were considered the most influential journals in this field. *International Journal of Molecular Sciences* had the most publications, and the most quantity of citations and the highest H-index were found in *Biomaterials*. The dual-map overlay revealed that publications in Molecular/Biology/Genetics and Health/Nursing/Medicine co-cited journals received the majority of the citations for studies from Molecular/Biology/Immunology and Medicine/Medical/Clinical. In terms of publication production and influence, Fu X stood out among the authors, and Pittenger MF took the top spot in co-citations. According to the keywords from the analysis, future research should concentrate on the mechanisms through which stem cells promote wound healing. We conducted a thorough analysis of the general information, knowledge base and research hotspots in the field of stem cells

Nianzhe Sun and Yu Sun contributed equally to this study.

and wound healing from 1999 to 2023 by using the VOSviewer, CiteSpace, and other bibliometric analysis tools. It not only provided valuable insights for scholars, but also served as a reliable reference that drives further development in the field and stimulates the interest of researchers.

KEYWORDS

bibliometric analysis, CiteSpace, stem cell, VOSviewer, wound healing

Key Messages

- The comprehensive study provided a panoramic view of the field by examining publications on the stem cell and wound healing from the beginning of database to 2023.
- The study summarized the main source of stem cells for regenerative medicine and mechanism of mesenchymal stem cells promoting wound healing based on the results of visualization.
- The paper revealed the research trends in stem cell and wound healing and aimed to provide reliable references for scholars.

1 | INTRODUCTION

Almost everyone is aware that stem cells are a type of undifferentiated, non-specific cells that can differentiate into any type of cell in an organism. They are typically found in adult tissues or embryos and have the ability to self-renew. Based on their differentiation potential, there are several types of stem cells, including totipotent, pluripotent, multipotent, oligopotent, and unipotent stem cells.[1] Additionally, they can be divided into induced pluripotent stem cells (iPSCs), fetal and adult, and embryonic stem cells depending on their origin.[2] The therapeutic effectiveness of stem cells in medicine has generated a lot of interest due to their unique properties, especially in regenerative medicine.[3] Stem cell therapy is a cutting-edge therapeutic method that uses the stem cells' unique properties, such as the ability of self-renewal and undifferentiation, to replace or repair defective human tissues and cells with foreign cells that are completely novel, functioning properly, and completely effective.[4] At present, stem cell therapy has become an emerging therapy after drugs and surgery. Clinical trials of stem cells have involved nearly 100 diseases, such as different tumours, cardiovascular disorders, Alzheimer's disease, diabetes, spinal cord injury and so on.[5]

Normal wound healing in our body is a continuous multi-stage process, including haemostasis, inflammation, proliferation and remodelling, which is affected and controlled by many factors.[6] If this process is disturbed, it can lead to problems with the normal repair process, manifested as non-healing or excessive healing of the wound.[7] According to existing studies, the causes of non-healing wounds include systemic factors, such as age, malnutrition, obesity, chronic disease status, smoking, drinking, and so forth, and local factors, such as vascular diseases, neurological diseases, infections, and improper treatment.[8] Nevertheless, regardless of the cause, non-healing wounds have similar characteristics: chronic persistent inflammation, fibroblast senescence, decreased growth factor activity and infection.[9] As a clinician, especially a surgeon, will encounter chronic non-healing wounds almost every day, including diabetic foot ulcers, pressure sores, and others. Therefore, non-healing wounds have become a common and serious clinical problem, brought serious burden to both patients and society. A study published in 2021 found that chronic wounds have a major financial impact on health care and damage the quality of life for almost 2.5% of Americans. Based on the background of an aging population and widespread obesity and diabetes, and the continuous issue of infections, chronic wounds are projected to remain a serious clinical, social, and economic challenge.[10] Platelet-rich plasma (PRP), regulated growth factors and cytokines, negative pressure therapy, biological dressings, and stem cell therapy are a few of the current methods utilized to speed up wound healing.[11–14] Previous researches have demonstrated that using the right stem cells in wound treatment can encourage angiogenesis, speed up skin cell growth and reepithelialization, control immune response and regulate collagen fibre remodelling, thus promoting wound healing, inhibiting scar hyperplasia and achieving favourable healing effect.[15,16] Stem cell therapy is believed to be an effective method for wounds that do not heal.

Numerous studies on stem cell treatment for wound healing have been published during the past 20 years.

These investigations, however, have not been organized and examined in a methodical manner. Additionally, there is still ongoing discussion on stem cell therapy indications, adverse effects of stem cell therapy (e.g., tumorigenesis),[5] and some ethical issues, which frequently puts clinicians in a challenging position when deciding on the best course of action. Clinical practitioners and researchers can better identify the best applications for stem cell in wound healing and gain insightful information about potential future technical developments by systematically analysing current research. Bibliometrics is a technique for methodically and impartially evaluating the scope, significance, and trends of scientific research by using statistical and quantitative analysis of literature data.[17] Nevertheless, no prior attempt has been made to use bibliometrics to analyse pertinent studies on the specific topic of stem cell and wound healing. Therefore, this analysis is aimed at examining published papers using bibliometrics techniques and information visualization is used to summarize how stem cell treatment is used in wounds that are difficult to heal. This article is also dedicated to add to the corpus of existing knowledge and recommend new study directions.

2 | MATERIALS AND METHODS

2.1 | Source database and data collection

The Web of Science Core Collection (WoSCC) was used to conduct an organized search to find publications that were indexed from the first publication to 1 August 2023, based on the main search terms associated with 'stem cell' and 'wound'. The database used for this study was Science Citation Index Expanded (SCI-Expanded), and English was chosen as the study's language. A detailed search strategy was found in Appendix. Only publications type with 'article' or 'review' were considered. Two reviewers (NS and YS) independently identified all relevant data and studies and omitted duplicate and irrelevant studies in order to guarantee the accuracy and reliability of the data included. Any disagreements between the two researchers (NS and YS) will be discussed and reviewed by a third party (PW and JT).

2.2 | Data extraction and analysis

We conducted series of accurate analysis to consider ranking and statistical evaluation of related data of most cited and co-cited countries, affiliations, authors, journals and references using Microsoft Excel 2021. Visual maps intuitively depicting the national distribution of publications had been drawn via Python (v 3.11.4, https://www.python.org/downloads/). Meanwhile, we also used the advanced and renowned VOSviewer software (v 1.6.19, Leiden University) to represent bibliometric maps to visually show the co-authorship, co-citation and co-occurrence between them. Each characteristic term, encompassing keywords, countries, affiliations, references, journals and authors, was presented by a node, therein the size and proximity of nodes represented the weight, frequency and cooperation intensity of these terms. Additionally, the thickness of the lines thoughtfully represented the strength of their cooperation, while the use of coloured circles to show specific term clusters was profound. It was common practice to do bibliometric analysis using CiteSpace, which was used to look into the research trends in a certain study field. CiteSpace (v 6.2. R4, Pro. Chaomei Chen from Drexel University) was used in this investigation to identify and extract references with the highest concentrations of citations, as well as overlay dual maps of journals. The following settings were made for CiteSpace: the link retaining factor was set to 3 (LRF = 3), the value for top N was set to 1 ($e = 1$), the time interval was specified as 1999–1 August 2023, each time slice represented a span of 2 years, the look back years were set to 5 (LBY = 5), links (strength: cosine, scope: within slices), selection criteria relied on the g-index with a threshold of 10 ($k = 10$), and the minimum duration was set to 1 (MD = 1). Furthermore, we also used R software (v.4.3.1, https://www.r-project.org/) to create word clouds of keywords, topic dendrograms of factorial analysis and thematic map in order to meticulously analyse the keywords usage and to thoroughly explore trends of the complex academic collaboration networks for further prediction.

3 | RESULTS

3.1 | Annual publication output and growth trend

20 436 publications in all were retrieved from the start of the search to 1 August 2023. After screening, some irrelevant and ineligible records were excluded with remaining 19 728 documents (Figure 1). During the set timespan, a steadily increasing trend was observed in the annual publication output. Due to incomplete data in 2023, the number of documents issued in 2022 reached the largest peak ($N = 1892$), 18 times more than that in 1999 ($N = 105$). Meanwhile, the average annual growth rate reached 13.4% and a considerable increase could be seen from 2007 to 2022 (Figure 2).

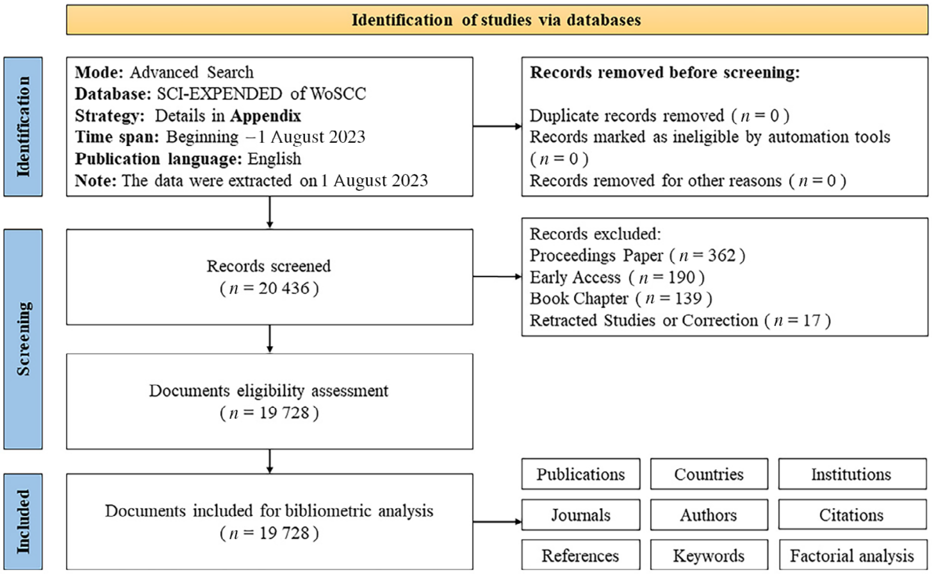

FIGURE 1 The flow diagram.

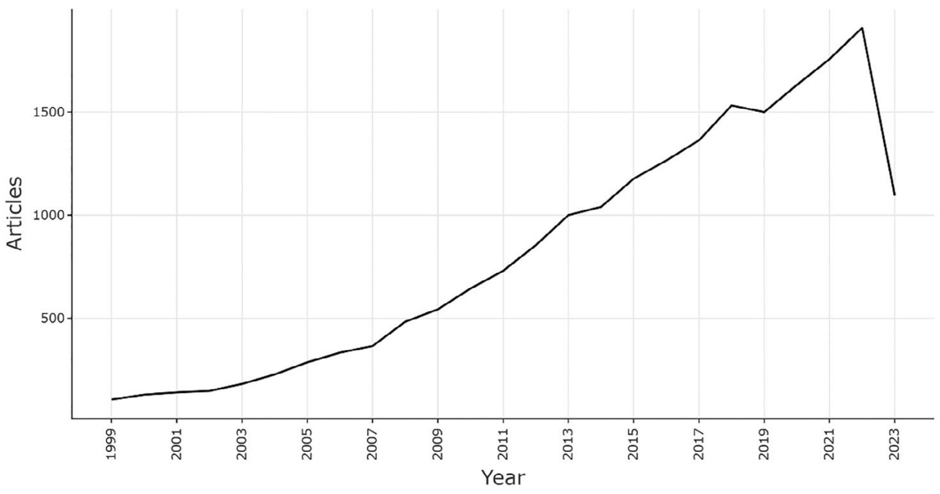

FIGURE 2 The annual dynamic growth trend of publications.

3.2 | Countries/regions and institutions analysis

A total of 119 countries and 13 225 institutions had made important contributions in the research area of stem cell and wound healing. The most frequent contributor was the United States with 22 743 publications, followed by China ($N = 22\,085$), Germany ($N = 5517$), Japan ($N = 4850$), and Italy ($N = 4334$), while there were less than 4000 publications in the remaining nations (Table 1). Single country publications (SCP) are independent studies or publications that concentrate on a single country, offering useful references for researching and assessing different facets of that country.[18] In contrast, multiple country publications (MCP) involves the cooperation of multiple countries, offering multifaceted understanding that promotes to comprehend the interactions between countries and the influencing factors on the trend of world development.[19,20] Interestingly, in addition to having the most publications, the United States also had the greatest SCP and MCP, indicating its strong research capabilities and wide-ranging engagement with other countries in this field (Figure 3A). From 1999 to 2023, the country-specific annual trend publications associated with stem cell and wound healing were shown in Figure 3B. The United States and China took the first and second positions in all countries. The United States' publications had steadily increased year by year. However, the annual publications of China were similar to others except the United States and was at a low level at first, but after 2012, China's publications in this area grew rapidly, and its growth rate exceeded that of the United States. At present, China's number of annual publications was close to but still not exceeding the United States, while the growth rate of other countries was still slow. The distribution of countries and their

TABLE 1 The top 10 prolific countries and affiliations involved in stem cell and wound healing.

Rank	Country	Publications	Affiliations	Publications
1	USA	22 743	Shanghai Jiao Tong University	770
2	China	22 085	Sun Yat-sen University	650
3	Germany	5517	University of Pittsburgh	615
4	Japan	4850	Zhejiang University	597
5	Italy	4334	Sichuan University	572
6	South Korea	3886	Stanford University	548
7	United Kingdom	3490	Seoul National University	487
8	Iran	3101	Harvard University	479
9	France	2605	Johns Hopkins University	469
10	Canada	2455	University of Toronto	458

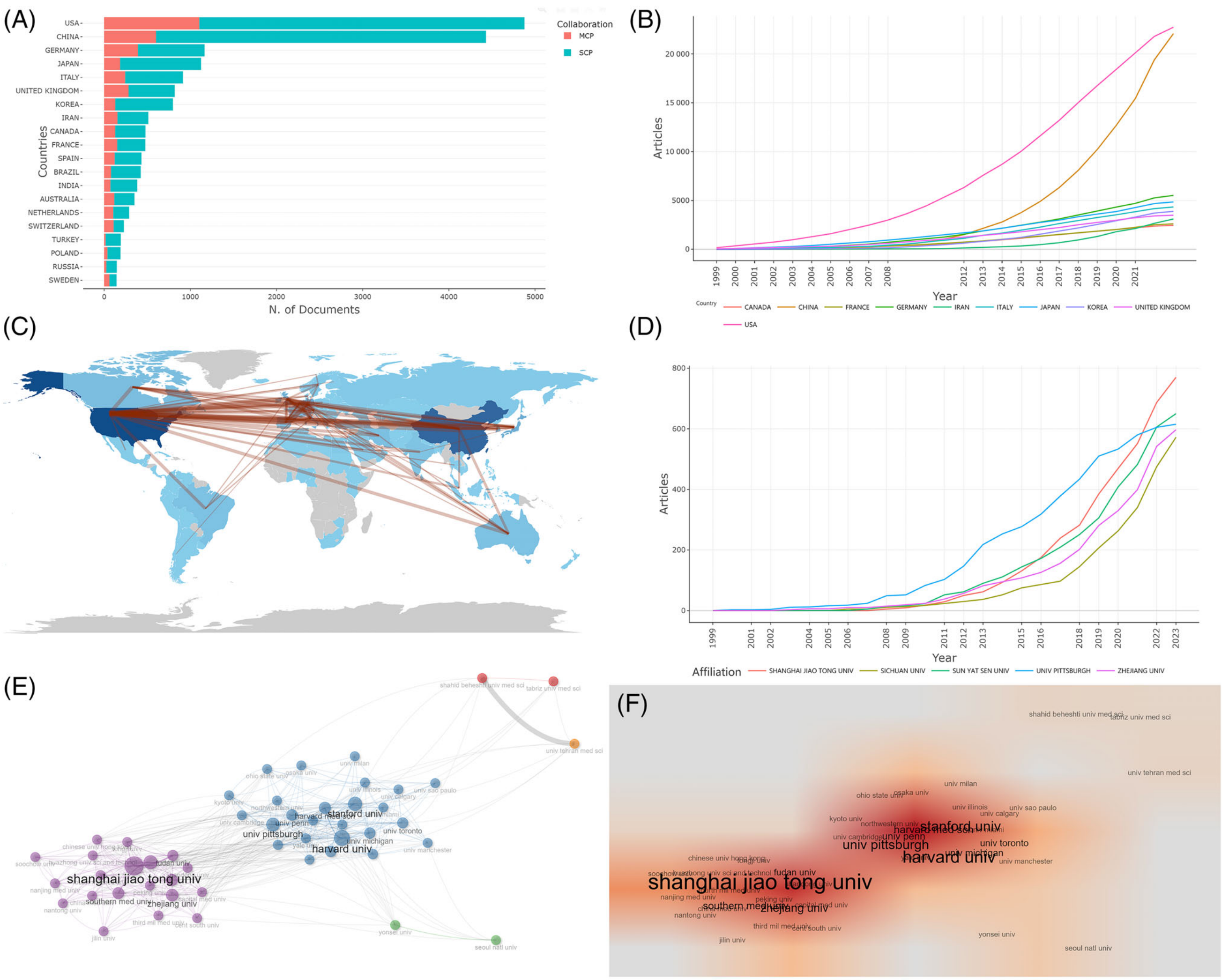

FIGURE 3 Analysis of countries and affiliations involved in stem cell and wound healing. (A) The top 20 most productive single country publications (SCP) and multiple country publications (MCP) countries. (B) The dynamic publications analysis of the top 10 most prolific countries. (C) The distribution and cooperative relationship of countries in terms of publications. (D) The dynamic publications analysis of the top 5 most productive institutions. (E) The cooperative relationship of institutions ($N = 50$) in terms of publications. (F) The visual density map of institutions about documents.

cooperative relationship network were depicted in Figure 3C. Obviously, the two most contributing countries were the United States and China due to the darker colour, which was consistent with the above results. Additionally, due to denser wiring, significant cooperation could be seen between the United States and China, Germany, and Japan. Nevertheless, the United States had not only published more papers but also cooperated with other countries the most. On the contrary, although China had published more papers, it did not engage in much international collaboration, so in the future, China should step up its collaboration with other nations in this area.

Table 1 contained a list of the top 10 institutions working in this field. Shanghai Jiao Tong University was the most notable institution, which produced 770 publications, Sun Yat-sen University came in second with 650 publications, and the University of Pittsburgh came in third with 615 publications. Figure 3D showed that from 1999 until 2021, University of Pittsburgh had the most publications in the discipline, but by the end of that year, Shanghai Jiao Tong University and Sun Yat-sen University had surpassed it. The university with the most papers published was found to be Shanghai Jiao Tong University, which was followed by Sun Yat-sen University, the University of Pittsburgh, Zhejiang University, and Sichuan University. In fact, all the 10 institutions had experienced an increase in the number of publications around 2010. Figure 3E showed the cooperative relationship of institutions with purple and blue nodes representing two clusters respectively. Nodes representing Shanghai Jiao Tong University and Harvard University were relatively large, indicating their dominance in this field. Positive cooperation between different institutions was observed. The density map of institutions also showed the dominance of Shanghai Jiao Tong University, Harvard University and Stanford University (Figure 3F).

3.3 | Authors and co-cited authors analysis

There were 95 511 researchers and 313 065 co-cited authors contributing to publications in this subject of stem cell and wound healing. The two most frequently published authors in this field were Fu X ($N = 96$) and Longaker MT ($N = 69$) (Table 2). Furthermore, Pittenger MF ($N = 1057$), Zhang Y ($N = 1012$), and Li Y ($N = 996$) were the three authors who had received the most co-citations. The networks of co-authorship and citation among specialists in the area of stem cells and wound healing were analysed using VOSviewer (Figure 4). Fu X ($N = 96$) and Longaker MT ($N = 69$) had substantially larger nodes than other authors because of their higher publication output, which corresponded to the outcomes in Table 2. The close collaborations centered on author Fu X between various authors were shown in Figure 4A's co-occurrence relationships, which also showed that researchers who were more active tended to collaborate more frequently with others. If two authors share a reference list and at least one of their publications can be found there, it's known as a co-citation.[21] Figure 4B displayed the network map centered on author Pittenger MF of the co-cited writers, showing that he had the highest number of collaborative relationships with other authors due to obviously more lines.

3.4 | Journals and co-cited academic journals analysis

The learned periodicals were concerned to be published in the research area of stem cell and wound healing added up to 2617, along with 33 346 co-cited journals. Table 3 showed that the 10 most potential journals by publication volume and the 10 most co-cited journals,

TABLE 2 The top 10 academic authors and co-cited authors involved in stem cell and wound.

Rank	Authors	Counts	Citations	Co-cited authors	Citations
1	Fu X	96	3219	Pittenger MF	1057
2	Longaker MT	69	7703	Zhang Y	1012
3	Gurtner GC	50	7629	Li Y	996
4	Fuchs E	43	8344	Zuk Pa	983
5	Dai J	37	1680	Caplan AI	947
6	Zhang W	37	926	Blanpain C	942
7	Li Y	37	1224	Wang Y	941
8	Wang Y	34	1064	Ito M	934
9	Reis RI	34	1352	Dominici M	909
10	Liu Y	33	871	Wu Y	901
#10	Li W	33	751		

Note: #10: The equal rank of 10th.

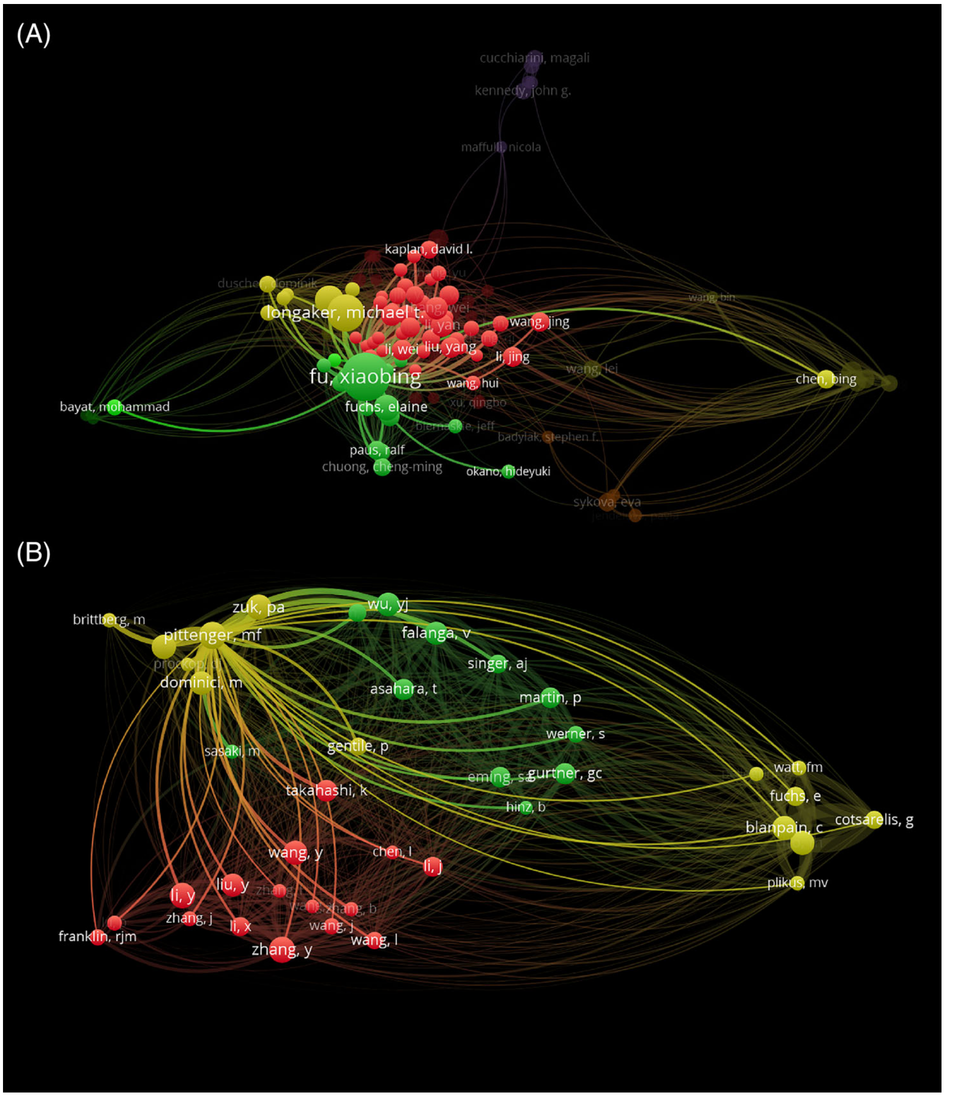

FIGURE 4 A network map showing authors centered on Author Fu X (A) and co-cited authors centered on Author Pittenger MF (B) publishing researches involved in stem cell and wound healing.

which suggested that *International Journal of Molecular Sciences* ($N = 418$) ranked first with the most publication volume. And the journal *Stem Cell Research & Therapy* ($N = 391$) ranked second, followed by *PLoS One* ($N = 382$) and *Scientific Reports* ($N = 271$). However, the H-index for *Biomaterials* was highest. In the co-cited journals, *Biomaterials* ($N = 25\,793$) ranked first, which was followed by *Proceedings of the National Academy of Sciences of the United States of America* ($N = 25\,392$) and *Nature* ($N = 24\,403$), whose citations all exceeded 20 000. And *Biomaterials* accounted for 14.03% of citations in the list, suggesting its high significance in this field and extensive links with other journals. The fact that all 10 of the most co-cited journals had citation counts of above 10 000 was remarkable, illustrating that the mutual cooperation between journals in this field was quite active.

Meanwhile, in terms of dynamic sources (Figure 5A), the publication volume of each journal was relatively small in this field before 2007. However, *Biomaterials* and *PLoS One* had experienced an increase in publication volume since 2007. Since then, the publication volume of *PLoS One* has increased rapidly, and it would remain the most-published journal until 2023. The rest of the documents from other sources, such as *International Journal of Molecular Sciences*, *Stem Cell Research & Therapy* and *Scientific Reports* also showed a rise in the number of publications between 2011 and 2013. It was worth noting that *International Journal of Molecular Sciences* and *Stem Cell Research & Therapy* ranked first and second respectively in terms of publication volume in 2023. That's not the end result due to incomplete data in 2023. Bradford suggested that the first zone's citations will originate from a tiny core group of journals when all references on a given topic are evenly divided into three zones. The second and third zone needs more journals than the previous zone does in order to receive the same number of citations. There is a diminishing productivity phenomenon from the first zone to the third zone, which is known

TABLE 3 The top 10 academic journals and co-cited journals involved in stem cell and wound healing.

Rank	Journals	Counts	H-index	G-index	M-index	Co-cited journals	Citations	H-index	G-index	M-index
1	*International Journal of Molecular Sciences*	418	45	78	3.462	*Biomaterials*	25 793	80	139	3.478
2	*Stem Cell Research & Therapy*	391	54	83	3.857	*PNAS*	25 392	78	133	3.12
3	*PLoS One*	382	62	96	3.444	*Nature*	24 403	40	45	1.667
4	*Scientific Reports*	271	45	66	3.75	*Cell*	18 265	38	68	1.583
5	*Biomaterials*	226	80	139	3.478	*Science*	18 162	31	50	1.632
6	*Wound Repair and Regeneration*	179	49	85	1.96	*PLoS One*	17 302	62	96	3.444
7	*Journal of Investigative Dermatology*	164	48	84	1.92	*Stem Cells*	14 327	60	114	2.5
8	*Acta Biomaterialia*	161	55	92	3.667	*Journal of Biological Chemistry*	14 160	29	50	1.381
9	*Stem Cells*	161	60	114	2.5	*Journal of Investigative Dermatology*	13 764	48	84	1.92
10	*Stem Cells International*	152	32	50	2.286	*Journal of Neuroscience*	12 273	55	83	2.2

Abbreviation: PNAS, *Proceedings of the National Academy of Sciences of the United States of America.*

as Bradford's scattering law. It is possible to utilize it to locate the journals with the highest citations in a certain field or topic.[22] In Figure 5B, we used Bradford's law to assess almost 20 journals as the source clustering, such as *International Journal of Molecular Sciences*, *Stem Cell Research & Therapy* and *PLoS One*. Furthermore, *Stem Cell Research & Therapy, International Journal of Molecular Sciences*, and *PLoS One* had more publication volume owing to larger nodes and were closely related to each other (Figure 5C). Additionally, the network map in Figure 5D suggested that *Biomaterials* had close associations with *Proceedings of the National Academy of Sciences of the United States of America*, *Nature*, *Science*, *PLoS One*.

A dual-map overlay was used to display the thematic distribution of journals in Figure 6. The links between the two sides were on behalf of the citation route, and the left part represented citing journals and the right part represented cited journals. Colours, such as green, orange, and purple trails, denoted citation linkages from left to right, while various clusters represented various regions. Two of the key citation pathways were orange, while one was green. The primary citation cluster was made up of articles from the Molecular/Biology/Immunology journals, and the primary co-cited cluster was made up of papers from the Health/Nursing/Medicine journals and the Molecular/Biology/Genetics journals according to the orange paths. The green line reflected that researches published in Molecular/Biology/Genetics journals was frequently co-cited by studies published in Medicine/Medical/Clinical journals.

3.5 | Analysis of keywords and thematic map

The top 100 most popular keywords were used to create a word cloud (Figure 7A), in which the phrase size denoted its occurrence frequency and the phrase colour represented the period of bursts. There were accumulatively most used 30 keywords demonstrating with research tree map in Figure 7B, among which stem cells (10%) ranked first, followed by expression (7%) and differentiation (7%). The collaborative relationship between keywords was depicted in Figure 7C. Due to their increased frequency, stem cells, expression, and differentiation had significantly larger nodes than others, which is consistent with the data shown above. Figure 7D was the thematic map analysis of the four identified clusters. It suggested that expression, proliferation and skin were more significant and promising keywords. Stem cells, expression and in-vitro were more important but not fully developed

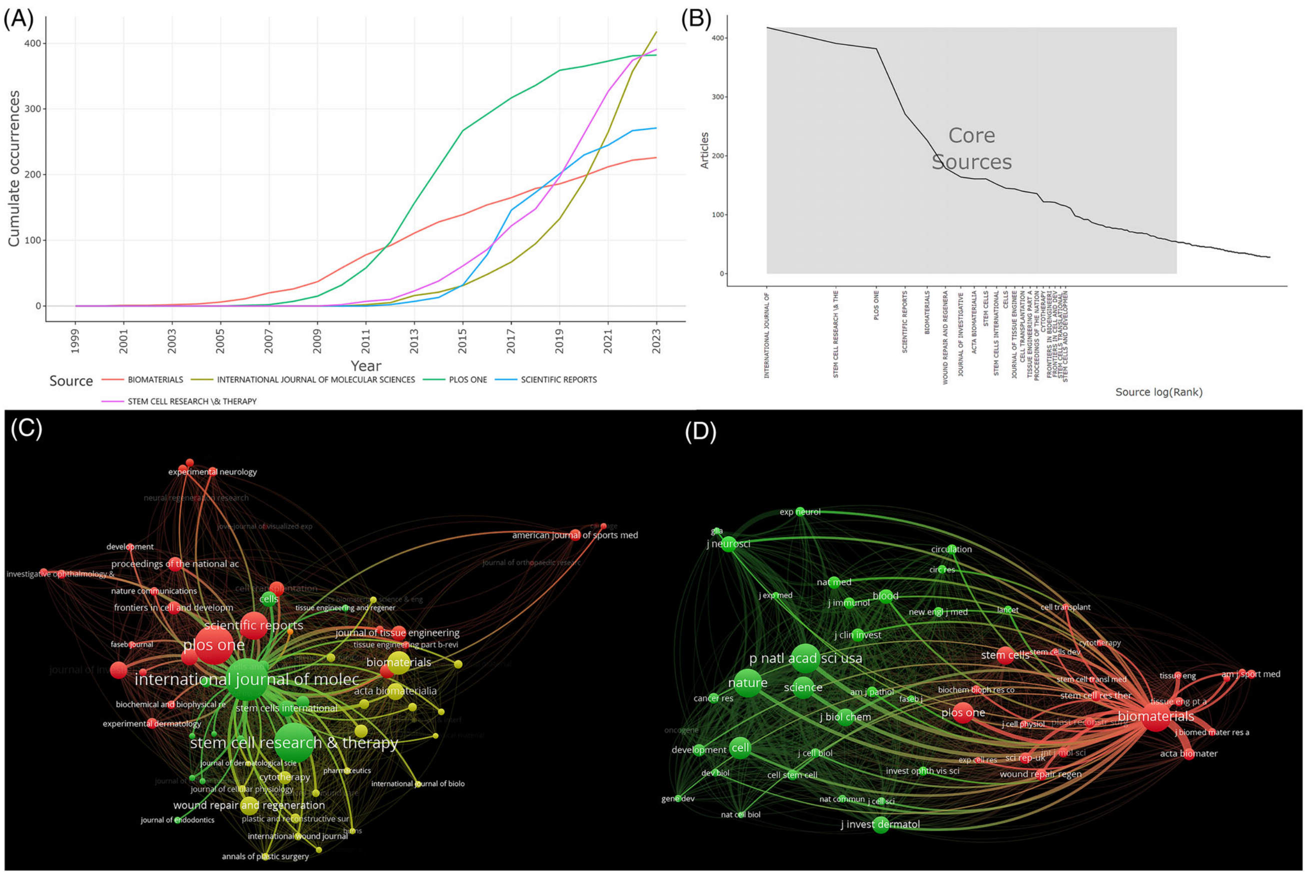

FIGURE 5 Analysis of journals and co-cited journals involved in stem cell and wound healing. (A) The dynamic analysis of the top 5 most prolific journals. (B) Core source clustering through Bradford's law. (C, D) A network map showing journals centered on *International Journal of Molecular Sciences* ($T \geq 50$, $N = 70$) and co-cited journals centered on *Biomaterials* ($T \geq 4000$, $N = 53$) publishing researches involved in stem cell and wound healing.

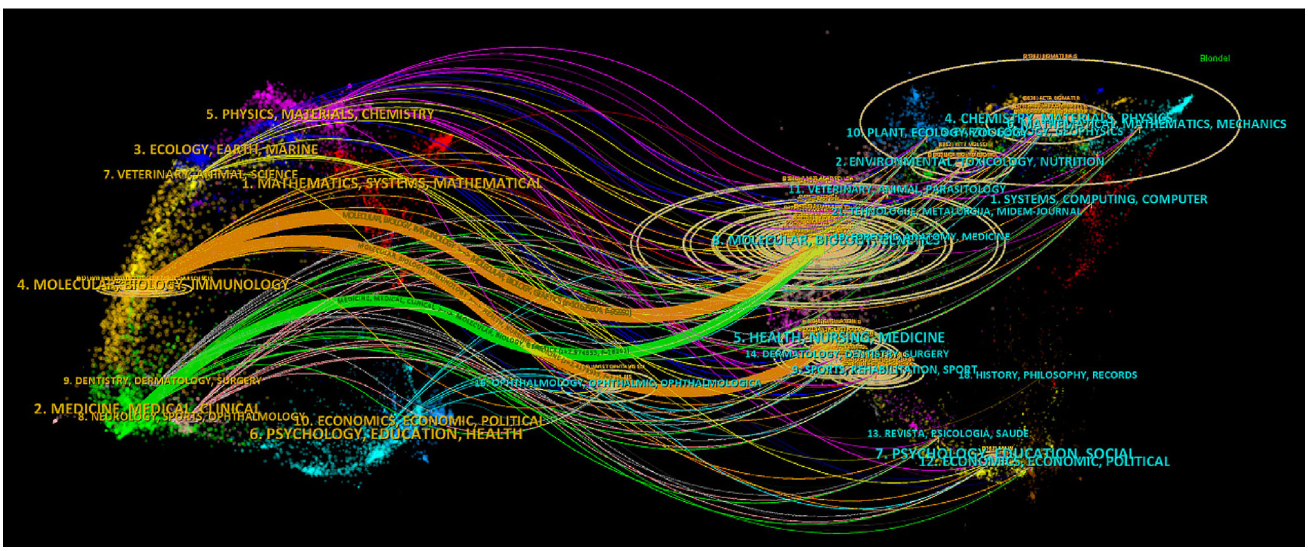

FIGURE 6 The dual-map overlay of journals related to stem cell and wound healing.

keywords. Articular cartilage defects and knee were marginal keywords due to their low density and centrality. Central nervous system, functional recovery and neural stem cell had well developed but not important, which may be related to the high professionalism of these keywords.

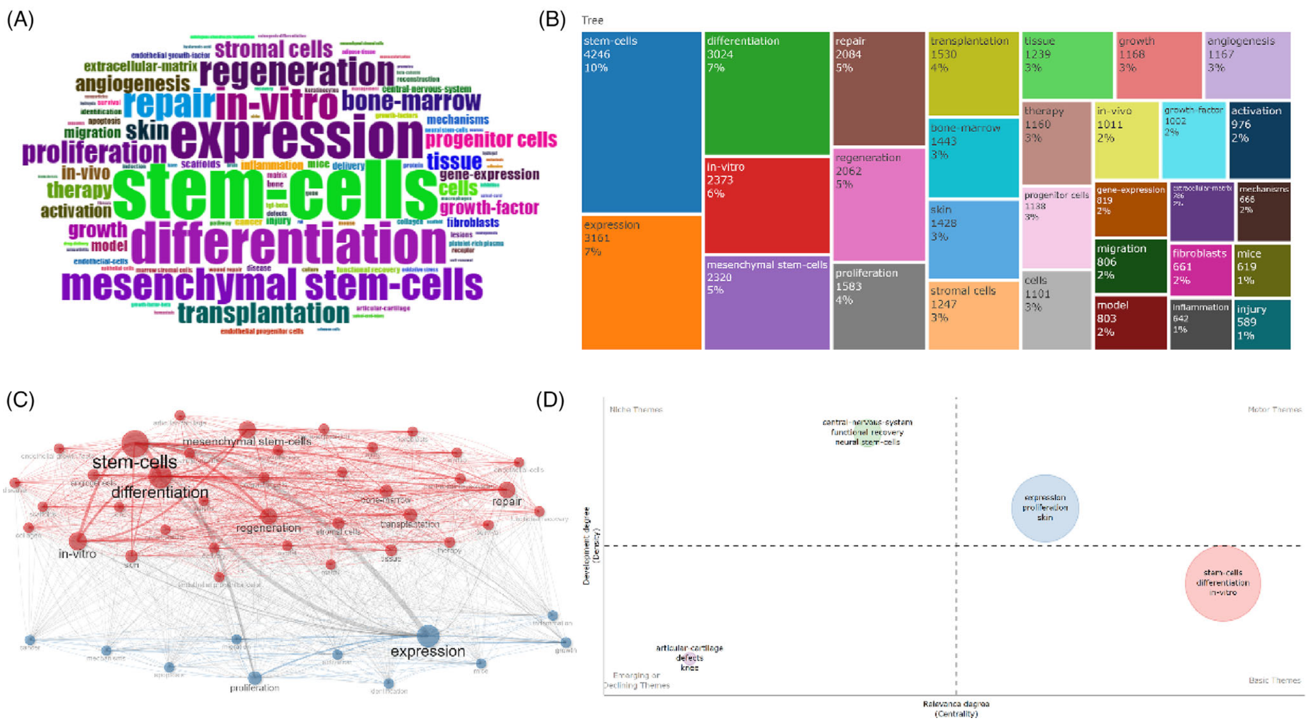

FIGURE 7 Analysis of keywords and thematic map involved in stem cell and wound healing. (A) The visualization keywords cloud ($N = 100$). (B) The proportional tree map of different keywords ($N = 30$). (C) The cooperative relationship of keywords ($N = 48$) in terms of publications. (D) Thematic map analysis of the four identified clusters.

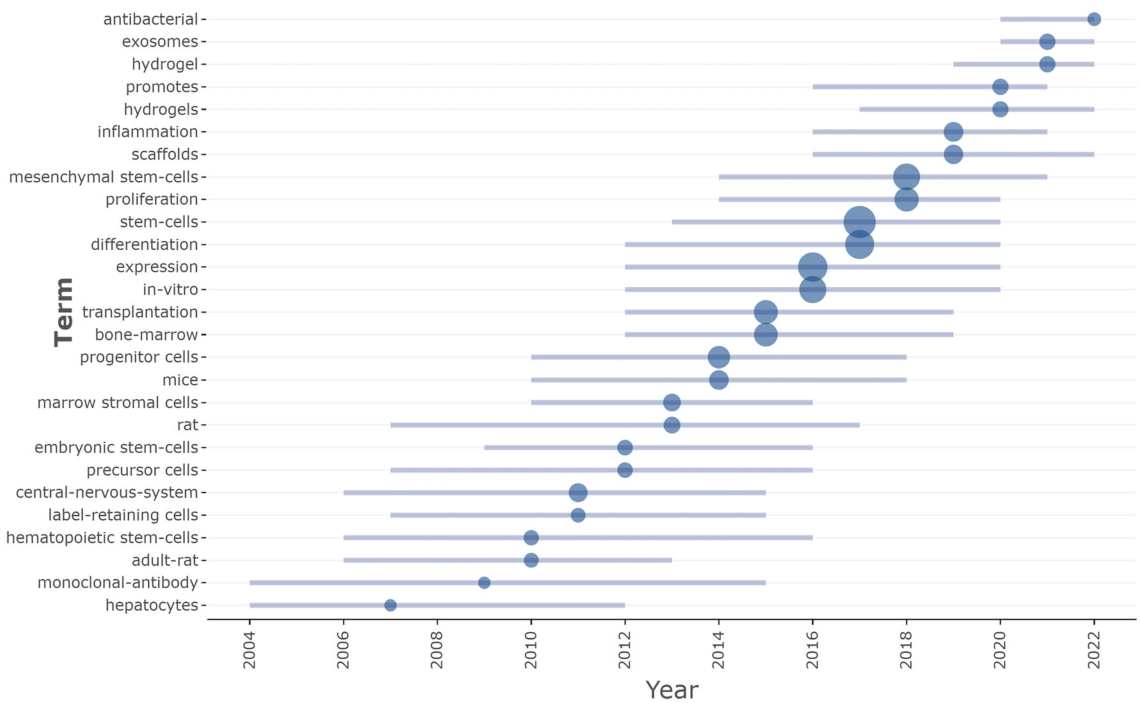

FIGURE 8 The analysis of keywords frequency and term bursts for topics that are trending.

The frequency and amplitude of keywords used in stem cell and wound healing studies were shown in Figure 8. Due to larger nodes, the following keywords had demonstrated relative consistency and high incidence during the last 20 years: stem cells, differentiation, expression, in-vitro, mesenchymal stem cell, and so forth,

TABLE 4 The top 10 references in terms of local citation about stem cell and wound healing.

Rank	Type	Document	LC	GC	LC/GC ratio (%)	NLC	NGC
1	Review	GURTNER GC, 2008, NATURE, DOI: 10.1038/nature07039	744	3892	19.12	83.55	37.07
2	Article	ITO M, 2005, NAT MED, DOI: 10.1038/nm1328	446	970	45.98	55.15	10.23
3	Article	SASAKI M, 2008, J IMMUNOL, DOI: 10.4049/jimmunol.180.4.2581	378	728	51.92	42.45	6.93
4	Article	KIM WS, 2007, J DERMATOL SCI, DOI: 10.1016/j.jdermsci.2007.05.018	367	639	57.43	32.99	6.21
5	Review	EMING SA, 2014, SCI TRANSL MED, DOI: 10.1126/scitranslmed.3009337	319	1638	19.47	66.22	30.63
6	Article	FALANGA V, 2007, TISSUE ENG, DOI: 10.1089/10.2006.0278	309	542	57.01	27.78	5.26
7	Article	ITO M, 2007, NATURE, DOI: 10.1038/nature05766	290	732	39.62	26.07	7.11
8	Article	BLANPAIN C, 2004, CELL, DOI: 10.1016/j.cell.2004.08.012	283	1052	26.90	29.56	9.78
9	Review	GUO S, 2010, J DENT RES, DOI: 10.1177/0022034509359125	266	2668	9.97	41.19	36.12
10	Article	FATHKE C, 2004, STEM CELLS, DOI: 10.1634/stemcells.22-5-812	222	374	59.36	23.19	3.48

Abbreviations: GC, global citations; LC, local citations; NGC, normalized global citations; NLC, normalized local citations.

with a concentration between 2012 and 2020. The results suggested that these research aspects had been continuously researched and given ongoing consideration in relation to stem cells and healing wounds. In addition, we also found some emerging topics in recent years, such as antibacterial, exosomes and hydrogel, and so forth.

3.6 | Analysis of references and co-cited references

The times that a publication is referenced by other publications in a specific region or nation is referred to as its local citation, whereas the times that a publication is referenced by other publications around the globe is referred to as its global citation.[23,24] A publication's impact and importance within its local domain can be evaluated using the ratio of local to global citations (LC/GC). The top 10 papers that had acquired considerable local citations were shown in Table 4 in this context. For example, Gurtner's review titled ‘Wound repair and regeneration’ published in *Nature* had the highest local citation count ($N = 744$).[25] The remaining nine references, with the number of local citations ranging from 222 to 446, would be deeply analysed in the discussion section. Furthermore, Carrie Fathke's research titled ‘Contribution of bone marrow-derived cells to skin: collagen deposition and wound repair’ published in *Stem Cells* had the highest LC/GC Ratio (59.36%),[26] which meant that the publication had a high influence in its local domain.

Citation bursts of references is a term that refers to researches within a given field which were received a lot many citations at any given time. It provides the exploration process and forecasts future study areas.[27] From 2004 to 2023, citation bursts occurred every year in Figure 9A with top 20 references with the strongest citation bursts. Among them, 25% (5/20) of the references had a value of strength of more than 12. Notably, the strongest burst (strength = 22.61) was the article ‘Regeneration of ischemic cardiac muscle and vascular endothelium by adult stem cells’ by Jackson,[28] bursting from 2004 to 2023. The following four references have their respective bursting years in 2012, 2012, 2017, and 2018. Overall, the top 20 references had a strength between 3.37 and 22.61 and a period between 4 and 19 years. The network map of entire references ($N = 50$) related to stem cells and wound healing was shown in Figure 9B. The three coloured nodes represent clusters of references on different topics. ‘Multilineage potential of adult human mesenchymal stem cells’ by Pittenger et al. in 1999[29] was the more important reference due to its larger node. Gurtner et al.'s review ‘Wound repair and regeneration’ in 2008[25] and Singer et al.'s review ‘Cutaneous wound healing’ in 1999[30] were notable references in red clustering, suggesting that this class of references mainly focused on the theme of wound healing.

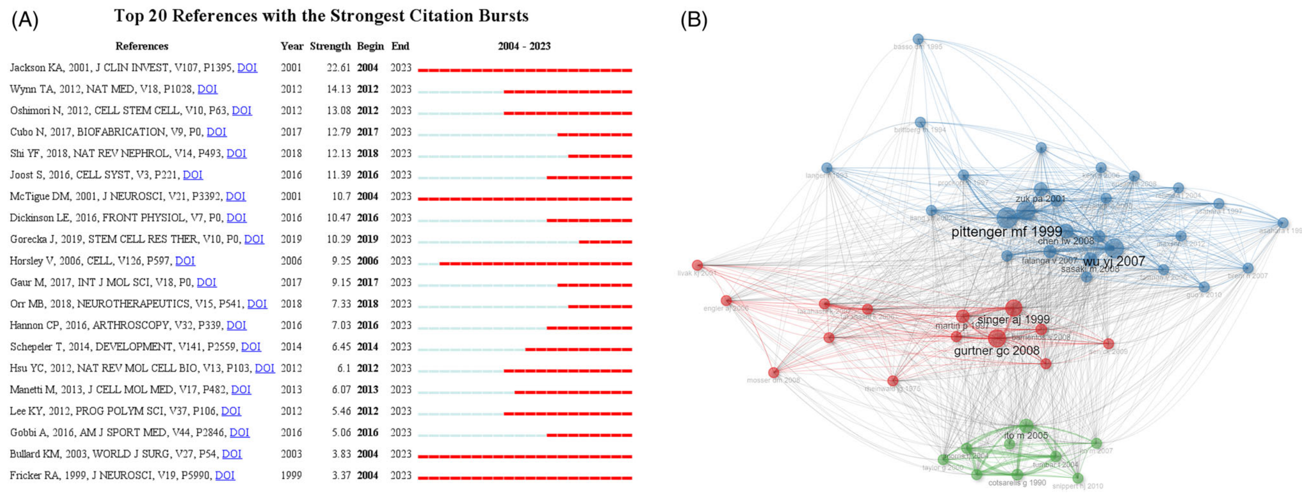

FIGURE 9 (A) Top 20 references with strong citation burstiness. The red bars mean some references cited frequently; the blue bars were references cited infrequently. (B) The network map of all references ($N = 50$) involved in stem cell and wound healing.

These representative references also showed a close co-occurrence relationship with each other and with other references.

3.7 | Factorial analysis

We further analysed the keywords using multiple correspondence analysis (MCA). MCA created two-dimensional diagrams by simplifying multidimensional data into low-dimensional forms and measuring keyword similarity using plane distance. When a keyword is close to the center, it indicates that the keyword is having more attention, and if it is further away from the center, it indicates less interest in the subject.[31] The best dimension reduction in MCA's first dimension and second dimension was shown in Figure 10A. Endothelial, growth factor, regeneration, stem cells, differentiation were terms with closer distance from central dots, which were all associated with the process by which stem cells functioned. Meanwhile, we performed hierarchical clustering dendrogram of the top 50 entries with high correlation (Figure 10B). The terms with the highest degree of correlation were much closer in hierarchical clustering dendrogram. Up to 10 levels could be calculated at most. The intricate hierarchical relationships suggested the fusion of disciplines and the heat of research in the field of competence. And at the lowest level of keywords, these classes were not mutually exclusive and there were overlaps between different items. With all top 50 entries roughly clustered into four categories based on term frequency and relevance, readers could have a quick and overview understanding of the distribution of hot research topics in this field.

4 | DISCUSSION

According to our bibliometric examination of research data from the WoSCC in the SCI-Expanded database from 1999 to 2023, 13 225 institutions from 119 different countries and regions produced overall 19 728 English research papers in 2617 scholarly publications. 1503 references were cited in total by these publications. These studies discussed the state of the subject at the moment, emerging trends, and hot topic of the future.

4.1 | General information

To our knowledge, this work was the first to perform a thorough bibliometric analysis of articles published between 1999 and 2023 that were related to stem cell and wound healing. The results we obtained indicated an upward trend in the annual publications in this area. The maximum annual publications happened in 2022, making it an important year in this area. The decrease in annual publications in 2023 might be due to that relatively close to the time of data collection and the data was incomplete.

We analysed the most prominent countries, institutions, authors and journals in the field. The country with the most publications were the United States, followed by China. Although the United States historically had the most publications, China had recently caught up to the United States in the aspect of publication volume. China was the only developing nation among the top 10, which indicated that there was a distinction between developed and developing nations in this area of study. Shanghai Jiao Tong University was the most contributive

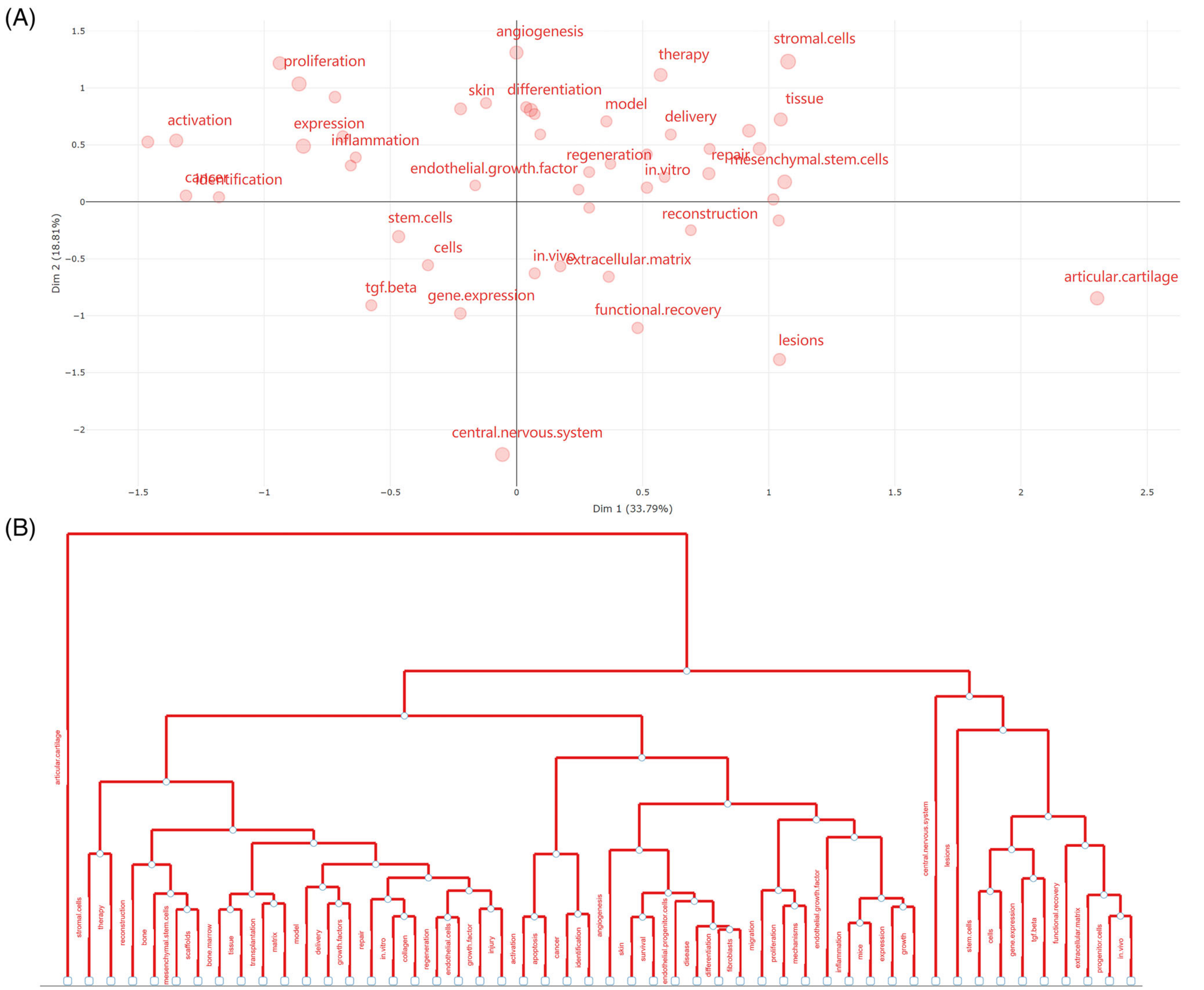

FIGURE 10 (A) Factorial map of different components of stem cell and wound healing. (B) Hierarchical clustering dendrogram of the top 50 entries with correlation.

institutions in the field, followed by Sun Yat-sen University and University of Pittsburgh. The majority of the top 10 leading institutions were from China and the United States, demonstrating the importance of these two countries in the stem cell and wound healing sector. Besides, active collaborations between different institutions could also be observed. Shanghai Jiao Tong University, Stanford University, and Harvard University collaborated with others actively. *International Journal of Molecular Sciences* and *Biomaterials* were considered the most influential journals with the most publications, and most citations and the highest H-index respectively, showing their significant academic influence. The dual-map overlay reflected that studies from Molecular/Biology/Genetics and Health/Nursing/Medicine co-cited journals were mainly cited by journals published in Molecular/Biology/Immunology and Medicine/Medical/Clinical, which implied that there were two major lines of inquiry into stem cell and wound healing, one of which concentrated on the basic research. The concentration in another direction was on basic to clinical translational research. In terms of publication production, Fu X stood out among the authors, and Pittenger MF took the top spot in co-citations, underscoring their enormous effect in the area of stem cell and wound healing. These active authors and co-authors showed sustained and fruitful cooperative relationships on the visualization map.

4.2 | Knowledge base

Local citation is frequently assessed by combining the references that cite it in order to ascertain the frequency of citations within the research topic.[32] These citing references show how frequently the pertinent research has been cited in other scholarly works. Core literature and significant research accomplishments on the topic are represented by the collection of highly cited local citation literature. As a result, local citation might be seen as a sign of a field's knowledge base. By assessing the research domain and choosing the top 10 commonly local cited references, we created a knowledge base for the research on 'stem cell and wound healing' in this study.

In 2009, the most widely cited paper was published by Gurtner et al.[25] In this review, they gave an overview of multicellular creatures' responses to tissue loss and highlighted areas where tissue regeneration had been promoted through developmental pathways. They reviewed classic clinical burden of fibrosis, wound repair across phylogeny, stages of wound repair, molecular mechanisms of wound repair, and epithelial stem-cell biology. Combining biomimetic scaffolds with electrical or mechanical environment modification (such as negative pressure wound treatment to speed healing), gene therapy and other approaches as 'soil', combined with stem cell therapy as 'seed', would improve human wound healing. In 2005, the document published by Ito et al.[33] showed that the hair follicle bulge's stem cells weren't vital for the epidermis survival and weren't often responsible for supplying epidermis with cells, but they were crucial for the process of healing a wound. The bulge cells were deployed in response to injury, leaving the stem cell niche promoting the regrowth of the epidermis. In 2008, Sasaki et al.[34] found that certain circumstances were necessary for MSC to successfully differentiate into keratinocytes in vitro. Additionally, they examined whether MSC moved and became engrafted into injured skin to improve wound healing by injecting MSC intravenously into injured mice. They explored the process of MSC recruitment and discovered that these cells had several chemokine receptors, particularly CCR7, a receptor for SLC/CCL21, which promoted migration of MSC. It was discovered that the MSC that were injected helped with wound healing by accumulating at the wound site. In 2007, Kim et al.[35] researched that adipose-derived stem cells (ADSCs) may play important roles in the healing of skin wounds, particularly in terms of fibroblast activation, proliferation, collagen production, and migratory capabilities. They discovered that ADSCs supported human dermal fibroblast (HDF) proliferation not only through direct contact between cells but also through paracrine activation. The migration of HDFs was stimulated by the conditioned media of ADSCs in in vitro wound healing models. In addition to in vitro evidence, in vivo animal studies had also confirmed the wound-healing effects of ADSCs. In 2014, Eming et al.[36] reviewed clinical needs of chronic wounds and scars, wound healing pathology, current treatment methods and limitations, and summarized the clinical methods based on repair mechanism. They proposed several emerging focus areas in wound healing, such as microbiome, aging, and personalized medicine approaches. And they pointed out that aging or underlying diseases, such as diabetes, could cause changes in the skin microbiome, but the mechanisms of how exactly these changes affected wound healing were unclear. The search for an objective biomarker or biological process that could distinguish normal tissue from diseased tissue (such as non-healing wounds or scar tissue) may be an emerging research direction for wound healing. In 2007, the successful application of topically administered autologous MSC to promote the healing of human and experimental murine wounds was studied by Falanga et al.[37] They researched that Autologous bone marrow-derived MSC could be safely and successfully delivered to wounds utilizing a fibrin spray system, according to their analysis of the fibrin delivery method, successfully accelerating wound healing in humans and experimental mice. In a study by Ito et al.,[38] it was demonstrated that adult mice with normal genetic could form new hair follicles after wounding. The Ctnnb1 gene was eliminated in these mice's epidermis after the utilization of tamoxifen. As a result, the growth of new hair follicles was completely inhibited, demonstrating that Wnt signalling in epidermal keratinocytes was necessary for hair follicle regeneration. They showed that a wound stimulus was sufficient to cause the regeneration of hair follicles from epithelial cells that did not typically generate hair. It was possible to manipulate the amount of hair follicles that form by exposing animals to Wnts through this de novo generation of hair follicles, which at the molecular level recapitulated embryogenesis in adult animals. This suggested the possibility of rebuilding hair follicles through wounding and Wnt pathway activation to treat hair loss, as well as treating acute wounds with modulators of the Wnt pathway to reduce scar formation. In 2004, Blanpain et al.[39] reported novel techniques that allowed for their clonal assessments and engraftment and showed the two characteristics that made up stem cells. In 2010, Guo et al.[40] discussed a number of factors that affected cutaneous wound healing as well as the possible molecular and cellular mechanisms at function. Local factors and systemic factors were the key elements that influence wound healing. The former included oxygenation, infection, foreign body, and venous sufficiency. However, the latter mainly included age and gender, sex hormones, ischemia, diseases (for example, diabetes, keloids, fibrosis, hereditary healing disorders, jaundice, uremia), medications (such as glucocorticoid steroids, non-steroidal anti-inflammatory drugs, chemotherapy), and so on. In 2004, Fathke et al.[26] demonstrated that for the regeneration of the epidermis, local cutaneous cells were necessary, but for the dermal fibroblast population, distant bone marrow-derived cells and the nearby undamaged dermal mesenchymal cells were also required.

Overall, the mechanism by which stem cells promoted wound healing was a common theme within the top 10 local cited references, which was consistent with the findings of a keyword analysis.

4.3 | Research hotspots

Based on the top 20 references with the strongest citation bursts, there were four references from 2004 to 2023 with the whole long-term citation bursts, revealing the research hotspots during the past and future timespan. Firstly, Fricker et al.[41] pointed out the potential pro-generative activity of progenitor cells relying on epidermal growth factor, basic fibroblast growth factor and leukaemia inhibitory growth factor, further providing a powerful and virtually unlimited source of cells for experimental and clinical transplantation. Subsequently, in 2001, Jackson et al.[28] showed the migration, differentiation, promoting tissue regeneration of haematopoietic stem cells and McTigue et al.[42] reported NG2-positive cells, a cell population involved in oligodendrocyte replacement to achieve tissue recovery, both of which explored the regeneration improvements efficiency from stem cell to promisingly offer new therapeutic avenues. Lastly, Bullard et al.[43] displayed the current biology of fetal wound healing on inflammatory, biological proteins, cell factors, enzymes and gene expressions. The aforementioned four long-term citations burst references represented the advancements and hotspots in the past years from different biology level, supplying the investigation foundations for future researches.

To understand the research trend of the topic 'stem cell and wound healing' more accurately, we investigated the trend topic of keywords over time. According to the keywords analysis, stem cell behaviour-related terms like expression, differentiation, proliferation, and so forth were used most frequently, indicating that these subfields were the most extensively researched area. Stem cells, expression, differentiation, in-vitro, and mesenchymal stem cell were also keywords with higher frequency and more extensive cooperation in the visual network diagram of keywords, suggesting the primary issue of this research field. In addition, there were some keywords that burst in recent years, which were worth noting, such as antibacterial.

Researches based on stem cells had given hopes of treating chronic non-healing wounds. However, the tumorigenicity of embryonic stem cells and iPSCs in vivo[44,45] as well as, most crucially, ethical issues[46] had restricted their usage in clinic. Therefore, we focused primarily on MSC since they were easily separated, significantly capable of self-renewal, and significantly differentiable. MSC had the pluripotent capacity to differentiate into both mesodermal and non-mesodermal cell lineages, which were known as a class of heterogeneous stem/progenitor cells, including bone cells, fat cells, chondrocytes, muscle cells, cardiomyocytes, fibroblasts, myofibroblasts, epithelial cells, and neurons.[47] MSC were found primarily in bone marrow, but had been proven to exist in many other tissues (Figure 11A), including the adipose (ADSCs), dental pulp (DPSCs), umbilical cord (UCMSCs), periodontal ligament (PDLSCs), tendon (TSPCs), and the exfoliated deciduous teeth (SHED).[48,49] One of the unique features of MSC was their ability to multidifferentiate in culture. Based on this, MSC had garnered a lot of interest in the area of regenerative medicine,[50] which had shown promising outcomes in the repair of injured tissue in recent years.[51,52] The direction of MSC differentiation was largely affected by the culture conditions in vitro, including biological signals and chemical signals, such as TGF-β, IGF-1, bFGF, Dexamethasone + isobutyl methyl xanthine + indomethacin, and so forth.[47] Additionally, researches had revealed that mechanical stimulation in vitro could also affect the differentiation of MSC. Sarraf et al.[53] found that after exposure to cyclical external stress, cloned MSC could differentiate into myo- and fibroblast-like cells. The tissue engineering of unique synthetic live tissue for transplantation in regenerative medicine might benefit from the application of this research. In fact, although a number of previous researches demonstrated the multilineage differentiation ability of MSC and some knowledge had been accumulated, little was known about the specific mechanism of their differentiation, resulting in this hotspot aspect. Interestingly, according to a growing body of researches, the therapeutic effects of MSC were more attributed to the modification of the host microenvironment, and that in addition to differentiation, the immune system's regulation (see below), the release of substances promoting tissue repair (such as pro-angiogenic factors), the attraction of endogenous MSC and the function of extracellular vesicles were some of the processes by which MSC affected the host.[54] These aspects were also the direction of future research.

MSC had been proven in numerous earlier studies to accelerate the healing of skin wounds (Figure 11B). For example, MSC cultured with collagen could speed up the wound healing of mice and promoted the repair of skin

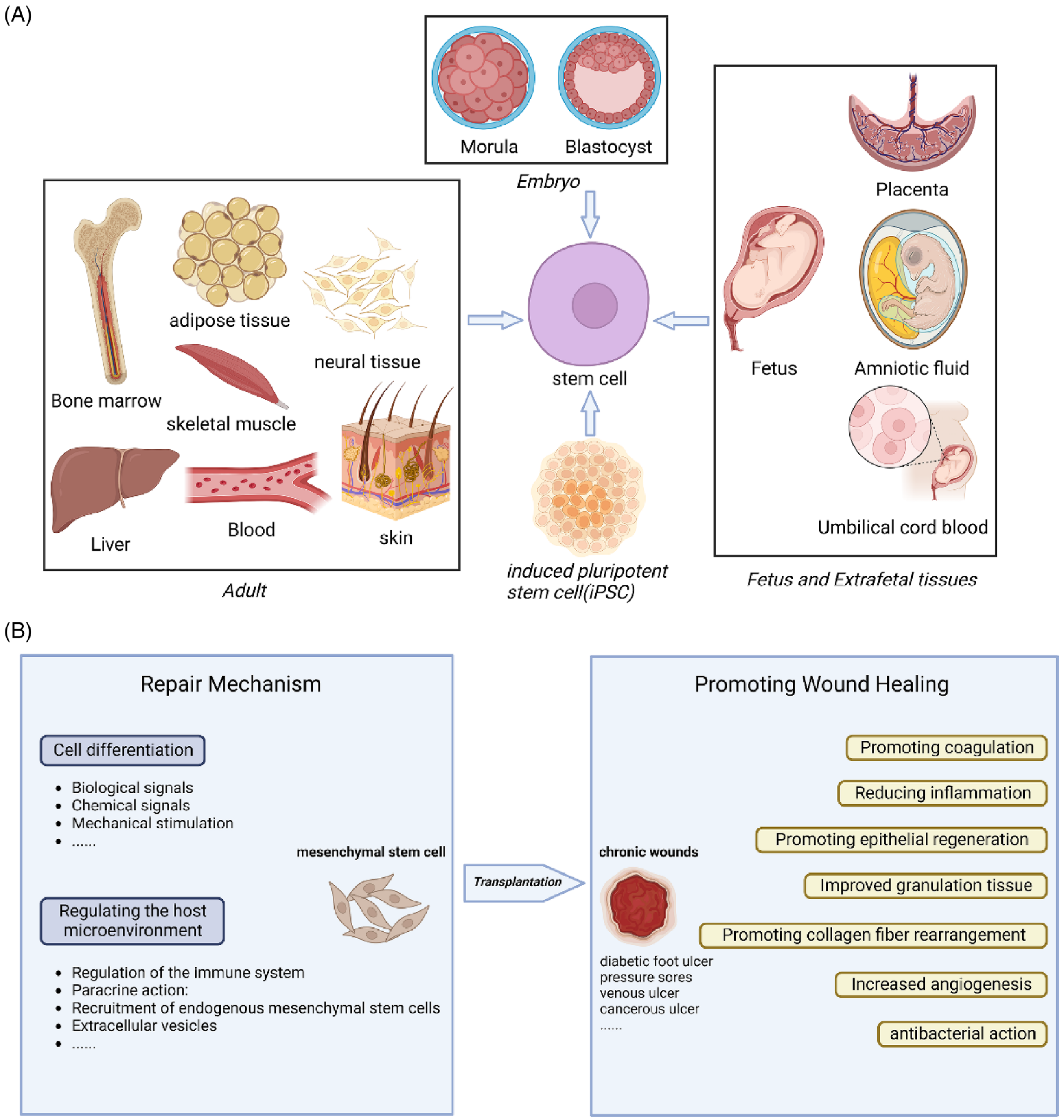

FIGURE 11 (A) The main source of stem cells for regenerative medicine. (B) Summary of mechanism of mesenchymal stem cells promoting wound healing.

injury, showing its effect in animal models.[55] Besides, A clinical trial of allogeneic ADSC-hydrogel complex for treating diabetic foot ulcers showed that it could promote the diabetic ulcer healing and significantly shorten healing time in the human body.[56] Currently, there is concern that MSC stimulated wound healing by two mechanisms: differentiating directly into resident cells and paracrine substances.[57] MSC had been linked to various stages of wound healing, according to studies. In the coagulation stage, MSC could promote coagulation by releasing tissue factor (TF). However, MSC also expressed phosphatidylserine, which, when moving from the cytoplasm to the cell surface, could activate thrombin-activating complex and blood coagulation. MSC could directly encourage the creation and activation of platelets, contributing to blood coagulation in this way. In addition, MSC may release some soluble factors affecting coagulation, and they also secreted extracellular vesicles inducing clotting through both intrinsic and extrinsic pathways of coagulation.[58,59] Overall, MSC could promote coagulation, which had a positive role in wound healing, but the potential thrombotic reactions should also be recognized. In the inflammatory phase, accumulation of local inflammatory factors occurred due to injury, which prevented wound healing. MSC regulated multiple immune cells through the immunomodulators they expressed. Liu et al. demonstrated that MSC-derived exosomes stimulated by melatonin could polarize macrophages from M1 phenotype to M2 phenotype, and the former was a pro-inflammatory phenotype while the latter had an anti-inflammatory effect. The transition of macrophage activation from the M1 phenotype to the M2 phenotype was a key step in wound healing and inflammation control, which might facilitate diabetic wound healing.[60] In fact, when the immune system was underactive, MSC could exacerbate inflammation, whereas they could also reduce inflammation when the immune system was overactive, which was called 'sensor and switcher of the immune system'.[61] In the proliferative phase, where wound filling and epithelial regeneration were the main goals, treatment with MSC could improve fibroblast survival and migration as well as extracellular matrix deposition, which would improve the healing effect.[62] Extracellular vesicles from MSC had helped a rat skin burn model's cutaneous wound healing by promoting the proliferation of epithelial cells. In contrast to collagen III, MSC improved the expression of CK19, PCNA, and collagen I in vivo.[63] At this stage, wound was mainly filled with granulation tissue. MSC promoted granulation tissue formation by improving fibroblast proliferation and myofibroblast activation, regulating inflammation response, and clearing infection.[15] In the maturation stage, the main goal of this stage was the normal arrangement of collagen fibres and functional angiogenesis. MSC could prevent scarring, by releasing numerous growth factors and cytokines with anti-fibrotic effects, such as adrenomedullin, hepatocyte growth factor (HGF), and IL-10.[64] There had also been evidence that exosomes of human placenta-derived MSC promote angiogenesis.[65] Numerous angiogenic factors were secreted by MSC, and at the same time MSC could promote endothelial cell proliferation, migration and protect endothelial cells from apoptosis,[54] so they had a significant ability to promote angiogenesis, all these were conducive to satisfactory wound healing. Data from a study of rat ADSCs implanted into rat wounds suggested that the MSC could not only differentiate directly into vascular endothelial cells but also secrete pro-angiogenic substances.[66] Continued research in these areas could enhance our identification of the mechanisms by which MSC promoted wound healing and facilitated the development of more effective treatment strategies. Furthermore, antibacterial has been a newly emerging keyword in recent years. Therefore, we paid attention to the antibacterial effect of stem cells. Earlier studies showed that MSC had obvious antibacterial effects, researchers found that human adipose-derived MSC could significantly inhibit the growth of *Staphylococcus aureus* in vitro, and 1, 25-dihydroxy vitamin D3 could increase the expression of LL-37 in MSC and enhance their antibacterial activity.[67] It was found that the antibacterial effect of MSC was mainly achieved by direct and indirect mechanisms. The direct mechanism mainly referred to the secretion of antimicrobial peptides (AMPs, which were a type of small peptides with an average length of 12 to 50 amino acids that had the ability to have an antibacterial, antibiofilm, and anti-inflammatory action through a number of different mechanisms[68]), mainly containing LL-37, β-defensin-2, hepcidin,[69] and other molecules by MSC, while the MSC regulation of the immune system was the indirect mechanism, such as increasing immune cell activation.[70] In the future, in-depth research on the antibacterial mechanism of stem cells and clinical trials in humans may be a research hotspot.

4.4 | Limitations

Using bibliometrics and visual analysis, this research investigates the hotspots and trends in the field of stem cell and wound healing. However, there are still certain limitations, though. First of all, it is difficult to find bibliometric tools and techniques that combine two databases for study. As a result, some study findings in other databases may be missed because our data is exclusively gathered from the WOS database and only includes English-language publications and reviews. Second, because of poor citation rates, some promising high-quality papers can go unnoticed. These articles could be more useful than ones with lots of citations. Finally, understanding future research trends may deviate or include subjective judgements due to the complexity and ambiguity of future events. This research offers a theoretical foundation for potential future research directions while reflecting current developments in the stem cell and wound healing fields.

5 | CONCLUSION

We conducted a thorough analysis of the general information, knowledge base and research hotspots in the field of stem cells and wound healing from 1999 to 2023 by using the VOSviewer, CiteSpace, and other bibliometric analysis tools. Notably, the United States had become one of the leading nations in this area. However, Shanghai Jiao Tong University was the most influential institution. Fu X and Pittenger MF were the two most-published and cited authors, respectively. *International Journal of Molecular Sciences* and *Biomaterials* were more valuable journals. At the same time, we built a knowledge base based on local cited references. Differentiation, expression, in-vitro, mesenchymal stem cell, and antibacterial were keywords worth noting. It was of great significance to further study the specific mechanism of stem cells promoting wound healing. In conclusion, this study provided insights into the results and trends in the field of stem cell and wound healing.

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CONFLICT OF INTEREST STATEMENT

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available in the supplementary material of this article.

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REFERENCES

1. Zakrzewski W, Dobrzyński M, Szymonowicz M, Rybak Z. Stem cells: past, present, and future. *Stem Cell Res Ther*. 2019;10(1):68.
2. Kolios G, Moodley Y. Introduction to stem cells and regenerative medicine. *Respiration*. 2013;85(1):3-10.
3. Rajabzadeh N, Fathi E, Farahzadi R. Stem cell-based regenerative medicine. *Stem Cell Investig*. 2019;6:19.
4. Hoang DM, Pham PT, Bach TQ, et al. Stem cell-based therapy for human diseases. *Signal Transduct Target Ther*. 2022;7(1):272.
5. Yamanaka S. Pluripotent stem cell-based cell therapy-promise and challenges. *Cell Stem Cell*. 2020;27(4):523-531.
6. Lindley LE, Stojadinovic O, Pastar I, Tomic-Canic M. Biology and biomarkers for wound healing. *Plast Reconstr Surg*. 2016;138(3 suppl):18s-28s.
7. Wilkinson HN, Hardman MJ. Wound healing: cellular mechanisms and pathological outcomes. *Open Biol*. 2020;10(9):200223.
8. Morton LM, Phillips TJ. Wound healing and treating wounds: differential diagnosis and evaluation of chronic wounds. *J Am Acad Dermatol*. 2016;74(4):589-605; quiz 605-6.
9. Martin P, Nunan R. Cellular and molecular mechanisms of repair in acute and chronic wound healing. *Br J Dermatol*. 2015;173(2):370-378.
10. Sen CK. Human wound and its burden: updated 2020 compendium of estimates. *Adv Wound Care (New Rochelle)*. 2021;10(5):281-292.
11. Oneto P, Etulain J. PRP in wound healing applications. *Platelets*. 2021;32(2):189-199.
12. Han G, Ceilley R. Chronic wound healing: a review of current management and treatments. *Adv Ther*. 2017;34(3):599-610.
13. Zubair M, Ahmad J. Role of growth factors and cytokines in diabetic foot ulcer healing: a detailed review. *Rev Endocr Metab Disord*. 2019;20(2):207-217.
14. Liang X, Lin F, Ding Y, et al. Conditioned medium from induced pluripotent stem cell-derived mesenchymal stem cells accelerates cutaneous wound healing through enhanced angiogenesis. *Stem Cell Res Ther*. 2021;12(1):295.
15. Jiang D, Scharffetter-Kochanek K. Mesenchymal stem cells adaptively respond to environmental cues thereby improving granulation tissue formation and wound healing. *Front Cell Dev Biol*. 2020;8:697.
16. Hassanshahi A, Hassanshahi M, Khabbazi S, et al. Adipose-derived stem cells for wound healing. *J Cell Physiol*. 2019;234(6):7903-7914.
17. Sun N, Ke L, Qing L, et al. The research landscape on vascularized composite allografts: a bibliometric analysis (2002-2021). *Am J Transl Res*. 2023;15(3):1569-1589.
18. Wondimagegn D, Whitehead CR, Cartmill C, et al. Faster, higher, stronger – together? A bibliometric analysis of author distribution in top medical education journals. *BMJ Glob Health*. 2023;8(6). doi:10.1136/bmjgh-2022-011656
19. Rawlings CM, McFarland DA. Influence flows in the academy: using affiliation networks to assess peer effects among researchers. *Soc Sci Res*. 2011;40(3):1001-1017.
20. Lee S, Bozeman B. The impact of research collaboration on scientific productivity. *Soc Stud Sci*. 2005;35(5):673-702.
21. Li M, Yuan Y, Zou T, Hou Z, Jin L, Wang B. Development trends of human organoid-based COVID-19 research based on bibliometric analysis. *Cell Prolif*. 2023;56:e13496.
22. Venable GT, Shepherd BA, Loftis CM, et al. Bradford's law: identification of the core journals for neurosurgery and its subspecialties. *J Neurosurg*. 2016;124(2):569-579.
23. Liu T, Yang L, Mao H, Ma F, Wang Y, Zhan Y. Knowledge domain and emerging trends in podocyte injury research from 1994 to 2021: a bibliometric and visualized analysis. *Front Pharmacol*. 2021;12:772386.
24. Hao X, Liu Y, Li X, Zheng J. Visualizing the history and perspectives of disaster medicine: a bibliometric analysis. *Disaster Med Public Health Prep*. 2019;13(5–6):966-973.
25. Gurtner GC, Werner S, Barrandon Y, Longaker MT. Wound repair and regeneration. *Nature*. 2008;453(7193):314-321.
26. Fathke C, Wilson L, Hutter J, et al. Contribution of bone marrow-derived cells to skin: collagen deposition and wound repair. *Stem Cells*. 2004;22(5):812-822.

27. Shen J, Shen H, Ke L, et al. Knowledge mapping of immunotherapy for hepatocellular carcinoma: a bibliometric study. *Front Immunol*. 2022;13:815575.
28. Jackson KA, Majka SM, Wang H, et al. Regeneration of ischemic cardiac muscle and vascular endothelium by adult stem cells. *J Clin Invest*. 2001;107(11):1395-1402.
29. Pittenger MF, Mackay AM, Beck SC, et al. Multilineage potential of adult human mesenchymal stem cells. *Science*. 1999;284(5411):143-147.
30. Singer AJ, Clark RA. Cutaneous wound healing. *N Engl J Med*. 1999;341(10):738-746.
31. Mostafa MM, Feizollah A, Anuar NB. Fifteen years of YouTube scholarly research: knowledge structure, collaborative networks, and trending topics. *Multimed Tools Appl*. 2023;82(8):12423-12443.
32. Xu Y, Gao Y, Jiang L, et al. Global trends in research on cervicogenic headache: a bibliometric analysis. *Front Neurol*. 2023;14:1169477.
33. Ito M, Liu Y, Yang Z, et al. Stem cells in the hair follicle bulge contribute to wound repair but not to homeostasis of the epidermis. *Nat Med*. 2005;11(12):1351-1354.
34. Sasaki M, Abe R, Fujita Y, Ando S, Inokuma D, Shimizu H. Mesenchymal stem cells are recruited into wounded skin and contribute to wound repair by transdifferentiation into multiple skin cell type. *J Immunol*. 2008;180(4):2581-2587.
35. Kim WS, Park BS, Sung JH, et al. Wound healing effect of adipose-derived stem cells: a critical role of secretory factors on human dermal fibroblasts. *J Dermatol Sci*. 2007;48(1):15-24.
36. Eming SA, Martin P, Tomic-Canic M. Wound repair and regeneration: mechanisms, signaling, and translation. *Sci Transl Med*. 2014;6(265):265sr6.
37. Falanga V, Iwamoto S, Chartier M, et al. Autologous bone marrow-derived cultured mesenchymal stem cells delivered in a fibrin spray accelerate healing in murine and human cutaneous wounds. *Tissue Eng*. 2007;13(6):1299-1312.
38. Ito M, Yang Z, Andl T, et al. Wnt-dependent de novo hair follicle regeneration in adult mouse skin after wounding. *Nature*. 2007;447(7142):316-320.
39. Blanpain C, Lowry WE, Geoghegan A, Polak L, Fuchs E. Self-renewal, multipotency, and the existence of two cell populations within an epithelial stem cell niche. *Cell*. 2004;118(5):635-648.
40. Guo S, Dipietro LA. Factors affecting wound healing. *J Dent Res*. 2010;89(3):219-229.
41. Fricker RA, Carpenter MK, Winkler C, Greco C, Gates MA, Björklund A. Site-specific migration and neuronal differentiation of human neural progenitor cells after transplantation in the adult rat brain. *J Neurosci*. 1999;19(14):5990-6005.
42. McTigue DM, Wei P, Stokes BT. Proliferation of NG2-positive cells and altered oligodendrocyte numbers in the contused rat spinal cord. *J Neurosci*. 2001;21(10):3392-3400.
43. Bullard KM, Longaker MT, Lorenz HP. Fetal wound healing: current biology. *World J Surg*. 2003;27(1):54-61.
44. Gutierrez-Aranda I, Ramos-Mejia V, Bueno C, et al. Human induced pluripotent stem cells develop teratoma more efficiently and faster than human embryonic stem cells regardless the site of injection. *Stem Cells*. 2010;28(9):1568-1570.
45. Ben-David U, Benvenisty N. The tumorigenicity of human embryonic and induced pluripotent stem cells. *Nat Rev Cancer*. 2011;11(4):268-277.
46. Lo B, Parham L. Ethical issues in stem cell research. *Endocr Rev*. 2009;30(3):204-213.
47. Liu ZJ, Zhuge Y, Velazquez OC. Trafficking and differentiation of mesenchymal stem cells. *J Cell Biochem*. 2009;106(6):984-991.
48. Liu P, An Y, Zhu T, et al. Mesenchymal stem cells: emerging concepts and recent advances in their roles in organismal homeostasis and therapy. *Front Cell Infect Microbiol*. 2023;13:1131218.
49. Bacakova L, Zarubova J, Travnickova M, et al. Stem cells: their source, potency and use in regenerative therapies with focus on adipose-derived stem cells - a review. *Biotechnol Adv*. 2018;36(4):1111-1126.
50. Hwang NS, Zhang C, Hwang YS, Varghese S. Mesenchymal stem cell differentiation and roles in regenerative medicine. *Wiley Interdiscip Rev Syst Biol Med*. 2009;1(1):97-106.
51. Oh EJ, Lee HW, Kalimuthu S, et al. In vivo migration of mesenchymal stem cells to burn injury sites and their therapeutic effects in a living mouse model. *J Control Release*. 2018;279:79-88.
52. Kawai T, Katagiri W, Osugi M, Sugimura Y, Hibi H, Ueda M. Secretomes from bone marrow-derived mesenchymal stromal cells enhance periodontal tissue regeneration. *Cytotherapy*. 2015;17(4):369-381.
53. Sarraf CE, Otto WR, Eastwood M. In vitro mesenchymal stem cell differentiation after mechanical stimulation. *Cell Prolif*. 2011;44(1):99-108.
54. Bronckaers A, Hilkens P, Martens W, et al. Mesenchymal stem/stromal cells as a pharmacological and therapeutic approach to accelerate angiogenesis. *Pharmacol Ther*. 2014;143(2):181-196.
55. Kou Z, Li B, Aierken A, et al. Mesenchymal stem cells pretreated with collagen promote skin wound-healing. *Int J Mol Sci*. 2023;24(10):8688.
56. Moon KC, Suh HS, Kim KB, et al. Potential of allogeneic adipose-derived stem cell-hydrogel complex for treating diabetic foot ulcers. *Diabetes*. 2019;68(4):837-846.
57. Sorrell JM, Caplan AI. Topical delivery of mesenchymal stem cells and their function in wounds. *Stem Cell Res Ther*. 2010;1(4):30.
58. Guillamat-Prats R. Role of mesenchymal stem/stromal cells in coagulation. *Int J Mol Sci*. 2022;23(18):10393.
59. Silachev DN, Goryunov KV, Shpilyuk MA, et al. Effect of MSCs and MSC-derived extracellular vesicles on human blood coagulation. *Cells*. 2019;8(3):258.
60. Liu W, Yu M, Xie D, et al. Melatonin-stimulated MSC-derived exosomes improve diabetic wound healing through regulating macrophage M1 and M2 polarization by targeting the PTEN/AKT pathway. *Stem Cell Res Ther*. 2020;11(1):259.
61. Jiang W, Xu J. Immune modulation by mesenchymal stem cells. *Cell Prolif*. 2020;53(1):e12712.
62. Yates CC, Rodrigues M, Nuschke A, et al. Multipotent stromal cells/mesenchymal stem cells and fibroblasts combine to minimize skin hypertrophic scarring. *Stem Cell Res Ther*. 2017;8(1):193.

63. Zhang B, Wang M, Gong A, et al. HucMSC-exosome mediated-Wnt4 signaling is required for cutaneous wound healing. *Stem Cells*. 2015;33(7):2158-2168.
64. Jackson WM, Nesti LJ, Tuan RS. Mesenchymal stem cell therapy for attenuation of scar formation during wound healing. *Stem Cell Res Ther*. 2012;3(3):20.
65. Komaki M, Numata Y, Morioka C, et al. Exosomes of human placenta-derived mesenchymal stem cells stimulate angiogenesis. *Stem Cell Res Ther*. 2017;8(1):219.
66. Nie C, Yang D, Xu J, Si Z, Jin X, Zhang J. Locally administered adipose-derived stem cells accelerate wound healing through differentiation and vasculogenesis. *Cell Transplant*. 2011;20(2):205-216.
67. Yagi H, Chen AF, Hirsch D, et al. Antimicrobial activity of mesenchymal stem cells against *Staphylococcus aureus*. *Stem Cell Res Ther*. 2020;11(1):293.
68. Luo Y, Song Y. Mechanism of antimicrobial peptides: antimicrobial, anti-inflammatory and antibiofilm activities. *Int J Mol Sci*. 2021;22(21):11401.
69. Esfandiyari R, Halabian R, Behzadi E, Sedighian H, Jafari R, Imani Fooladi AA. Performance evaluation of antimicrobial peptide ll-37 and hepcidin and β-defensin-2 secreted by mesenchymal stem cells. *Heliyon*. 2019;5(10):e02652.
70. Alcayaga-Miranda F, Cuenca J, Khoury M. Antimicrobial activity of mesenchymal stem cells: current status and new perspectives of antimicrobial peptide-based therapies. *Front Immunol*. 2017;8:339.

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APPENDIX

Search strategy in Web of Science Core Collection (Aug 1, 2023)
#1 (((TS=(healing*)) OR TS=(regeneration*)) OR TS=(repair*)) OR TS=(reconstruction*)
#2 (((((TS=(wound*)) OR TS=(ulcer*)) OR TS=(incision*)) OR TS=(lesion*)) OR TS=(vulnus*)) OR TS=(skin*)
#3 #1 AND #2
#4 ((((((((TS=(stem cell*)) OR TS=(bone marrow)) OR TS=(progenitor cell*)) OR TS=(lipoaspirate cell*)) OR TS=(mononuclear cell*)) OR TS=(mesenchymal stem cell*)) OR TS=(adipose-derived stem cell*)) OR TS=(mesenchymal stromal cell*)) OR TS=(epidermal stem cell*)
#5 #3 AND #4
#6 DT=(Article OR Review)
#7 #5 AND #6