

Bibliometric Analysis of Research Trends and Hotspots in Circular RNAs and Breast Cancer (2002–2022)

Sixia Zhong, Xiuli Zhang *, Yun Li, Meili Zhang and Huannan Cao

¹Department of Basic Sciences, Changchun University of Science and Technology, Changchun 130600, Jilin Province, China.

Correspondence to: Xiuli Zhang, Department of Basic Sciences, Changchun University of Science and Technology, Changchun 130600, Jilin Province, China.

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ABSTRACT

A bibliometric analysis aims to evaluate research hotspots and emerging trends in breast cancer and circular RNA, providing fresh perspectives for future research in this field.

Methods: This study employs bibliometric analysis tools, including VOSviewer and CiteSpace, to examine the literature on breast cancer and circular RNAs published between 2002 and 2022. The analysis focuses on bibliometric characteristics such as publication volume, country/region distribution, institutional affiliations, publishing journals, citation frequency, H-index, and research hotspots.

Results: Through a comprehensive review of the Web of Science database, 787 relevant publications were identified. Over the two decades, the number of articles has exhibited a growing trend. China leads in research output within this field, followed by significant contributions from institutions in the United States and Iran. Fang Lin is the most prolific author, with other notable contributors including Yang Burton B., Tang Hailin, Wang Xuehui, and Xie Xiaoming. The journals "Frontiers in Oncology" and "Molecular Cancer" have the highest number of publications in this domain. Research on tumor cell proliferation and migration continues to be a major focus. Over time, keyword trends have shifted from terms like "cell growth," "messenger RNAs," and "biomarker" to "long noncoding RNAs" and "sponge," reflecting ongoing advancements in the field. These emerging keywords suggest that "long noncoding RNAs" and "sponge" are poised to become key research areas in the future.

Conclusion: Bibliometric analysis offers valuable insights into the research landscape of breast cancer and circular RNAs. Recent studies have increasingly focused on the mechanisms underlying breast cancer and the biological functions of circular RNAs, highlighting the growing significance of this research area.

Keywords:

Artificial Intelligence, Detection, Microorganisms, Microscopy

Introduction

According to the World Health Organization, in 2020, 2.26 million women worldwide were diagnosed with breast cancer, resulting in 685,000 deaths. By the end of 2020, 7.8 million women had been diagnosed with breast cancer in the past five years, making it the most common cancer type globally. It accounts for approximately 30% of all cancer cases and 15%

of female cancer deaths. Despite significant advances in early diagnosis, surgery, chemotherapy, radiotherapy, endocrine therapy, and targeted therapy, breast cancer remains the leading cause of cancer-related deaths among women in over 100 countries [1-5]. Circular RNAs (circRNAs) are single-stranded RNA transcripts without 5' caps or 3' polyadenylated tails, generated through back-splicing from precursor mRNAs, and characterized by a covalently closed loop structure [6]. More than 40 years ago, viroids were first discovered as circular RNA molecules [7]. Subsequently,

circular RNAs were observed in the cytoplasm of eukaryotic cell lines through electron microscopy [8]. At that time, these molecules were considered "junk" produced by aberrant splicing events, with only the testis-specific circular RNAs from the Sex-determining Region Y (Sry) gene in mouse testes thought to potentially have a function[9,10]. In recent years, with the development of high-throughput sequencing technology (RNA-seq) and specific bioinformatics algorithms, thousands of circular RNAs have been identified in various species, including fungi, protozoa, plants, worms, fish, insects, and mammals [11-15]. Studies have found that certain circular RNAs exhibit cell- or tissue-specific expression in eukaryotes and display high stability and evolutionary conservation [16-18]. Evidence suggests that circular RNAs may play important roles in regulating gene expression through multiple mechanisms, such as acting as miRNA sponges, interacting with RNA-binding proteins, serving as intermediates in alternative splicing, templates for protein translation, and transcriptional regulators [19]. Recent research indicates that circular RNAs are involved in the pathological processes of many human diseases, especially cancer [20-23]. Currently, the mechanisms of circular RNAs in breast cancer are not well understood. However, research on breast cancer and circular RNAs has rapidly developed over the past decade.

Identifying new advancements and trends in the field has become challenging due to the rapid development of research on breast cancer and circular RNAs. Bibliometric analysis holds significant value in describing the current status, publication trends, and scientific output of researchers and institutions, as well as identifying future research hotspots [24]. Additionally, assessing the quality of relevant academic achievements is crucial for researchers, universities, and decision-makers in government departments, helping them to formulate strategies [25]. Bibliometric analysis provides a reliable basis for standardizing academic quality and offering useful information globally [26].

To date, this method has been used to estimate research trends in various medical fields, such as heart transplantation and familial hypercholesterolemia, as well as in non-medical fields [27-29].

Therefore, this study collected quantitative and qualitative data in the field of breast cancer and circular RNAs research, identifying the most productive countries, institutions, authors, and journals based on the number of publications or citations. The research objective is to conduct the first comprehensive bibliometric analysis of breast cancer and circular RNAs research over the past decade. This will provide scholars entering or about to enter the field with new insights into the current status, emerging trends, and future research hotspots in breast cancer and circular RNAs research.

Materials and Methods

Data Source and Search Strategy

On October 14, 2023, a literature search was conducted using the online version of the Web of Science Core Collection (WoSCC, Clarivate Analytics, Philadelphia, PA) database. The WoSCC database is considered one of the most comprehensive, systematic, and authoritative sources worldwide, covering over 12,000 influential journals and encompassing high-quality literature in biomedical, natural, and social sciences. It is widely used for bibliometric analysis and research on scientific literature visualization [30,31].

The search parameters were set as follows: Topic: [circular RNA] and Topic: [breast cancer], Time span: (2002 to 2022); Literature types: (articles and reviews); Language limit: English. All records (including title, author, keywords, source, abstract, and references) were exported in plain text format. The retrieval was conducted in one day (October 14, 2023) to avoid changes due to daily database updates.

Data Extraction and Analysis

All records retrieved from the WoSCC were independently downloaded by the author Sixiazhong and imported into Microsoft Excel 2016 for further data processing. Metrics such as the annual number of publications, countries /

regions, source journals, institutions, authors, keywords, and citation frequencies were extracted and statistically analyzed. Additionally, the Impact Factor (IF) and classifications from the Journal Citation Reports (JCR) were used to evaluate the quality of scientific information. The IF represents the average number of citations per article in a journal over the most recent two-year period [32]. JCR assigns each scientific journal to the appropriate IF category and ranks them within specific fields (Q1, Q2, Q3, and Q4) [33]. The IF and JCR classifications used in this study are based on 2022 data. Furthermore, the H-index was applied as another metric. The H-index is defined as the number of h papers published by a researcher that have each been cited at least h times, with a higher H-index indicating greater academic influence. The H-index is often regarded as an important indicator for evaluating a researcher's scientific output and academic standing and is also useful for assessing the academic output capacity of countries, institutions, or journals [34].

Visualized Analysis

Using VOSviewer 1.6.19 (Centre for Science and Technology Studies, Leiden University, The Netherlands), we created a visualization map where nodes represent countries, institutions, authors, or keywords, connected through co-authorship, citation, co-citation, and co-occurrence analysis. The size of each node is determined by the weight of the element, such as the number of publications, citations, or frequency of occurrences. Each node was assigned a color, with the same color indicating the same cluster, representing a collection of items with similar attributes within the network [35]. The links between nodes represent associations between elements, and the thickness of the links indicates the strength of these associations. Total Link Strength (TLS) was used to quantitatively assess the links. Similar analytical methods were employed to create visualization maps of highly cited documents, countries or regions, institutions, journals, journals, and authors across different periods to depict the evolution of these elements. Additionally, VOSviewer was used to categorize keywords with high co-occurrence

frequencies into clusters and to create a density visualization map.

CiteSpace V (version 6.2.R4, Drexel University) was used to: (i) generate visual maps of the cited references network from the time zone view, and (ii) detect burst analysis of co-occurring keywords. The parameter settings for CiteSpace were as follows: time slice (2002-2022), with each slice being one year, item source (all selected), node type (one at a time), selection condition (50), pruning (Pathfinder), visualization (cluster view static, show merged networks). The detailed workflow of literature screening and data analysis is illustrated in

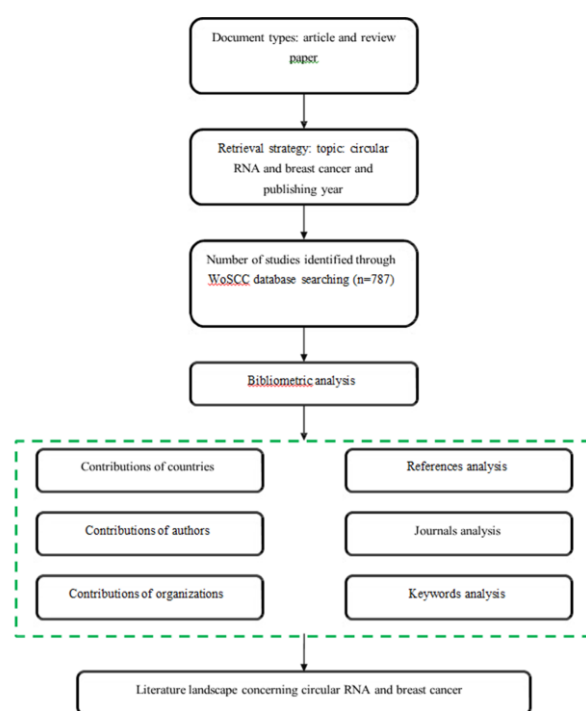


Figure 1: Flow diagram of literature filtering

Results

Publication Outputs and Citation Trends

Based on the growth trend shown in Figure 2, the study period was divided into three phases: (i) 2002-2011: Initial Phase, with in citation rate; (ii) 2012-2015: Slow Growth Phase, with annual publications ranging between 2-6, maintaining a stable growth rate; and (iii) 2016-2022: Rapid Development Phase. In 2020, the number of publications on circular RNAs and breast cancer exceeded 100 for the first time. By 2021, the annual number of publications surpassed 200, with a total of 6,807 citations. As of the

retrieval date, these publications have been cited 27,966 times, with an average of 35.53 citations per paper. In the Initial Phase, research in this field was relatively limited and underdeveloped, with a low number of citations. However,

Since 2019, annual citations have exceeded 2,000, showing a steady growth trend. This sustained growth reflects the increasing importance and attention given to circular RNAs and breast cancer research, indicating that this field is gaining more recognition within the academic community.

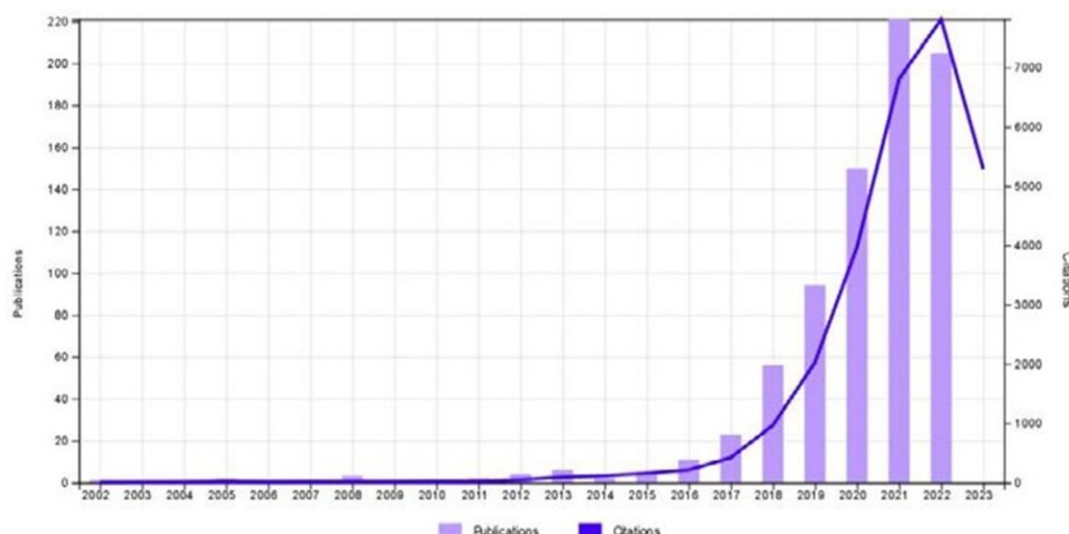


Figure 2: Global trend of annual publications and citations related to circular RNA and breast cancer research from 2002 to 2022.

Contributions of Countries

Among the 787 papers, researchers hail from 52 countries or regions. From 2002 to 2022, the top ten countries in terms of global article output are shown in Figure 3A. The majority of papers originate from China (612 papers, accounting for 77.76%), followed by the United States (51 papers, 6.48%), Iran (48 papers, 6.10%), India (24 papers, 3.05%), and Italy (21 papers, 2.67%) (Table 1).

To ensure the reliability and statistical significance of the analysis, we set the VOSviewer parameters to include countries with at least five publications. A total of 52 countries were included, of which 21 met this threshold. The citation relationships between different countries/regions are shown in the citation network map (Figure 3B). Among the top ten countries in terms of citation count, China ranks highest (citations = 20,650), followed by the United States. (citations = 3,975), Canada (citations = 1,283), Singapore (citations = 1,192), and Italy (citations = 1,039), with the latter three having comparable citation counts (Figure 3C). In terms of the number of

cited documents, China ranks first (documents = 612), followed by the United States (documents = 51) and Iran (documents = 48) (Figure 3D). Among the top ten countries in terms of total link strength, China ranks highest (Total Link Strength, TLS = 2,207), followed by Iran (TLS = 620) and the United States (TLS = 522) (Figure 3E). China has the strongest connections with Iran and the United States, highlighting the leading positions of China and the United States in circular RNA and breast cancer research.

The international collaboration map shows the close cooperative relationships between countries/regions (Figure 3F). China is at the center of circular RNA and breast cancer research, with the highest total link strength (TLS = 52), a total of 612 publications, and 20,650 citations. China has particularly strong ties with the United States, Iran, and Singapore.

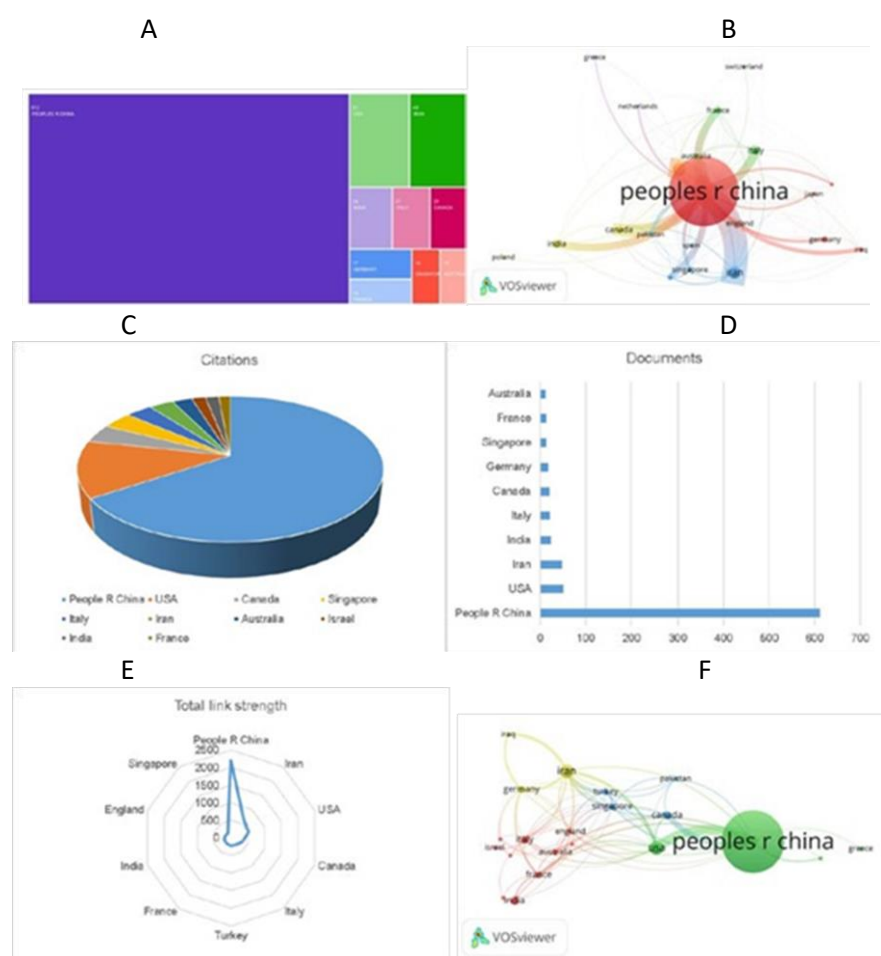


Figure 3: (A) The top 10 countries in terms of article output on circular RNA and breast cancer research from 2002 to 2022. (B) Citation network map showing the relationships between different countries/regions with at least five publications. (C) The top 10 countries by citation count. (D) The top 10 countries by the number of cited documents. (E) The top 10 countries by total link strength of citations.(F) Close cooperation relationships between countries/regions, with line thickness reflecting the frequency of cooperation. Thicker lines indicate stronger cooperation.

Countries	Record count	% of 787
people r china	612	77.76%
USA	51	6.48%
Iran	48	6.10%
India	24	3.05%
Italy	21	2.67%
Canada	20	2.54%
Germany	17	2.16%
France	14	1.78%
Singapore	14	1.78%
Australia	13	1.65%

Table 1: The top 10 countries by global article output in circular RNA and breast cancer research.

Contributions of Organizations

The 787 articles were published by 852 institutions. The top ten high-output institutions, all from China, are shown in Table2. Nanjing Medical University (TP = 60) is the most prolific institution, followed by Sun Yat-sen University (TP = 42), Zhengzhou University (TP = 23), and Tongji University (TP = 21). Using VOSviewer, we created a network visualization of institutions that published more than five papers. Figure 4 displays the cooperation network among institutions, with 63 projects forming nine different colored clusters. In the ranking of the

top ten institutions by total link strength (TLS) (Table 3), four institutions are from China: Nanjing Medical University (TLS= 53), Southeast University (TLS = 24), Sun Yat-sen University (TLS = 24), and Jilin University (TLS = 17). Nanjing Medical University has the highest total link strength (TLS = 53), followed by Southeast University (TLS = 24) and Sun Yat-sen University (TLS = 24), both with equal total link strength. Notably, Southeast University performs best in terms of the average number of citations per publication (CPP = 102.69), indicating its high impact in the field of circular RNA and breast cancer research

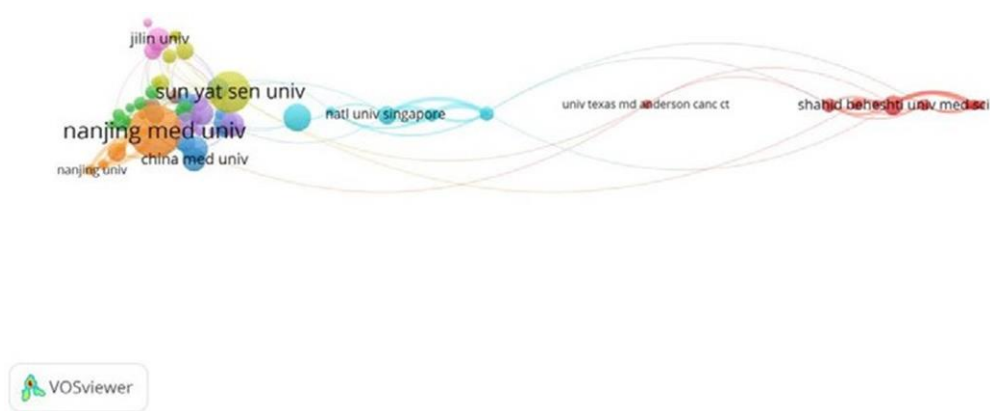


Figure 4: Network visualization of institution collaboration analysis based on VOS viewer.

organization	TP	TC	CPP	TLS
nanjing medical university	60	2519	41.98	53
sun yat -sen university	42	2941	70.02	24
zhengzhou university	23	857	37.26	2
tongji university	21	473	22.52	12
qingdao university	19	296	15.58	14
jilin university	18	1097	60.94	17
shandong university	18	728	40.44	9
huazhong university science and technology	18	480	26.67	8
central south university	18	460	25.56	5
China medical university	18	230	12.78	1

CPP,Number of citations per publication:CPP= TC/TP;TC,Total number of citations of total publications;TP,Total number of publications;TLS,Total link strength

Table 2: The top 10 most productive institutions in circular RNA and breast cancer research.

Organization	TP	TC	CPP	TLS
nanjing medical university	60	2519	41.98	53
southeast university	13	1335	102.69	24
sun yat-sen university	42	2941	70.02	24
Shahid Beheshti University of Medical Sciences	14	135	9.64	23
Islamic Azad University	9	294	32.67	20
National University of Singapore	13	1185	91.15	20
University of Tehran	8	353	44.1	19
Hawler Medical University	6	32	5.33	17
jilin University	18	1097	60.94	17
University of Toronto	12	1013	84.42	17

CPP, Number of citations per publication: $CPP = TC/TP$; TC, Total number of citations of total

publications; TP, Total number of publications; TLS, Total link strength

Table 3: The top 10 institutions by total collaboration link strength in circular RNA and breast cancer research.

Authors and Co-cited Authors

A total of 4,038 authors contributed to the research output, with 3,454 authors having published only one article. To identify the most influential experts in the field of breast cancer and circular RNAs over the past twenty years, we ranked the top fifteen authors based on total publications (TP) and H-index. As shown in Table 4, Fang Lin from Anhui Agricultural University ranks first in terms of the number of papers (TP = 14, CPP = 17.71, H-index =

Yang, Burton B. from the University of Toronto has the highest average citations per paper (TP = 11, CPP = 91.82, H-index = 58). Among the top fifteen most prolific authors, twelve are from China, two from the United States, and one from Turkey. Chen Bing, Li Yaming, Wang Lijuan, Yang Qifeng, and Zhao Wenjing have the highest total link strength (TLS = 63, TC = 570, TP = 8, CPP = 71.25), indicating a close collaborative relationship.

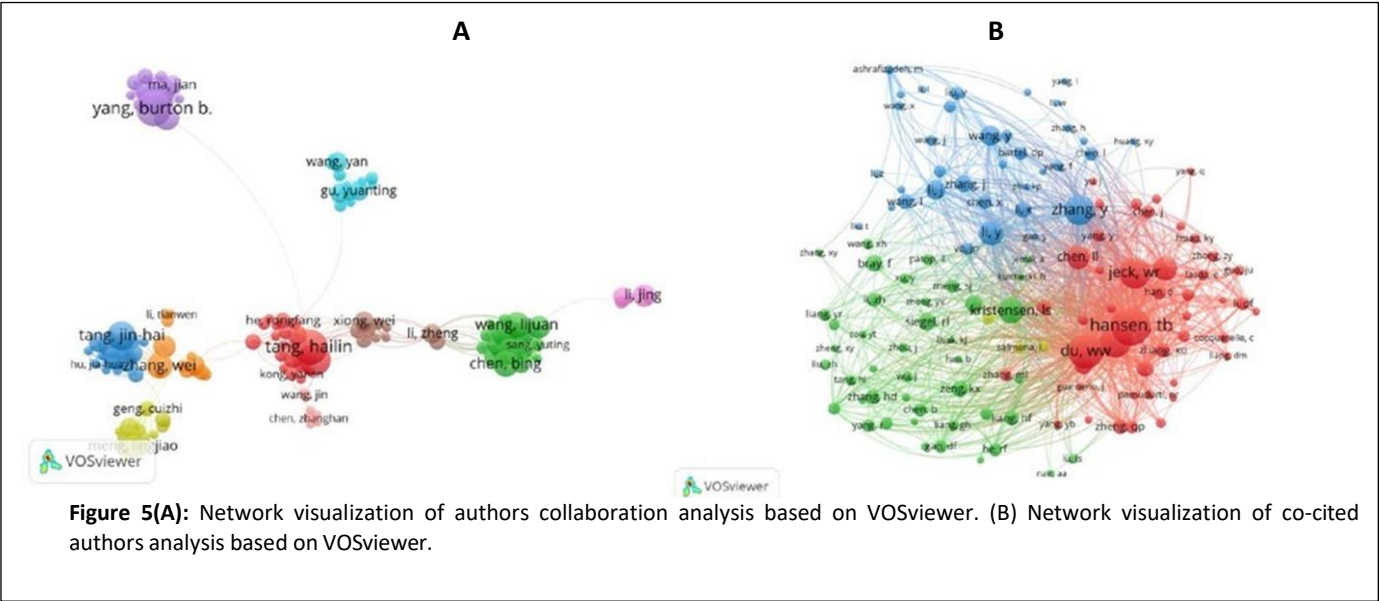
Author	TP	TC	CPP	TLS	H-index	Organization
fang , lin	14	248	17.71	34	56	Anhui Agricultural University
yang , burton b.	11	1010	91.82	48	58	University of Toronto
tang , hailin	11	940	85.45	26	52	Sun Yat Sen University
wang , xuehui	10	229	22.9	31	27	Sanya Tropical Fisheries Research Institute
xie , xiaoming	10	892	89.2	25	51	Beijing University of Chinese Medicine
du , willian w.	9	763	84.78	47	34	University of Toronto
tang , jin-hai	9	324	36	47	51	Dalian Medical University
chen , bing	8	570	71.25	63	23	Jiangsu Key Lab Mol & Translat Canc Res
li , yaming	8	570	71.25	63	39	Hosp China Med Univ 1
wang , lijuan	8	570	71.25	63	28	Shandong University
yang , qifeng	8	570	71.25	63	87	Zhejiang University
zhao , wenjing	8	570	71.25	63	19	Southern University of Science & Technology
wu , nan	8	492	61.5	41	59	Binzhou Medical University
ji , changle	8	96	12	29	11	Tongji University
zarrabi , ali	8	384	48	18	52	Istinye University

CPP, Number of citations per publication: $CPP = TC/TP$; TC, Total number of citations of total

publications; TP, Total number of publications; TLS, Total link strength

Table 4: The top 15 most productive authors on circular RNA and breast cancer.

Using VOSviewer, we set the minimum number of published papers threshold to three and found that the most prolific authors also have tight collaboration networks (Figure 5A). Set the minimum citation threshold to 40, creating a co-citation network of authors that includes 126 nodes, 7,737 links, and 4 clusters. (Figure 5B).



Journals and Co-cited Journals

The 787 articles on circular RNAs and breast cancer were published in 284 academic journals. The top ten high-output journals published a total of 191 papers, accounting for approximately 24% of the total output (Table 5). "Frontiers in Oncology" and "Molecular Cancer" lead in total output (TP), but "Molecular Cancer" surpasses "Frontiers in Oncology" in total citations (TC = 2,877), average citations (AC = 106.56), H-index (H-index = 126), and impact factor (IF = 37.3), indicating its significant status in the field of circular RNAs and breast cancer.

Rank	Journal	TP	TC	AC	H-index	JCR	IF2022
1	frontiers in oncology	27	298	11.037	83	Q2	4.7
2	molecular cancer	27	2877	106.5556	126	Q1	37.3
3	cancer management and research	20	440	22	40	Q3	3.3
4	cancer cell international	17	238	14	56	Q2	5.8
5	molecular therapy-nucleic acids	16	588	36.75	59	Q1	8.8
6	cell death & disease	15	926	61.7333	111	Q1	9
7	international journal of molecular sciences	15	1174	78.2667	162	Q1	6.2
8	oncotargets and therapy	15	245	16.3333	60	Q2	4
9	cancers	13	170	13.0769	76	Q1	5.2
10	frontiers in cell and developmental biology	13	252	19.3846	53	Q1	5.5

IF,Impact Factor; JCR,Journal Citation Reports; TC,Total number of citations of total

publications;TP,Total number of publications;AC=TC/TP,Average citations.

Table 5: The top 11 most productive journals on circular RNA and breast cancer

Based on network analysis, the citation patterns of 61 journals were divided into seven clusters, forming a total of 801 links (Figure 6A). The co-citation relationships between different journals are shown in Figure 6B, which includes 232 items forming five

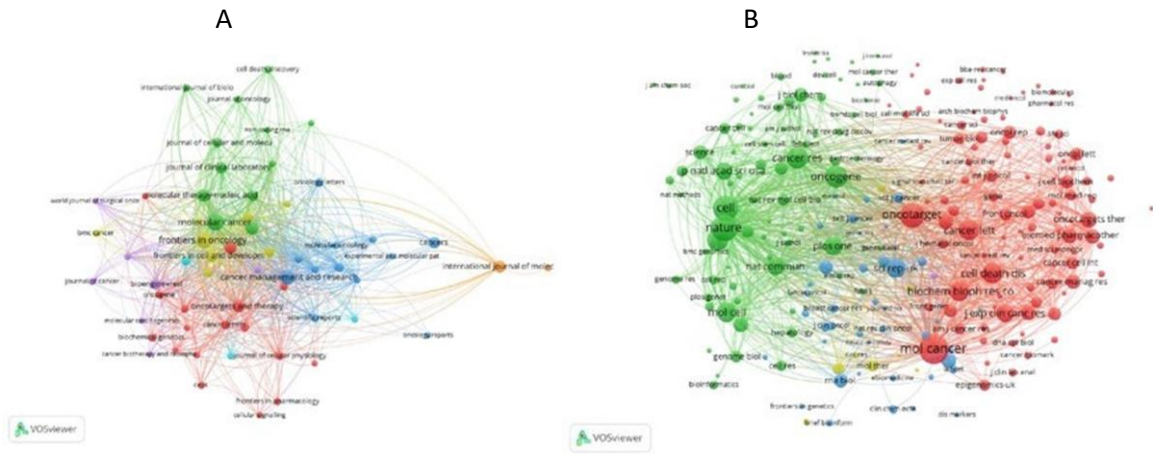


Figure 6: (A) Network visualization of journals analysis based on VOSviewer. (B) Network visualization of co-cited journals analysis

References and Co-cited References

To further explore development trends, we analyzed the ten most-cited documents during the study period (Table 6). These documents include one review and nine research papers, with total citation counts ranging from 103 to 266. The most-cited article is a 2013 study by Thomas B. Hansen (266 citations), followed by a

2013 study by Sebastian Memczak (261 citations). Both articles discuss how circular RNAs mediate protein translation expression by regulating the activity of miR-7, revealing previously unrecognized regulatory potential of coding sequences. Overall, newly published articles have lower citation rates, so the current citation counts may underestimate their actual value.

Rank	Title	Year	Journal	First author	TC
1	Natural RNA circles function as efficient microRNA sponges	2013	Nature	Hansen, TB	266
2	Circular RNAs are a large class of animal RNAs with regulatory potency	2013	Nature	Memczak, S	261
3	Circular RNAs are abundant, conserved, and associated with ALU repeats	2013	RNA	Jeck, WR	176
4	Exon-intron circular RNAs regulate transcription in the nucleus	2015	Nature Structural& Molecular Biology	Li, Zhaoyong	126
5	Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries	2018	Ca-Cancer J Clin	Freddie Bray BSc	123
6	circRNA Biogenesis Competes with Pre-mRNA Splicing	2014	Molecular Cell	Ashwal-Fluss, R	114

TC,Total number of citations of total publications

Table 6: The top 10 references on circularRNA and breast cancer with the most co-citations.

Figure 7 presents a co-citation analysis based on CiteSpace, showing 172 documents cited more than five times annually in the field of breast cancer and circular RNAs. Visualizing these documents in a timeline analysis reflects the temporal characteristics of research hotspots in this field. Based on the log-likelihood ratio (LLR)

algorithm, nine cluster labels representing hot topics were selected (Table 7) and ranked in Figure 7. Along the dashed lines connecting each label, larger circles indicate higher citation frequencies, and warmer-colored lines indicate later publication dates.

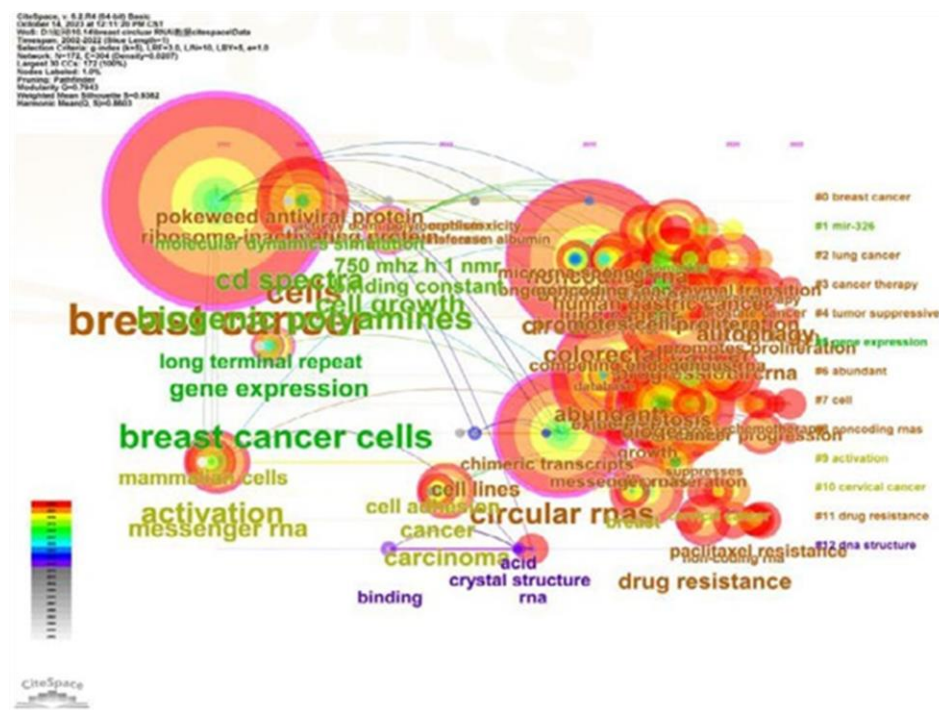


Figure 7: Timeline view of the top 13 most co-cited references on circular RNA and breast cancer using CiteSpace software. For each cluster, the position of each node indicates the publication time of the document, and the node size represents the number of citations.

Cluster ID	Size	Silhouette	Mean(Year)	Label (LLR)
0	20	0.99	2006	breast cancer
1	17	0.992	2008	mir-326
2	17	0.986	2017	lung cancer
3	14	1	2019	cancer therapy
4	13	0.846	2019	tumor suppressive
5	13	0.974	2004	gene expression
6	12	1	2018	abundant
7	11	0.982	2019	cell
8	11	0.857	2016	noncoding mas

LLR: Loglikelihood ratio

Table 7: Main clusters of co-cited references

Cluster 0 (breast cancer) and Cluster 5 (gene expression) appeared the earliest, indicating that early breast cancer research focused on gene expression. Cluster 3 (cancer therapy) and Cluster 4 (tumor suppression) are current research hot topics, reflecting the high current interest in

tumor suppressor genes and cancer therapy.

Keywords Analysis of Research Hotspots

The co-occurrence frequency of keywords can indicate scientific hotspots within a specific research theme,

serving as an important method for tracking scientific development. This study extracted 2,909 keywords from 787 articles and listed the top 20 keywords based on co-occurrence frequency using VOSviewer software, as shown in Table 8. First, a density map was generated using 72 keywords with co- occurrence frequencies exceeding 20 times, visually depicting the distribution of popular themes in the field. As shown in Figure 8A, "circular RNA," "breast cancer," "expression," "proliferation," "invasion," and "metastasis" are significant elements of the density map. Next, a cluster analysis was performed on the selected keywords.

Each cluster was labeled with index terms extracted from the keywords. After calculation, the 72 high-frequency keywords formed four clusters (Figure 8B), representing the main research directions in this field: Cluster 1 (red circles, 31 keywords): Focuses on various diseases related to breast cancer and circular RNAs, with keywords including "cell lung-cancer," "colorectal-cancer," and "gastric- cancer." Cluster 2 (green circles, 23 keywords): Focuses on the clinical diagnosis of breast cancer and circular RNAs, with keywords including "diagnosis," "resistance," and "prognosis."

Keyword	Occurrences	TLS
circular <u>ma</u>	280	1480
breast cancer	255	1240
breast-cancer	241	1231
expression	189	1074
proliferation	188	1095
circular <u>mas</u>	169	861
progression	147	873
metastasis	145	935
invasion	143	879
migration	117	726
cells	94	484
<u>circma</u>	92	587
biomarker	89	533
cancer	78	475
growth	74	452
promotes	69	438
hepatocellular-carcinoma	64	391
<u>circmas</u>	62	396
apoptosis	61	340
colorectal-cancer	60	376

TLS:TLS.Total link strength

Table 8: The top 20 keywords in the co-occurrence frequency of circular RNA and breast cancer.

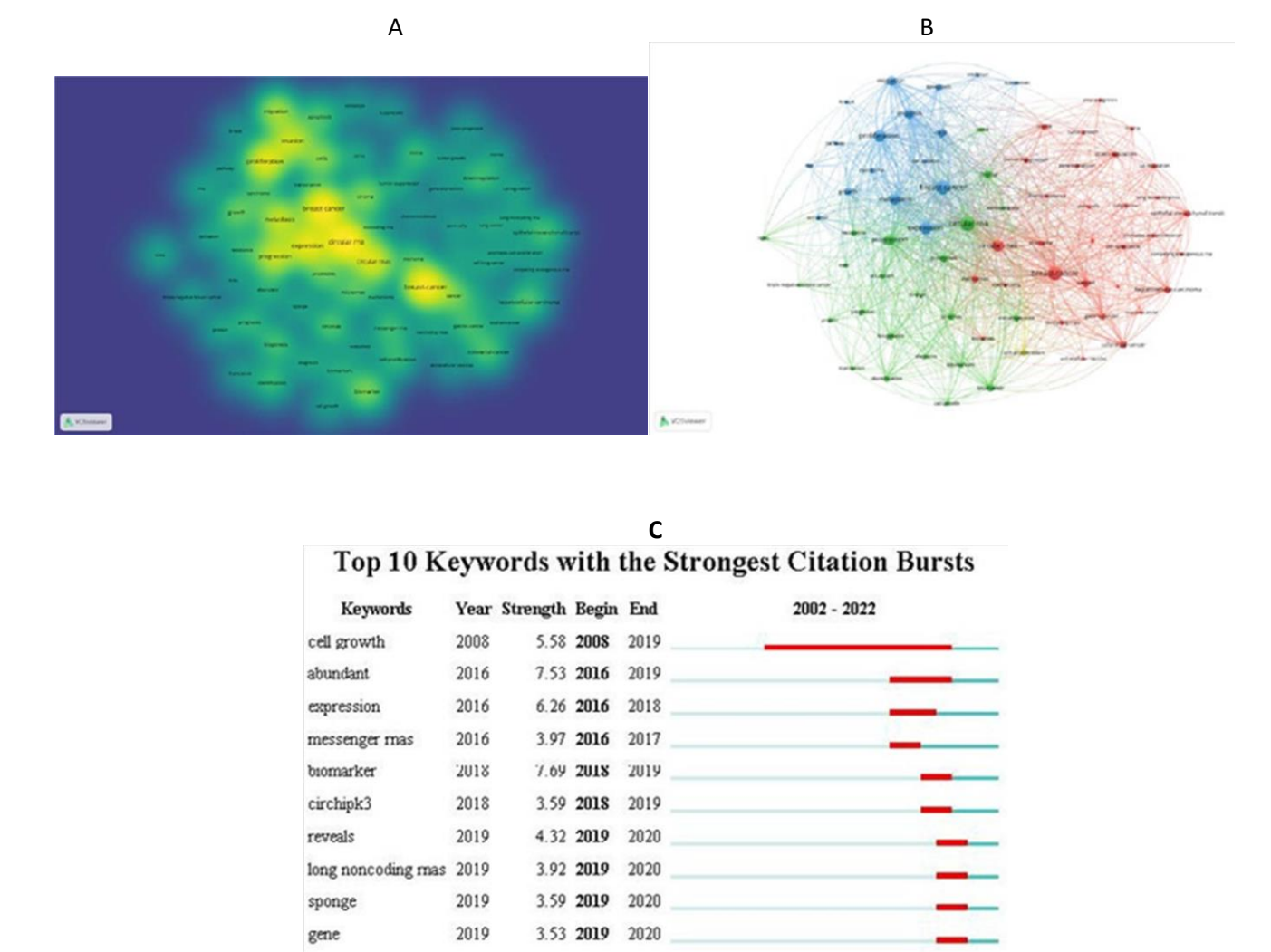


Figure 8: (A) Density map of keywords generated by VOSviewer. (B) Keyword co-occurrence analysis on breast cancer and circular RNA research using VOSviewer. (C) Top 10 keywords with the strongest citation bursts (sorted by the beginning year of the burst). Notes: The blue bars indicate the reference had been published; the red bars indicate citation bursts.

Cluster 3 (blue circles, 17 keywords): Focuses on the mechanisms of action of breast cancer and circular RNAs, with keywords including "activation," "apoptosis," "invasion," and "proliferation." Cluster 4 (yellow circle, 1 keyword): Labeled as "cell-proliferation." Finally, we identified the top 10 potential keywords, which are considered indicators of research frontiers or emerging trends over time. As shown in Figure 8C, since 2018, the keywords with citation bursts include "biomarker" (7.69), "circhipk3" (3.59), "long noncoding RNAs" (3.92), and "sponge" (3.59). These keywords represent the research frontiers in the study of breast cancer and circular RNAs. H-index=56), followed by Yang, Burton B. from the University of Toronto (TP=11, CPP=91.82, H-index=58),

and Tang Hailin from Sun Yat-sen University (TP=11, CPP=85.45, H-index=52), who have played significant roles in this field. Additionally, Yang, Burton B. from the University of Toronto stands out in terms of single article citations (TP=11, CPP=91.82, H-index=58), contributing many high-quality articles to this field.

Discussion

We conducted a bibliometric analysis of 787 documents related to breast cancer and circular RNAs from the WoSCC database, covering the period from 2002 to 2022. This analysis revealed several key insights. Firstly, this has been an active research field in recent years. From 2002 to 2015, there was almost no growth in the number of research

papers on breast cancer and circular RNAs globally. However, since 2016, there has been an explosive increase in the number of research papers in this field. Through bibliometric analysis of countries, institutions, authors, and journals, we observed changes in global research trends.

China has the highest output of publications in this field, followed by the United States and Iran. All top ten high-output institutions are from China, with most collaborative research conducted domestically. European countries have relatively close collaborations, while cooperation among other countries is limited. Notably, Nanjing Medical University, Sun Yat-sen University, and Southeast University have close ties. Strengthening international cooperation, removing academic barriers, and promoting the development of breast cancer and circular RNA research is crucial.

In the co-author analysis, Fang Lin from Anhui Agricultural University has published the most papers (TP=14, CPP=17.71). Among the top ten journals, except for "Frontiers in Oncology" (impact factor 4.7), "Cancer Management and Research" (impact factor 3.3), and "OncoTargets and Therapy" (impact factor 4), the remaining journals have relatively high impact factors (greater than 5.0). "Frontiers in Oncology" and "Molecular Cancer" tie for the first place in the number of papers (TP), but "Molecular Cancer" surpasses "Frontiers in Oncology" in total citations (TC=2877), average citations (AC=106.56), H-index (H-index=126), and impact factor (IF=37.3). Furthermore, "Molecular Cancer" has the highest co-citation count at 1,894 times, indicating its significant status in the field of circular RNAs and breast cancer. According to the 2022 JCR standards, among the top ten most active journals, six are classified as Q1, three as Q2, and one as Q3. The downregulation of circular RNA gene expression promotes the proliferation, invasion, and migration of non-small cell lung cancer (NSCLC) cells by regulating protein expression [36-38]. Circular RNAs also play significant roles in various cancers. In breast cancer, they promote the development of multiple myeloma the

through the miR-1180/yes-associated protein pathway and facilitate the progression of Mantle Cell Lymphoma via pathways involving three lncRNAs (MALAT1, NEAT1, and XIST), five microRNAs (hsa-miR-129-5p, hsa-miR-3163, hsa-miR-4662a-5p, hsa-miR-101-3p, and hsa-miR-186-5p), and five mRNAs (NOTCH1, FMR1, ABCB1, TWIST1, and VEGFA) [39,40]. Additionally, circular RNAs reduce the proliferation, invasion, and migration of Wilms tumor cells through the miR-145-5p pathway, inhibit the growth and migration of bladder cancer cells through the C-MYC pathway, and suppress the growth and migration of colon cancer cells through pathways involving miR-150-5p, c-Myc, cyclin D1, p53, caspase-3, PARP, PTEN, PI3K, AKT, JAK2, and STAT5 [41-43]. Circular RNAs also inhibit the growth of hepatocellular carcinoma through pathways involving miR-892a and miR-328-3p, HIF1AN, HDGF, PI3K-AKT, the Rapamycin kinase complex 1/ β -catenin, NOTCH2, BIRC5, SURVIVIN, and MYC [44].

Circular RNAs regulate carcinogenesis and cancer progression by acting as microRNA sponges, encoding proteins, and interacting with proteins [45]. In breast cancer, researchers detected 3,093 circular RNAs, with 18 exhibiting differential expression between adriamycin (ADM)-resistant and parental MCF-7 cells. Through quantitative real-time polymerase chain reaction (qPCR) analysis, they found that Homo sapiens (hsa)_circ_0006528 was significantly upregulated in ADM-resistant cancer cells. When the expression of hsa_circ_0006528 was inhibited by small interfering RNA, the sensitivity of breast cancer cells to ADM significantly increased. Concurrently, the downregulation of hsa_circ_0006528 was associated with increased expression of miRNA-7-5p. This suggests that the hsa_circ_0006528/miR-7-5p/RAF1 axis plays a regulatory role in ADM-resistant breast cancer [46]. Additionally, circABCB10 has been reported to promote breast cancer proliferation and inhibit apoptosis by acting as a sponge for miRNA-1271 [47]. Studies have also found that the miR-1275-ATG7/ULK1-autophagic axis and miR-92b-3p pathway promote autophagy and proliferation of breast cancer cells, while the miR-190a-3p/TP53INP1 axis pathway induces apoptosis in triple-

negative breast cancer cells [22,48,49].

To our knowledge, this is the first bibliometric analysis of the literature on breast cancer and circular RNAs, describing milestones and trends over the past twenty years. The advantages of this analysis lie in its objectivity and its ability to demonstrate development directions in the field while highlighting areas that have not been thoroughly studied. However, several limitations exist. Firstly, our data is solely from the WoSCC database, excluding other databases (such as PubMed), printed publications, and video materials, which may result in the omission of certain articles. Secondly, our selective analysis of the characteristics of the information might overlook some key points and details. Lastly, bibliometric methods have inherent limitations and cannot correct for factors such as population size, overall research output, gross domestic product, and research investment resources. Nevertheless, we have attempted to comprehensively analyze the development and research content of breast cancer and circular RNAs, aiming to summarize the discipline and provide guidance during this period of rapid development in this field.

Conclusion

In summary, research on the mechanisms of breast cancer related to the biological functions of circular RNAs is increasing, with "Molecular Cancer" being the most influential journal in this field. China leads in both output and scientific impact. Among institutions, Nanjing Medical University is the top producer and also has the highest total link strength. Fang Lin from Anhui Agricultural University ranks first in the number of papers, while Yang, Burton B. from the University of Toronto has the highest number of citations per paper. The research hotspots in this field focus on "expression," "proliferation," "invasion," and "metastasis." The research is primarily based on basic studies, concentrating on animal and cellular levels. Future research directions include "biomarker," "circchipk3," "long noncoding RNAs," and "sponge."

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