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Fundamental knowledge and research regarding the role of immunity in triple-negative breast cancer from 2014–2024: A bibliometric analysis

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ABSTRACT

Immunity has vital research value and promising applications in triple-negative breast cancer (TNBC). Nevertheless, few bibliometric analyses have systematically investigated this area. This study aimed to comprehensively review the collaboration and impact of countries, institutions, authors, and journals on the role of immunity in TNBC from a bibliometric perspective, evaluate the keyword co-occurrence of the knowledge structure, and identify hot trends and emerging topics. Articles and reviews related to immunity in TNBC were retrieved from the Web of Science core collection using subject search. A bibliometric study was conducted primarily using CiteSpace and VOSviewer. A total of 3,104 articles and reviews were included from January 1, 2014, through December 31, 2024. The number of articles on immunization in TNBC is rising. These publications are mainly from 415 institutions in 82 countries, led by China and the USA. Among these publications, *Lajos Pusztai* published the most papers, while *Peter Schmid* was co-cited the most. The most productive journals focused on molecular biology, biological immunology, and clinical medicine. Furthermore, co-citation analysis revealed that tumor microenvironment, biomarkers, and immune checkpoint inhibitors are current and developing research areas. The keywords *"immunotherapy"* and *"nanoparticles"* are also likely to be new trends and focal points for future research. This study adopted bibliometric and visualization methods to provide a comprehensive review of the research on immunization in TNBC. This article will help researchers better understand the dynamic evolution of the role of immunity in TNBC and identify areas for future research.

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Introduction

Breast cancer is the most common malignancy worldwide, and the incidence is increasing (>0.5% per year), with triple-negative breast cancer (TNBC) accounting for 15–20% of all breast cancers.[1–3] TNBC is defined by the lack of expression of estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 (HER2).[4–6] Compared to hormone receptor-positive or HER2-positive breast cancer, TNBC is highly aggressive throughout the clinical course, with higher recurrence rates, greater metastatic potential, and shorter overall survival.[7,8] TNBC remains the most therapeutically challenging subtype of breast cancer,[9] necessitating further research for effective treatment measures.

The immune system can recognize and control tumor growth, but tumor cells can avoid immune recognition and elimination.[10] In recent decades, tremendous progress has been made in understanding tumor immune evasion, leading to novel approaches to stop tumor immune escape and thus ensure elimination of cancer cells.[11] Tumor immunotherapy encompasses the treatment of tumors by stimulating and enhancing the immune function or regulating the immune response through biological agents.[12,13] With the development of immune checkpoint inhibitors for solid tumors and the validation of TNBC immunogenicity, immunotherapy is attracting increasing attention.[13] Although TNBC has limited options for systemic therapy, it is more likely to respond to immune checkpoint blockade therapy than other breast cancer subtypes due to higher immunogenicity, higher enrichment of tumor-infiltrating lymphocytes (TILs), and higher levels of programmed cell death ligand 1 (PD-L1) expression.[14] Therefore, it is necessary to explore the potential application of immunotherapy in TNBC. Currently, many researchers are using multi-omics data for bioinformatics analysis to identify critical immune checkpoints, followed by further mechanistic validation to explore the feasibility of translating these immune checkpoints into clinical therapies.[15] Meanwhile, various immunotherapeutic strategies, including immune checkpoint blockade, vaccination, and adoptive cell transfer, have been widely investigated in clinical research of TNBC.[16]

Bibliometric analysis uses collaborative network analysis and literature co-citation analysis to evaluate the quality of a study.[17] It quantitatively assesses the knowledge generated over time by analyzing the research profiles of different countries, institutions, and researchers, thus providing a knowledge map of the development and evolution of scientific knowledge in the field of study.[18,19] Therefore, this study aimed to analyze

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the literature on the role of immunity in TNBC using bibliometric methods from January 1, 2014, to December 31, 2024, and ensure better understanding of the current status and trends of these studies by analyzing their main characteristics.

Materials and methods

Data collection

The Web of Science (WoS) has been accepted by many researchers as a high-quality digital literature resource database and is considered the most suitable database for bibliometric analysis.[20] This study was based on the Science Citation Index-Expanded (SCI-Expanded) of the Web of Science Core Collection (WoSCC) to collect and analyze the data. The literature obtained from this database ensures the accuracy and authority of the conclusions. To avoid errors and omissions due to the constant updating of the database, the literature search and data download were completed in one day (December 31, 2024), covering the period from January 1, 2014, to December 31, 2024. The search formula was set as *TS = ("Triple-negative breast cancer" OR "Triple-negative breast carcinoma" OR "TNBC") AND TS= ("Immune" OR "Immunity" OR "Immunization" OR "Immuno")*. Only articles and reviews were included, and non-English articles were excluded. Then, the search results were exported as text, with the record content as *"Full Record and Cited References"* in *"Plain Text File"* format. We ultimately analyzed 3,104 pieces of literature, and the detailed process of literature selection is illustrated in Figure 1.

Data analysis and visualization

We derived citation reports and search results from the WoSCC database, including the annual number of articles published, annual number of citations, number of publications for different countries and institutions, and number of categories. The obtained data were imported into Microsoft Excel 2019, Tableau Public, VOSviewer, CiteSpace, and online Bibliometric Platform (https://bibliometric.com/) for further analysis.[21–23] Excel was used to process the raw data; for example, in keyword co-occurrence analysis, keywords in different formats but with the same or similar meanings were merged. Tableau Public was the product of a computer science project at Stanford University to explore, create, and publicly share data visualization items online, and we used it to produce a world map describing the volume of publications. We created a network of national and regional collaborations through an online website (https://bibliometric.com/).

VOSviewer, developed by the Science and Technology Research Center of Leiden University, is a software tool for building and visualizing bibliometric networks.[24] We used the VOSviewer software to plot country cooperation network maps, institutional cooperation density maps, and keyword co-

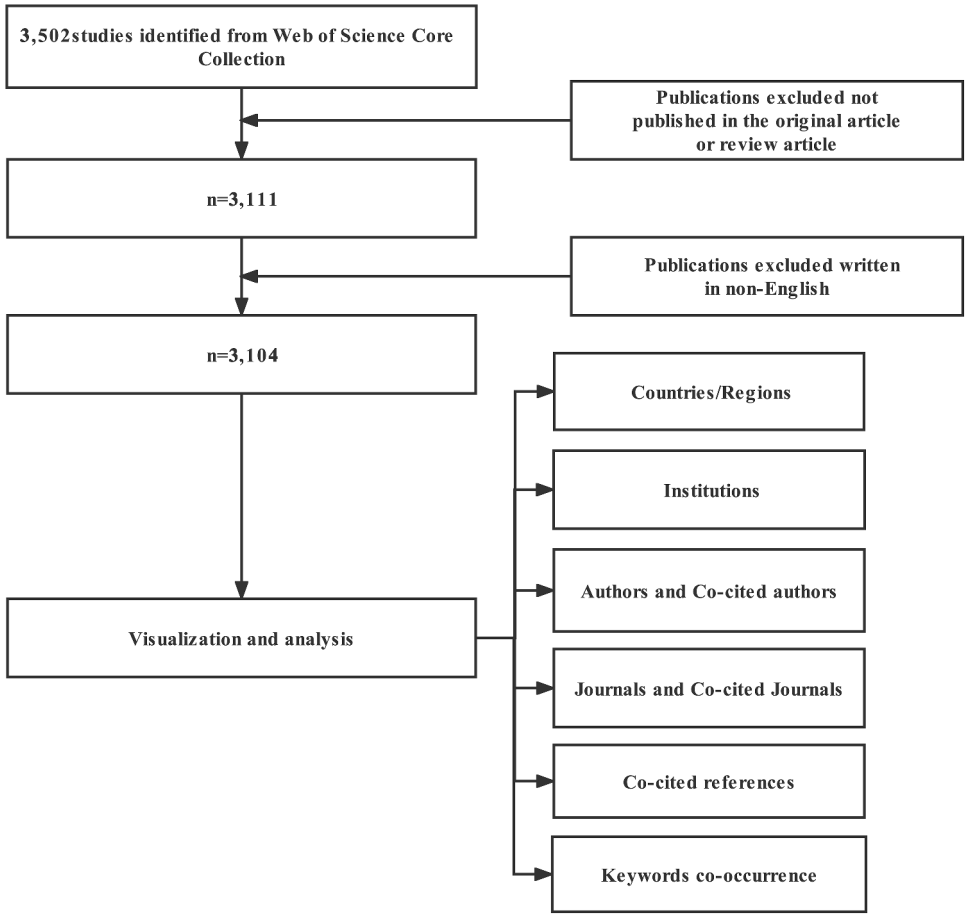

Figure 1. Flowchart of this study.

occurrence network maps. For all elements of the VOSviewer analysis, we chose the total count method, which means that all analysis methods were given the same weight. For the cooperative network graph of countries, the minimum number of documents for a country was set to 10. For the institutional cooperative density graph, the minimum number of documents for an institution was set to 5, chosen for the keyword co-occurrence analysis. We first excluded keywords that appeared in the search formula, merged synonyms, and then included keywords that appeared more than 30 times in the analysis.

CiteSpace, developed by Prof. *Chaomei Chen*, is a tool designed for visual analysis of academic literature in a field of study or a discipline for research.[25,26] In our study, we used CiteSpace for country/institution/author collaboration network analysis, co-citation analysis (as well as cluster analysis), and journal bipartite graph overlay analysis to gain a more comprehensive understanding of the knowledge structure of the field and the direction of research.[27] The minimum burst duration was set at 1 year. The time slices were 1 year each from January 2010 to August 2022. The *"Selection Criteria"* was set to *"g-index"* where k = 25, *"Pruning"* was selected as *"Pruning sliced networks,"* and other parameters were set to default values. To identify the important pivot points in a domain, we manually clicked *"Compute Node Centrality"* in the menu to calculate the centrality of each node; nodes with centrality >0.1 were considered to have a pivotal role in the network.

Results

Distribution of publications and citations

After literature selection, 3,104 publications were obtained from the WoSCC, including 2,571 articles (82.83%) and 533 reviews (17.17%). As of December 31, 2024, all the literature had been cited 99,567 times (84.303 times without self-citations), with an average of 32.08 citations per article. These publications were from 82 countries/regions, 415 institutions, 604 journals, and 762 authors. As shown in Figure 2, the number of published articles and citation frequencies have been increasing annually since 2014, with a noticeable surge occurring from 2019 to 2021. Over the past 10 years, the research has received increasing academic attention, maintaining high publication levels over the last five years. Meanwhile, the upward trend slowed between 2021 and 2022, but regained its growth momentum after 2022.

Distribution of countries/regions

All publications are distributed in 82 countries and regions. Immune-related studies in TNBC are mainly concentrated in China, the USA, and European countries (Figure 3a). We have ranked the top 10 high-output countries and regions by the number of publications (Table 1). The top three countries in terms of the number of articles published in this field are China, the USA, and Italy. In addition, the cooperation network analysis in Figure 3b shows that the most frequent cooperation occurred between the USA and China, followed by the USA and Japan. Next, we used VOSviewer software to create a citation density map (Figure 3c), where the red color signifies a higher number of citations for the literature published by each country. The closer the countries are to each other, the more frequently they have collaborated. Notably, the USA has shown exceptionally high activity in this field. In addition, we used Citespace to visualize and analyze the centrality of each country and region. As shown in Figure 3d, the circle size represents the volume of publications and the connecting curves represent the intensity of collaboration. The difference is that the color inside the circle represents the time from 2014 to 2024 when the literature was published, the cooler colors represent the earlier time, the warmer colors represent closer to the current time, and the purple outer circle represents centrality. The result shows that the USAhas higher centrality of research results, indicating that it is more significant and influential in this field. In

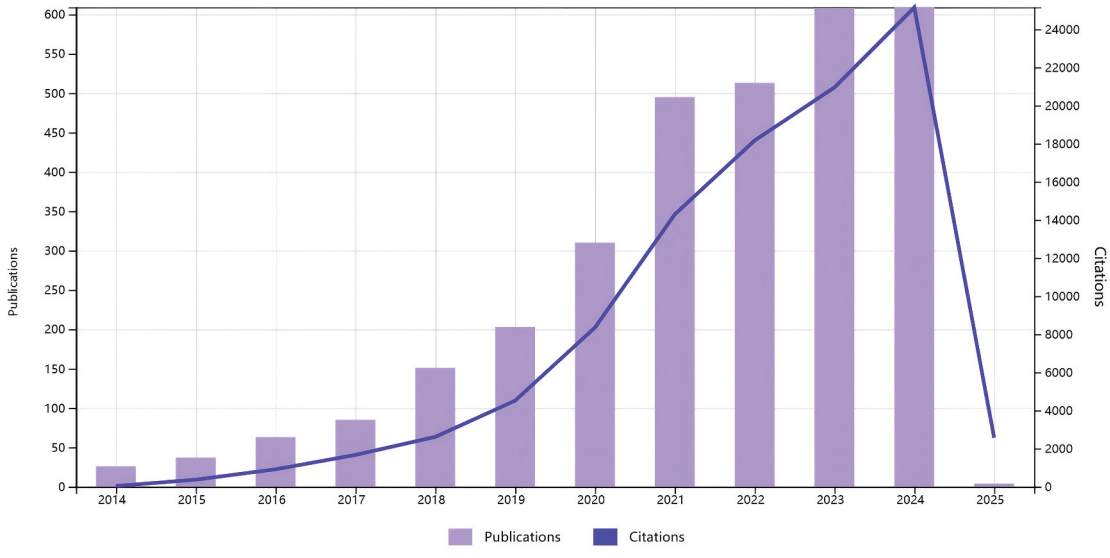

Figure 2. Trends in the annual number of publications and citations.

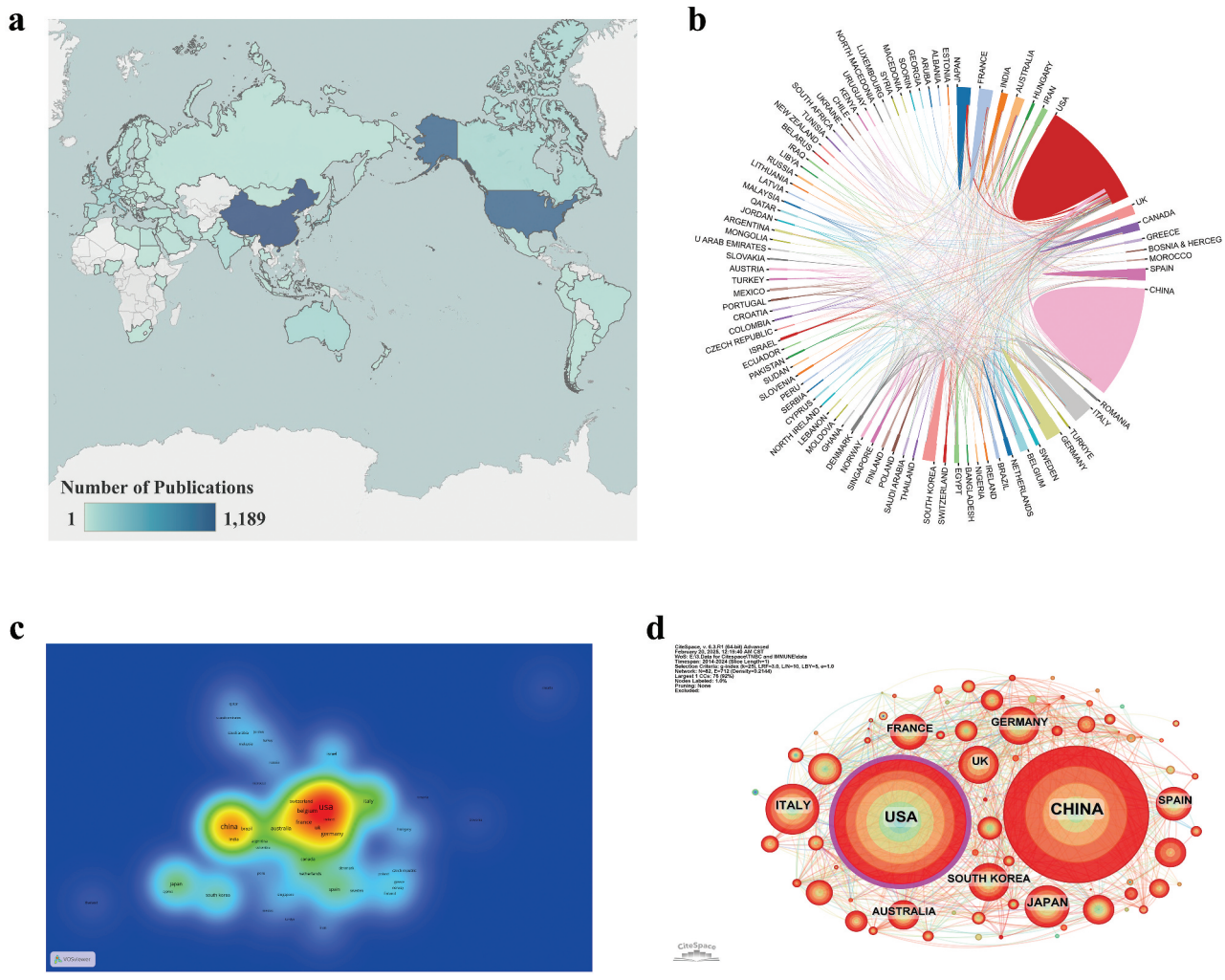

Figure 3. Contributions of different countries and regions to publications. (a) Geographic map of research countries and regions. (b) The network map of collaboration between countries/regions. (c) Cooperation network visualization between countries and regions. (d) Centrality visualization between countries and regions.

addition, the results show that compared with the United States, China's research results are mainly concentrated in recent years, while the United States, Germany and other countries have a lot of research results in earlier years. In recent years, the number of published articles in China has increased rapidly year by year, and the growth momentum is getting stronger and stronger, while the number of published articles in the United States and other countries has shown a slow growth trend. China's rapid growth in TNBC and immunology has helped to raise the level of research in this field globally.

Visual analysis of the institutions

We performed a visual analysis of the research institutions in this field and listed the top 10 research institutions in terms of the number of publications in Table 1. The *Fudan Univ* (97 articles) from China is the leading institution, followed by *Chinese Acad Sci* (80 articles) from China and *Dana Farber Canc Inst* (67 articles) from the USA. The size of the nodes represents the number of papers issued by the institution, and the connection lines between the nodes indicate the frequency of cooperation. The most influential institutions in the study have purple outer rings (Figure 4a). The top 10 institutions

Table 1. The top 10 high-output countries/regions and institutions.

Rank	Countries/Regions	Number of publications	Centrality	Institution	Number of publications	Centrality
1	China	1189	0.04	Fudan Univ	97	0.06
2	USA	1023	0.37	Chinese Acad Sci	80	0.05
3	Italy	199	0.08	Dana Farber Canc Inst	67	0.05
4	Japan	150	0.06	Univ Texas MD Anderson Canc Ctr	66	0.11
5	UK	148	0.07	Sun Yat Sen Univ	65	0.06
6	Germany	145	0.03	Harvard Med Sch	64	0.03
7	France	132	0.08	Univ Milan	57	0.03
8	South Korea	129	0	Zhejiang Univ	56	0
9	Australia	111	0.07	Shanghai Jiao Tong Univ	50	0.02
10	Spain	98	0.05	China Med Univ	49	0.04

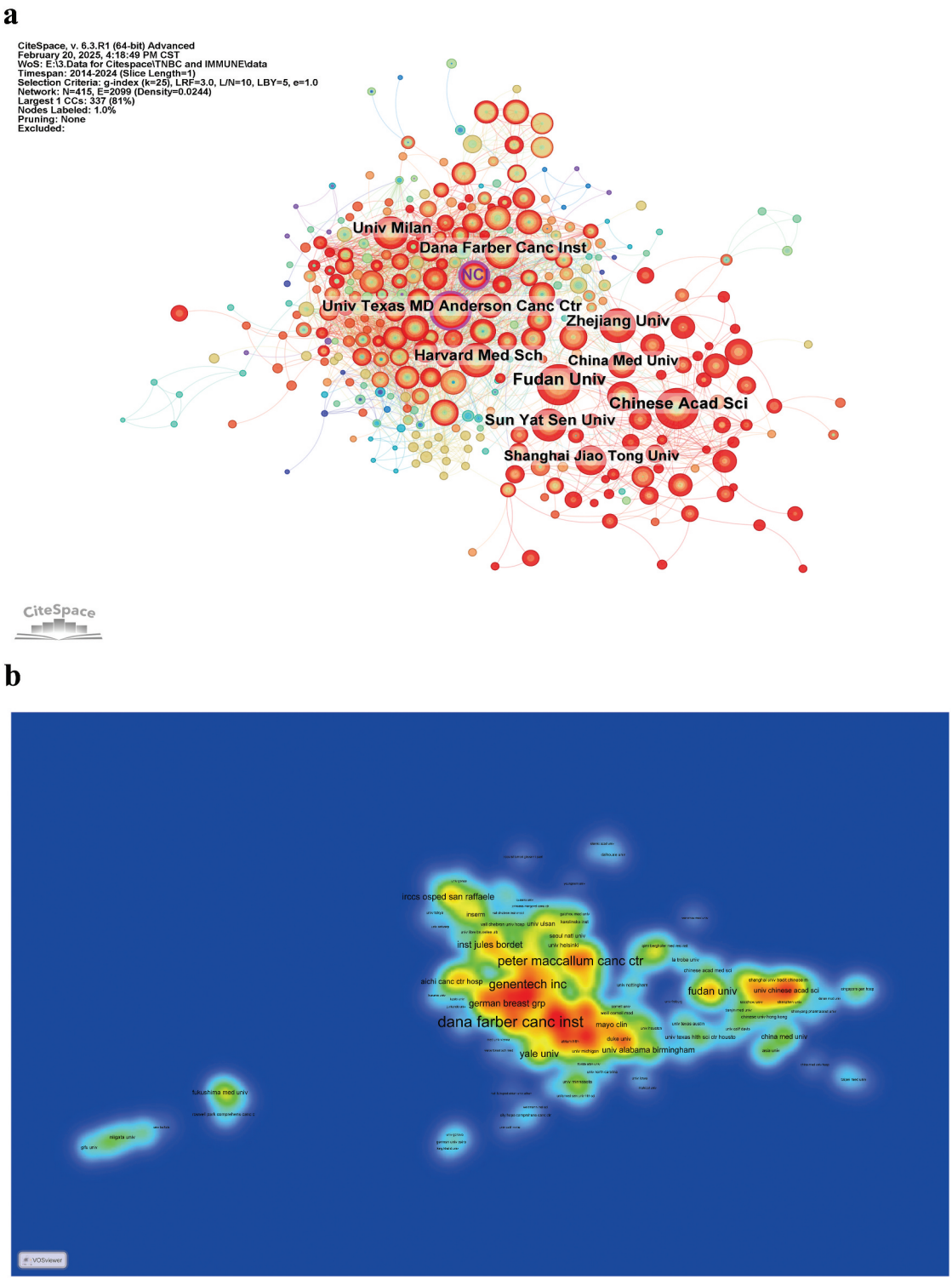

Figure 4. Contributions of different institutions to publications. (a) Cooperation network visualization between institutions. (b) Density map of institutions.

with the frequency of cooperation are marked with black text, and the number of NCI publications is not in the top 10, but it still has a purple outer ring. This indicates the high impact of *MD Anderson Cancer Center* and *NCI* research results and the frequency of collaboration with other institutions around the world at the center of the global collaboration network. Besides, Figure 4b is a density graph of cooperation between institutions, where the red color signifies higher intensity of cooperation between institutions. Although *Fukushima Medical University* from Japan has 32 publications, it has few collaborations with other countries around the world, and most of the collaborating institutions are in Japan; thus, it is in a relatively marginal position in Figures 4a,b. In addition, the results show that compared with the USA, many institutions in China are mainly focused on the year 2022–2024, while the number of research institutions in the USA is

relatively more balanced. In some European countries, the peak occurred around 2020, but it has decreased in recent years. This difference may be related to funding input, policy adjustments, and different countries' research priorities in the field of TNBC. The rapid growth in the number of publications published by Chinese research institutions has promoted the academic influence of TNBC immunotherapy. However, despite the increasing contribution of China in TNBC-related research, it is still necessary to strengthen research depth and innovation through cooperation with the USA and other countries to further improve the international recognition of TNBC treatment strategies and clinical conversion efficiency.

Visual analysis of authors and co-cited authors

The collaborative network of authors allows the comparison of authorship volume between authors and shows the intensity of collaboration between authors.[28] Co-cited authors refer to two or more authors who are cited together by another paper or papers, constituting a co-citation relationship. Co-citation authorship analysis can be used to find influential authors in a specific field. It can reveal the authors' papers that are often cited together.[29] In our analysis, 947 authors and 40,395 co-citations were associated with the role of immunity in TNBC. As shown in Table 2, *Lajos Pusztai* of *Yale-New Haven Hospital* had the most publications in this field ($n = 34$), followed by *Kazuaki Takabe* ($n = 31$), *Zhi-Ming Shao* ($n = 30$), *Masanori Oshi* ($n = 29$), and *Sherene Loi* ($n = 28$). Among the top 10 co-cited authors, *Peter Schmid* (n = 1,004) was the most cited author, followed by *Carsten Denkert* ($n = 650$) and *Sherene Loi* ($n = 645$).

Figure 5a shows the collaboration network among authors: node size represents the number of published papers, and line thickness indicates the intensity of collaboration. Cool circles and lines indicate early publication and collaboration, warm circles and lines indicate recent publication and collaboration. The top 10 authors who publish and actively collaborate with other countries and institutions were identified. Figure 5b demonstrates the co-citation relationship: node size represents the total citation frequency, and line thickness represents the co-citation intensity. The cool color line indicates early co-citation, and the warm color line indicates recent co-citation. A total of 25 authors with more than 200 citations were identified. Lajos Pusztai, Zhi-Ming Shao, Sherene Loi, Roberto Salgado, Sara M Tolaney and Giuseppe Curigliano not only publish a large number of articles, but also maintain frequent collaboration with other authors. Zhi-Ming Shao's coauthors, from Fudan University in China, are primarily based in China, while the other five researchers are at the center of a global collaboration network. In contrast, authors like Kazuaki Takabe and three others are positioned at the periphery of the collaboration network and rarely cooperate with other major researchers worldwide.

Visual analysis of journals and co-cited journals

To search for the most productive and influential journals, we used VOSviewer to visualize published journals on TNBC concerning immunity. The results showed that 3,104 articles were published in 604 academic journals. As shown in Table 3, *Cancers* (145 articles, impact factor (IF): 4.5003) published the most articles in this field, followed by *Frontiers in Oncology* (109 articles, IF: 3.5000) and *Frontiers in Immunology* (98 articles, IF: 5.6998). Among the top 10 journals in terms of the number of publications, 8 of them were in the Q1 division of the Journal Citation Report (JCR 2024), and 2 had an IF of more than 10, the highest being *Cancer Research* with an IF of 12.5001 (Table 3). The analysis of journal co-citations shows the contribution and influence of each journal to the field. Among the 6,862co-cited journals, 6 journals had more than 4,000 citations. As shown in Table 3, the *Journal of Clinical Oncology* had the most citations (citation: 6,862, IF: 42.1006), followed by *Clinical Cancer Research* (citation: 5,623, IF: 9.9995) and *Annals of Oncology* (citation: 5,336, IF: 56.6983). According to the JCR 2024, 90% were in Division 1 of the JCR, excluding *Breast Cancer Research and Treatment* (Q2). The dual-map overlay of journal analysis is a visual analysis method used to analyze, compare, and contrast the thematic connections between citing journals and cited journals.[30] The method introduces a dual-map topic overlay design on the global scientific map that visualizes the distribution of journals across topics, citation links, and central themes of research in a particular field.[30,31] Figure 6 shows a dual-map overlay regarding TNBC and immune-related journals published between 2014 and 2024. The left side is the citing map while the right side is the cited map. Each colored curve starts from a topic in the citation chart and points to a topic in the cited chart, and curves with the same starting point and same landing point converge. The colors of the curves represent different categories, and the thicker the

Table 2. The top 10 authors and co-cited authors.

Rank	Author	Count	Centrality	Co-cited author	Co-citations	Centrality
1	Lajos Pusztai	34	0.04	Peter Schmid	1,004	0.02
2	Kazuaki Takabe	31	0	Carsten Denkert	650	0.03
3	Zhi-Ming Shao	30	0	Sherene Loi	645	0.04
4	Masanori Oshi	29	0	Sylvia Adams	620	0.02
5	Sherene Loi	28	0.01	Elizabeth A Mittendorf	566	0.05
6	Roberto Salgado	27	0.02	Leisha A Emens	561	0.04
7	Sara M Tolaney	25	0.01	Brian D Lehmann	547	0.05
8	Giuseppe Curigliano	23	0.01	Giampaolo Bianchini	501	0.02
9	Li Yan	23	0	Rita Nanda	458	0.02
10	Itaru Endo	20	0	Javier Cortes	445	0.01

Figure 5. Visualization map of research authors. (a) Cooperation network visualization between authors. (b) Co-citation analysis network of co-cited authors.

curve, the stronger the citation relationship between the two topics. In the citing map, the more papers a journal has in the field, the longer the vertical axis of the ellipse, while the more authors, the longer the horizontal axis of the ellipse.[30] Figure 6 shows that articles published in molecular/biology/genetics journals were frequently cited by molecular/biology/immunology and medicine/medical/clinical journals.

Table 3. The top 10 journals and co-cited journals.

Rank	Journal	Count	JCR	IF (2024)	Co-cited journal	Citation	JCR	IF (2024)
1	Cancers	145	Q1	4.5003	Journal of Clinical Oncology	6,862	Q1	42.1006
2	Frontiers in Oncology	109	Q2	3.5000	Clinical Cancer Research	5,623	Q1	9.9995
3	Frontiers in Immunology	98	Q1	5.6998	Annals of Oncology	5,336	Q1	56.6983
4	International Journal of Molecular Sciences	68	Q1	4.9000	Cancer Research	5,302	Q1	12.5001
5	Scientific Reports	59	Q1	3.8001	New England Journal of Medicine	4,423	Q1	96.1978
6	Breast Cancer Research and Treatment	57	Q2	2.9997	Nature	4,187	Q1	50.5012
7	Journal for Immunotherapy of Cancer	52	Q1	10.3005	Breast Cancer Research and Treatment	2,979	Q2	2.9997
8	Breast Cancer Research	48	Q1	6.1004	Cell	2,776	Q1	45.4993
9	Clinical Cancer Research	48	Q1	9.9995	Nature Communications	2,756	Q1	14.7007
10	Cancer Research	38	Q1	12.5001	PNAS	2,619	Q1	9.4006

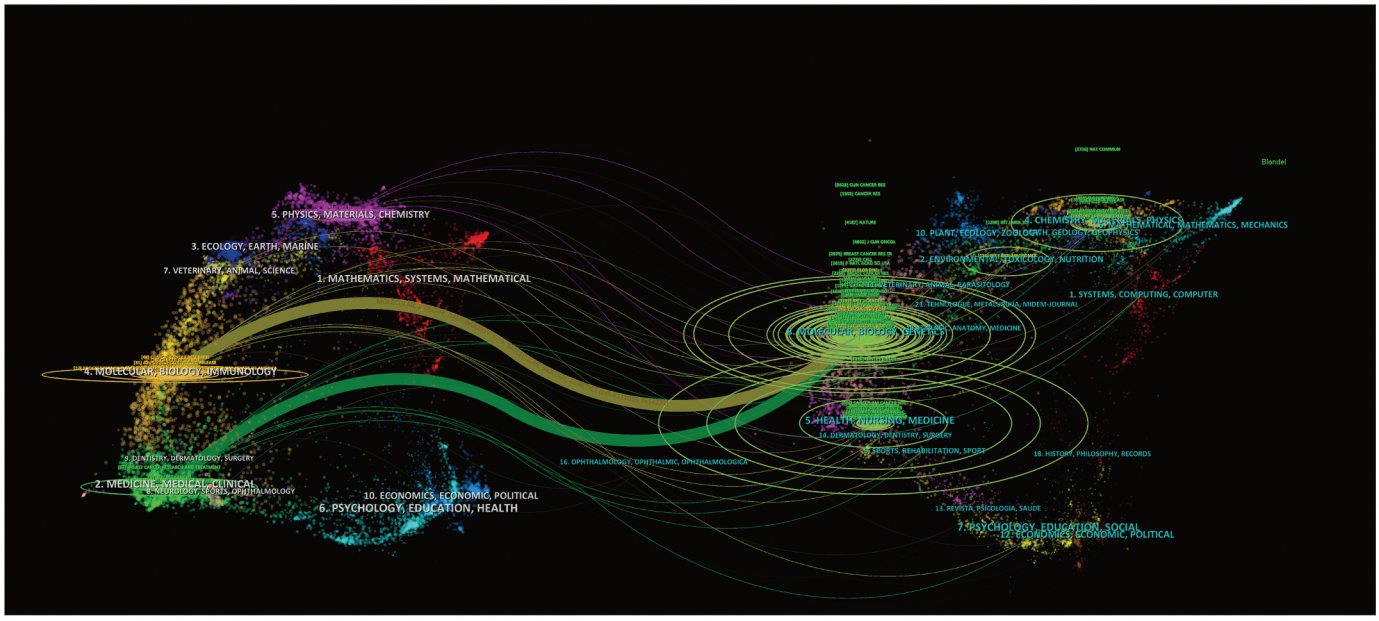

Figure 6. The dual-map overlay of journals.

Visual analysis of co-cited references

The top 10 co-cited references are listed in Table 4. All the 10 references have a JCR division of Q1, indicating the high quality and impact of co-cited references for studies on TNBC and immunity. The first author of the most co-cited reference was *Peter Schmid*, which had a co-citation of 540. The following article, also authored by *Peter Schmid*, as the first author, comes next in citation count. Notably, *Peter Schmid* contributed to three-tenths of the top 10 co-cited references, two of which were published in the *New England Journal Of Medicine* (Q1, IF: 96.1978) and one in *Lancet Oncology* (Q1, IF: 41.6016). The Citespace software was used to visualize the co-citation of references (Figure 7a), and there are 10 co-citation clusters (Figure 7b). The node size represents the number of co-citations of the reference, with the higher the number of co-citations, the larger the node. The connecting lines between the nodes represent the co-citation relationship between the two references. The more the two references are cited together, the higher the co-citation intensity and the thicker the lines. The colors of the nodes and connecting lines represent the time when the co-citation relationship occurred, with cooler colors representing earlier co-citation relationships and warmer colors representing more recent co-citation relationships. The clusters were listed from 2014 to 2024: *"systematic review"* (Cluster 0), *"pd-l1 expression"* (Cluster 1), *"tumor-infiltrating lymphocyte"* (Cluster 2), *"b cell"* (Cluster 3), *"new therapeutic strategies"* (Cluster 4), *"targeted therapy"* (Cluster 5), *"pd-l1 testing"* (Cluster 6), *"learning model"* (Cluster 7), *"favorable tumor"* (Cluster 8), *"cart-t cell therapy"* (Cluster 9), *"ido inhibitor"* (Cluster 10) and *"isocitrate dehydrogenase"* (Cluster 13). Of note, three references of *Peter Schmid* have been frequently cited together with other articles in the last five years, which also confirms his significant contribution to the study of TNBC and immunity. This finding is consistent with the results of the analysis of co-cited authors.

Visual analysis of keyword co-occurrence

Keywords are standardized terms from titles and texts, which are used to elaborate on the subject of the literature, as well as to make information easier to save and disseminate.[32] In studying the structure of a collection of literature, keywords can be used to accurately identify research frontiers and

Table 4. The top 10 co-cited references.

Rank	Title	Publication year	Co-citations	Source	JCR
1	Atezolizumab and Nab-Paclitaxel in Advanced Triple-Negative Breast Cancer	2018	540	New England Journal Of Medicine	Q1
2	Pembrolizumab for Early Triple-Negative Breast Cancer	2020	360	New England Journal Of Medicine	Q1
3	Pembrolizumab plus chemotherapy versus placebo plus chemotherapy for previously untreated locally recurrent inoperable or metastatic triple-negative breast cancer (KEYNOTE-355): A randomized, placebo-controlled, double-blind, phase 3 clinical trial	2020	320	Lancet	Q1
4	Atezolizumab plus nab-paclitaxel as first-line treatment for unresectable, locally advanced or metastatic triple-negative breast cancer (IMpassion130): updated efficacy results from a randomized, double-blind, placebo-controlled, phase 3 trial	2020	274	Lancet Oncology	Q1
5	Tumour-infiltrating lymphocytes and prognosis in different subtypes of breast cancer: A pooled analysis of 3771 patients treated with neoadjuvant therapy	2018	272	Lancet Oncology	Q1
6	Pembrolizumab monotherapy for previously treated metastatic triple-negative breast cancer: Cohort A of the phase II KEYNOTE-086 study	2019	254	Annals Of Oncology	Q1
7	Neoadjuvant atezolizumab in combination with sequential nab-paclitaxel and anthracycline-based chemotherapy versus placebo and chemotherapy in patients with early-stage triple-negative breast cancer (IMpassion031): A randomized, double-blind, phase 3 trial	2020	244	Lancet	Q1
8	Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries	2021	238	CA: A Cancer Journal for Clinicians	Q1
9	Long-term Clinical Outcomes and Biomarker Analyses of Atezolizumab Therapy for Patients With Metastatic Triple-Negative Breast Cancer: A Phase 1 Study	2019	228	JAMA Oncology	Q1
10	Pembrolizumab in Patients With Advanced Triple-Negative Breast Cancer: Phase Ib KEYNOTE-012 Study	2016	214	Journal Of Clinical Oncology	Q1

hotspots. In addition to the search terms, the total keywords (including author keywords and added keywords) extracted from the 3,104 publications were analyzed by VOSviewer software. A total of 8,308 keywords were extracted, 34 of which appeared more than 100 times. As seen in Figure 8 and Table 5, *"expression"* appeared most frequently with 1,694 occurrences, followed by *"immunotherapy"* ($n = 769$), *"tumor-infiltrating lymphocytes"* ($n = 442$), *"chemotherapy"* ($n = 431$), and *"survival"* ($n = 373$). In the keyword co-occurrence visualization graph, keywords are marked with different colors according to their average years of publications. As shown in Figure 8, the keywords *"tumor-infiltrating lymphocytes," "prognostic value," "neoadjuvant chemotherapy,"* and *"subtypes"* mainly appeared in the early years, while the keywords *"immunotherapy," "immune checkpoint inhibitors," "pd-l1,"* and *"tumor microenvironment"* mainly appeared in the recent years. Notably, the nodes *"tumor microenvironment," "paclitaxel," "pembrolizumab plus chemotherapy,"* and *"atezolizumab"* are in yellow, indicating that these areas have become increasingly popular in recent years and may become a hot topic in the future. Distinct from co-citation analysis, keyword co-occurrence analysis can reveal some new words, such as *"nanoparticles,"* and *"immunotherapy,"* which may also become a hot topic for future research.

Discussion

TNBC remains the most therapeutically challenging subtype of breast cancer due to its highly aggressive nature, high recurrence rate, high metastatic potential, and short overall survival. The role of immunity in TNBC, especially immunotherapy of TNBC, has received increasing attention in recent years with the development of immune checkpoint inhibitors for the treatment of solid tumors and the validation of TNBC immunogenicity. Due to the higher immunogenicity, TILs enrichment, and PD-L1 expression levels of TNBC, patients with TNBC can benefit from immunotherapy. Therefore, it is necessary to understand the immunotherapy methods for TNBC and conduct further in-depth studies. Based on more than a decade of research on the role of immunity in TNBC, we conducted the bibliometric analysis of the knowledge base and structure of the field to clarify the evolutionary trends of knowledge in this field. In this study, we primarily used Citespace and VOSviewer to evaluate the collaborative network maps of countries and regions, institutions, and authors from 3,104 retrieved articles. Subsequently, we derived the subject knowledge migrations trajectories by overlaying the journal biplot analysis. Finally, we derived the knowledge base and structure and research hotspots on the role of immunity in TNBC at various periods through literature co-citation and keyword co-occurrence analysis.

From the analysis of the trend of publication, it can be seen that from 2019 to 2021 and after 2022, the number of literatures and the frequency of citations have accelerated significantly, while the growth rate has slowed down significantly between 2021 and 2022. The large increase in literature around 2019 May be attributed to significant advances within the field of research and increased academic attention to breast cancer research. However, the COVID-19 outbreak in late 2019 appears to have led to a temporary disruption in research activities and a slowdown in the publication process. While the pandemic has led to an increase in research in some related fields, some non-epidemic-related areas of research may have been adversely affected. After 2022, as the impact of the epidemic gradually subsided, the growth rate of this field resumed and continued the rapid development trend of pre-epidemic research.

Regarding the map of scientific contributions and collaboration networks by country and region, China, the USA, and Italy are the top three high-producing countries. The American sociologist *Freeman L.* (*Freeman, 1979*) proposed the index "*betweenness centrality*" to measure the centrality of

Figure 7. Network visualization map of cited references. (a) Co-citation network of references. (b) Cluster analysis of references.

a node in a graph relative to other nodes, which is mainly used to measure the value of the bridge function of a node in the whole network structure and can be used to assess its influence in the whole set of nodes.[33,34] The USA has the highest centrality (0.37), and it plays a key bridging role in the worldwide network of country cooperation. Compared to the USA, China

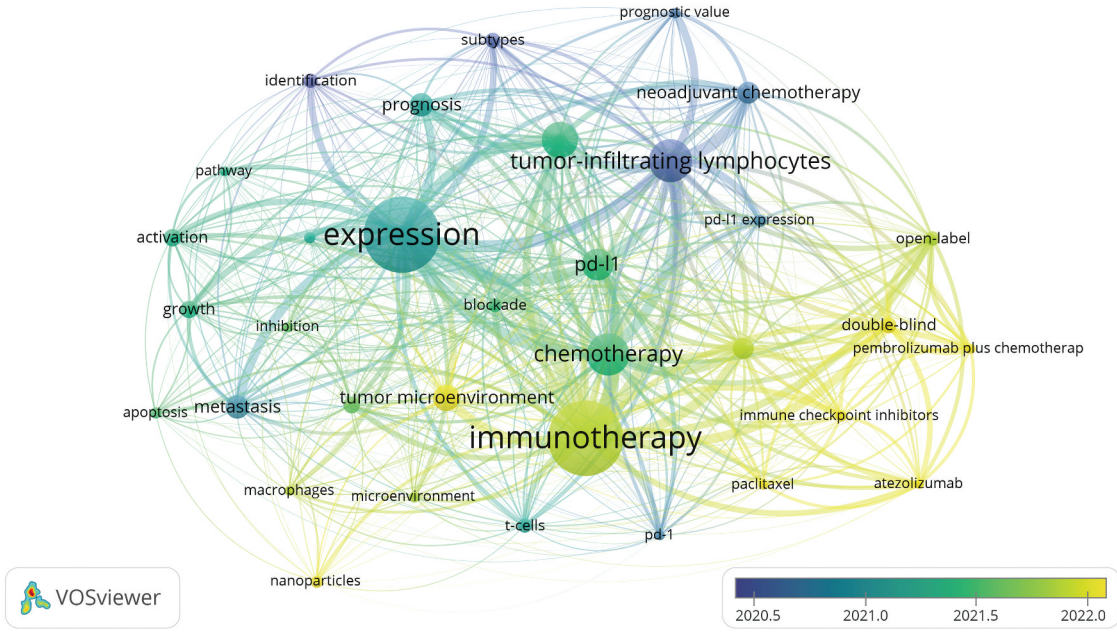

Figure 8. Visual analysis of keyword co-occurrence. Different colors of the nodes and connecting lines indicate the average year of keyword co-occurrence according to the bar on the bottom right corner.

Table 5. The top 30 keywords.

Rank	Keyword	Occurrences	Total link strength	Rank	Keyword	Occurrences	Total link strength	Rank	Keyword	Occurrences	Total link strength
1	expression	770	1,694	11	pembrolizumab	214	762	21	pd-l1 expression	123	430
2	immunotherapy	769	1,844	12	growth	181	387	22	nanoparticles	122	173
3	tumor-infiltrating lymphocytes	442	1,354	13	activation	180	394	23	immune checkpoint inhibitors	121	462
4	chemotherapy	431	1,146	14	resistance	169	400	24	apoptosis	117	208
5	survival	373	936	15	double-blind	163	647	25	receptor	117	278
6	pd-l1	321	921	16	subtypes	157	413	26	microenvironment	114	274
7	tumor microenvironment	270	583	17	open-label	150	572	27	prognostic value	113	315
8	prognosis	242	520	18	t-cells	150	385	28	inhibition	112	250
9	metastasis	241	491	19	identification	147	318	29	atezolizumab	106	486
10	neoadjuvant chemotherapy	224	625	20	blockade	142	412	30	pembrolizumab plus chemotherapy	105	431

has a higher number of publications but lower centrality, which is due to the large number of papers published in China alone, resulting in poor centrality. Next, concerning the research contributions of institutions and the collaborative network map, the top 10 institutions are from three countries, China, the USA, and Italy. The *Univ Texas MD Anderson Canc Ctr* ranked fourth in terms of the number of published papers, but it was the only one among these 10 institutions whose centrality was greater than 0.1(0.11). Although the number of publications of *NCI* did not rank among the top ten, its centrality index reached 0.1. In contrast, although *Fudan Univ* ranks first in terms of the number of published papers (97), its centrality is less than 0.1(0.06). Notably, despite its late start (2018), *Chinese Acad Sci* was ranked second in terms of the number of publications (80) and forth in terms of centrality. Moreover, we found extensive collaborations between the *Dana-Farber Cancer Institute*, *Peter MacCallum Cancer Center*, and other institutions, highlighting their great contribution to the study of the role of immunity in TNBC. In contrast, *Fukushima Medical University* from Japan has developed a certain scale of publications, but it remains spatially distant from the global collaborative network, indicating that its research lacks extensive global collaboration and ought to strengthen it. In addition, we observe that although China's research institutions started late compared to Europe and the United States, they are growing fast. This trend can be attributed to China's rapid economic and technological development in recent years. However, we also note that the overall impact of China's research output remains relatively low. This may be due to the fact that most of the research results have only recently been published, and some valuable findings have not yet accumulated a large number of citations. At the same time, the substantial research output helps to enhance China's influence in the field of TNBC immunotherapy, further improving the country's TNBC diagnosis and treatment standards. The USA and China collectively account for 71.26% of global publications in this field. Their collaborations, such as large-scale clinical trials and extensive patient sample studies, provide a solid foundation for deeper research efforts. This cooperation contributes to improving TNBC prognosis,

ultimately enhancing the quality of life for TNBC patients worldwide.

To identify the most prolific authors, we ranked authors according to their total number of publications on the role of immunity in TNBC and evaluated them in combination with other indicators.[35,36] Lajos Pusztai (34 articles) had the highest number of published articles, followed by Kazuaki Takabe (31 articles), *Zhi-Ming Shao* (30 articles), *Masanori Oshi* (29 articles), and *Sherene Loi* (28 articles). The analysis showed a relatively low centrality (≤0.01), which signifies the lack of communication and collaboration among authors in this field. The collaborative network map showed a dispersed distribution of researchers in this research area, and major researchers, such as *Masanori Oshi, Li Yan* and *Itaru Endo*, did not form a collaborative network, indicating lack of academic communication and collaborative research. Therefore, scholars worldwide should break down academic barriers and engage in more collaborations and exchanges to advance research on the development of immunity in TNBC. Among all cited authors, only *Peter Schmid* has a co-citation frequency exceeding 1000 times (1,004 times). Furthermore, our analysis indicates that Sherene Loi simultaneously ranked among the top ten in both rankings. *Sherene Loi et.al.* found that high levels of TILs were associated with a better prognosis in patients with TNBC, and immunomodulation could be a new treatment approach for TNBC.[37,38] This outstanding academic pioneer has provided a solid knowledge foundation for the subsequent researchers in this field.

Journal and co-citation journal analysis can provide a lot of information, which can help researchers to choose the right journal to submit their papers.[39] Our study found that publications in the top 10 most active journals accounted for about a quarter (23.26%) of all papers in this field, indicating a relative concentration of published research in this area. *Cancers* (145 articles) published the most articles, while the *Journal of Clinical Oncology* attracted the most co-citations. Both journals are about molecular biology and immunology, as well as clinical medicine, which is consistent with the double map overlay analysis. The journal biplot overlay analysis graph demonstrated two major citation paths from molecular/biology/genetics co-cited journals to molecular/biology/immunology journals and from molecular/biology/genetics co-cited journals to medicine/medical/clinical journals, implying that research related to the role of immunity in TNBC has evolved from molecular biology to clinical medicine.[40] We found that journals with IF > 8 accounted for the majority of the top 10 journals (30%) and co-cited journals (90%), indicating that these journals received more literature and contributed more to the scholarship in this field, which reminds scholars interested in this field to focus more on these journals.

Co-citation analysis of references helped us to find the most influential literature on the role of immunity in TNBC.[41] *Peter Schmid* contributed to three of the top 10 journals in terms of co-citation ranking. All three were clinical trials, two on the PD-L1 inhibitor atezolizumab and one on the programmed cell death protein 1 (PD-1) inhibitor pembrolizumab.[42–44] In addition, there was a study on TILs and TNBC prognosis. A large number of studies demonstrating the role of immunity in TNBC have heavily referenced PD-1/PD-L1 and immune checkpoint inhibitors, and it is foreseeable that a large number of studies will remain focused on PD-1/PD-L1 in the future.[45] Subsequently, keyword co-occurrence analysis can explore the hot spots and frontiers of research on immunity in TNBC. The keyword co-occurrence analysis is a further extension and expansion of the hotspots, and *"tumor microenvironment," "paclitaxel," "pembrolizumab plus chemotherapy,"* and *"atezolizumab"* are some of the most studied keywords in this field today. Unlike tumor cells, stromal cell types within the tumor microenvironment are genetically stable and are therefore an attractive therapeutic target to reduce the risk of drug resistance and tumor recurrence.[46] TNBC constitutes a highly diverse group of cancers, and the delineation of their subtypes is necessary to better define molecular-based therapies; thus, locating appropriate biomarker locus is extremely significant for TNBC[47]. Jindong Xie used multi-omics data for bioinformatics analysis and identified the disulfidptosis regulator, glycogen synthase 1 (GYS1) as a promising target for triple-negative breast cancer, which was validated through both in vitro and in vivo experiments.[15] Additionally, various immunotherapies such as immune checkpoint blockade, vaccination, and adoptive cell transfer have been extensively investigated in the clinical studies of TNBC.[16] The immune checkpoint inhibitors, pembrolizumab and atezolizumab, can block the PD-1/PD-L1 pathway and are already under investigation in phase III clinical studies.[47,48] Furthermore, we analyzed the research results in this field in different periods and found that in 2014, both *Sylvia Adams* and *Sherene Loi* verified that TILs are a reliable prognostic factor in TNBC and that higher TIL levels are significantly associated with a reduced rate of distant recurrence in primary TNBC.[49,50] Meanwhile, *Elizabeth A Mittendorf* demonstrated that PD-L1 was expressed in 20% of TNBC, suggesting PD-L1 as a potential therapeutic target for TNBC.[51] A large number of studies on immune checkpoint inhibitors have emerged in recent years, with pembrolizumab and atezolizumab receiving the most attention; clinical studies on their combination with other chemotherapeutic drugs are also becoming popular.[43,44,52–55] Clinical data show proof-of-principle studies on the use of immune checkpoint inhibitors in advanced TNBC, indicating the potential benefit of immunotherapy for patients with TNBC.[56] In the future, the discovery of more immune checkpoints and the translation of basic research results to the clinic will continue to be hot topics in this research field.

Keyword co-occurrence analysis shows that nanoparticles and immunotherapy may be future research hotspots. With the continuous progress of nanoparticle drug delivery technology, its application in tumors, especially triple-negative breast cancer, is becoming more and more widespread. As an emerging drug delivery technology, nanoparticles show great potential in immunotherapy. With their unique physicochemical properties, nanoparticles can improve the efficiency of the delivery of immunomodulatory molecules and tumor antigens while reducing systemic toxicity in conventional therapies.[57,58] Through rational design, nanoparticles can accurately target key cells in the tumor microenvironment, enhance the efficiency of antigen presentation and effectively activate T cells, thus significantly enhancing the effect of immunotherapy. In

addition, nanoparticles can be used as carriers to deliver immune checkpoint inhibitors, increasing their concentration at the tumor site and attenuating the immunosuppressive state in the tumor microenvironment, thereby improving therapeutic response.[59,60] More importantly, nanoparticles provide a multifunctional platform for immunotherapy, enabling multi-level synergies to enhance the overall effect of tumor immunotherapy by simultaneously loading immune adjuvants, anti-cancer drugs, and regulatory factors.[61,62] In the future, with the continuous progress of nanoparticle technology, its application in immunotherapy will further promote the development of personalized and precision therapy.

In a previous bibliometric study, which used TNBC and neoadjuvant therapy as keywords, the authors concluded that combination therapies, including immunotherapy, could represent the future direction for TNBC neoadjuvant treatment.[63] This study provided valuable insights into the current research landscape, the latest advances, and emerging trends in TNBC neoadjuvant therapy. Building on these findings, our study suggests that utilizing nanoparticles as carriers for immunotherapy combined with other drug treatments is likely to be a promising trend for future TNBC treatment strategies. In this study, we explicitly described and assessed the knowledge structure and dynamic evolution of the role of immunity in TNBC through bibliometric analysis and visualized knowledge maps. However, we need to acknowledge some limitations. The data were retrieved only from the WoSCC database, and some important articles published in other databases, such as Scopus, may have been missed. However, WoSCC is an authoritative and comprehensive database, which represents most of the information to some extent, and therefore is most often used as a data source for bibliometrics.[64,65] At the time of this study, new articles on the role of immunity in TNBC were still being published, resulting in omissions.

Conclusion

This study innovatively combined multi-omics data with cutting-edge bioinformatics methods to systematically analyze the key drivers and research hotspots in the field of TNBC immunotherapy. Through the introduction of dynamic cooperative network analysis, this study reveals the collaborative relationship between different countries, institutions and researchers and its evolution trend, and uses advanced co-occurrence analysis tools such as CiteSpace and VOSviewer to provide a panoramic view of the current research status in the field of TNBC immunotherapy, and deeply explore the potential scientific frontier. In particular, the rapid development of the emerging field of nanoparticle immunotherapy. This study summarized the main biomarkers related to TNBC immunotherapy and their clinical application potential, providing an important reference for precision treatment strategies, and comprehensively looking forward to future research directions. In the future, it is suggested to focus on the in-depth study of the interaction mechanism between tumor microenvironment and immune microenvironment, promote the clinical validation of nanoparticle delivery technology, strengthen international cooperation to improve research efficiency and universality, explore new methods of multi-omics data integration, use artificial intelligence and machine learning to explore new therapeutic targets and biomarkers, and promote the development of precision immunotherapy.

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Authors' contributions

KXC and LNC designed the manuscript; XDL drafted the manuscript; HR collected related data; CL conducted the bibliometric analysis; KXC and LNC revised the image and manuscript. All authors reviewed and approved the manuscript.

Availability of data and material

The dataset for this study can be found in the Web of Science (http://www.webofknowledge.com).

Ethical approval

Ethical approval and patient consent are not required since this is a bibliometric analysis based on published studies.

Informed consent

All analyses were based on previously published studies; thus, no informed consent is required.

Abbreviations

TNBC	triple-negative breast cancer
HER2	human epidermal growth factor receptor 2
TILs	tumor-infiltrating lymphocytes
PD-L1	programmed cell death ligand 1
WoS	Web of Science
SCI-Expanded	Science Citation Index-Expanded
WoSCC	Web of Science Core Collection
PD-1	programmed cell death protein 1

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