Article

Bibliometric and visual analysis of research on chemoresistance mechanisms in triple-negative breast cancer, 2015–2025

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Abstract

Objective: To characterize publication patterns, collaboration networks, and research themes in the literature captured by a predefined search on triple-negative breast cancer (TNBC) chemoresistance.

Methods: The Web of Science Core Collection (WoSCC) was searched for English-language articles and reviews published from January 1, 2015, to December 8, 2025. The query combined TNBC with cisplatin, paclitaxel, doxorubicin, or gemcitabine and terms related to chemoresistance and mechanisms. After screening, 212 records were analyzed using CiteSpace, VOSviewer, and the bibliometrix R package.

Results: Annual output increased from 5 publications in 2015 to 39 in 2025; 92 publications (43.40%) appeared during 2023–2025. China contributed 98 publications (46.23%) but had lower betweenness centrality (0.15) than the United States (0.34) and India (0.28). Oncology and biochemistry and molecular biology were the leading disciplines. Keyword and burst analyses identified persistent attention to chemoresistance, apoptosis, and signaling pathways, with recent activity in proliferation, gene expression, and phosphorylation. Nanomedicine and metabolism appeared as research themes, but the bibliometric data do not establish clinical efficacy.

Conclusion: TNBC chemoresistance research develops rapidly. Current studies focus on molecular mechanisms and novel therapies. This study constitutes an exploratory bibliometric analysis based on 212 records from the Web of Science Core Collection; however, it does not represent the entirety of the literature on chemotherapy resistance in TNBC. It is necessary to strengthen international cooperation. Its findings describe research activity rather than treatment effectiveness and should not be generalized to all TNBC systemic therapies.

Keywords: TNBC, chemoresistance, bibliometric analysis, drug resistance mechanism

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Introduction

Breast cancer is the most frequently diagnosed cancer in women worldwide and remains a leading cause of cancer mortality[1]. Triple-negative breast cancer (TNBC) is defined by the absence of estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 expression. It accounts for approximately 10–15% of breast cancers and is characterized by marked molecular heterogeneity, early recurrence, and limited subtype-specific treatment options [2,3]. Cytotoxic chemotherapy — principally anthracycline-, taxane-, and platinum-containing regimens — remains a major component of systemic treatment, although treatment choices vary by disease stage and biomarker status [4,5]. Intrinsic or acquired chemoresistance limits durable response and contributes to relapse and metastatic progression [5–9].

Bibliometric analysis quantitatively describes publication output, citation structure, collaboration, and thematic evolution. When transparently reported, it can complement—but does not replace — systematic reviews or clinical evidence synthesis [10,11]. CiteSpace and VOSviewer support co-citation, co-occurrence, and network mapping, whereas bibliometrix provides complementary descriptive analyses [11,12,16].

This study mapped the literature captured by a prespecified Web of Science search on TNBC chemoresistance from 2015 through 2025. This study applied bibliometric methodologies to systematically analyze and integrate research on the mechanisms of chemoresistance in TNBC. The results elucidate the current research landscape, major thematic concentrations, and emerging trends in this field. The scope was chemoresistance associated with four named cytotoxic agents (cisplatin, paclitaxel, doxorubicin, and gemcitabine). Immune-evasion and immunotherapy-related findings are discussed only when they intersect with mechanisms of response to cytotoxic treatment; resistance to immune- checkpoint inhibitors as an independent treatment category was not comprehensively searched and is outside the primary scope. The analysis therefore identifies patterns within the retrieved corpus rather than providing an exhaustive account of all treatment resistance in TNBC.

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Materials and Methods

Literature search and search strategy

The Web of Science Core Collection (WoSCC; https://www.webofscience.com) was searched using the following query: TS=(("triple negative breast cancer" OR TNBC) AND (cisplatin OR paclitaxel OR doxorubicin OR gemcitabine) AND (chemoresistance OR "acquired resistance") AND (mechanisms OR pathways)). Filters were document type (Article or Review), language (English), and publication date (January 1, 2015, to December 8, 2025). The search returned 267 records. One researcher conducted the preliminary screening, and uncertain records were resolved through discussion with a second researcher; 212 records met the eligibility criteria. It should be noted that this study did not employ an independent dual-reviewer screening protocol. Instead, one researcher conducted an initial screening of titles and abstracts to exclude records that clearly did not meet the inclusion criteria, including non-articles/reviews, non-English language documents, irrelevant studies, and records with incomplete bibliographic data; for records whose eligibility status was unclear, the first researcher consulted a second researcher, and a final consensus was reached through discussion. In this phase, a total of 55 records were excluded. Subsequently, an internal deduplication step was performed using CiteSpace, during which no duplicate records were identified (n=0).

These four cytotoxic chemotherapeutic agents (cisplatin, paclitaxel, doxorubicin, gemcitabine) were predefined as search entries in the initial study design. They represent the most commonly used first-line conventional chemotherapeutic agents for TNBC and were selected as core drugs in previously published bibliometric studies of TNBC chemoresistance. We acknowledge that this drug set excludes carboplatin, eribulin, capecitabine, antibody-drug conjugates and other newer agents, which inevitably restricts the scope of our corpus.

Inclusion and exclusion criteria

Eligible records were peer-reviewed research articles or reviews, written in English, published within the prespecified date range, and addressing TNBC chemoresistance or its mechanistic pathways within the operational search scope.

Records were excluded if they were duplicates; were unrelated to TNBC chemoresistance; lacked essential bibliographic information, such as author or institutional data; were conference proceedings, books, guidelines, news items, or other nonjournal material; or had been retracted.

Data processing and visualization analysis

Bibliographic records were imported into CiteSpace 6.4.R1, VOSviewer 1.6.20, and R with bibliometrix 5.2.1. Duplicate records were removed before analysis. Annual output, countries/regions, institutions, authors, journals, disciplines, references, and keywords were analyzed. Excel 2024 was used for data organization and line charts.

VOSviewer analyses used full counting. A similarity threshold of 0.1 was applied, and nodes with an occurrence frequency of at least 2 were retained for collaboration-network construction.

The CiteSpace output embedded in the manuscript documented a 2015–2025 time span with a 1-year slice length and g-index selection (k=25), with LRF=2.5, L/N=10, LBY=5, and e=1.0. Cosine similarity was used for link strength, and the displayed networks were generated without pruning. These settings were applied to the reported co-occurrence, co-citation, and collaboration visualizations.

In the visualizations, node size represents frequency, link thickness represents relationship strength, and node color indicates the time of occurrence. Nodes with betweenness centrality of at least 0.10 are highlighted by a purple rim. Modularity Q and weighted mean silhouette S were used to assess keyword-cluster structure.

International collaboration rate was calculated as the number of publications coauthored across countries divided by 212 and multiplied by 100%. Interinstitutional collaboration rate was calculated as the number of publications coauthored across institutions divided by 212 and multiplied by 100% (Figure 1).

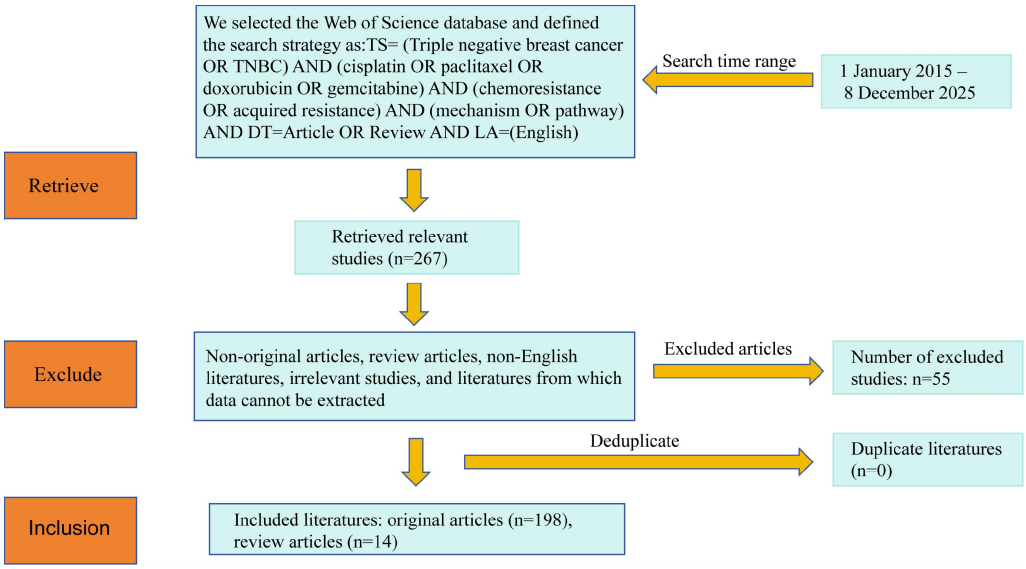

Figure 1. Study-selection flow diagram. The WoSCC search identified 267 records; 212 articles and reviews were retained after eligibility screening.

Results

Publication trends

The search identified 267 records, of which 212 articles and reviews published between 2015 and 2025 were retained (Figure 2). The annual number of publications has overall shown a sustained upward trend, with a marked acceleration in recent years. The 92 publications issued during 2023–2025 represented 43.40% of the 212-record corpus (Figure 2B), indicating a recent increase in publication activity.

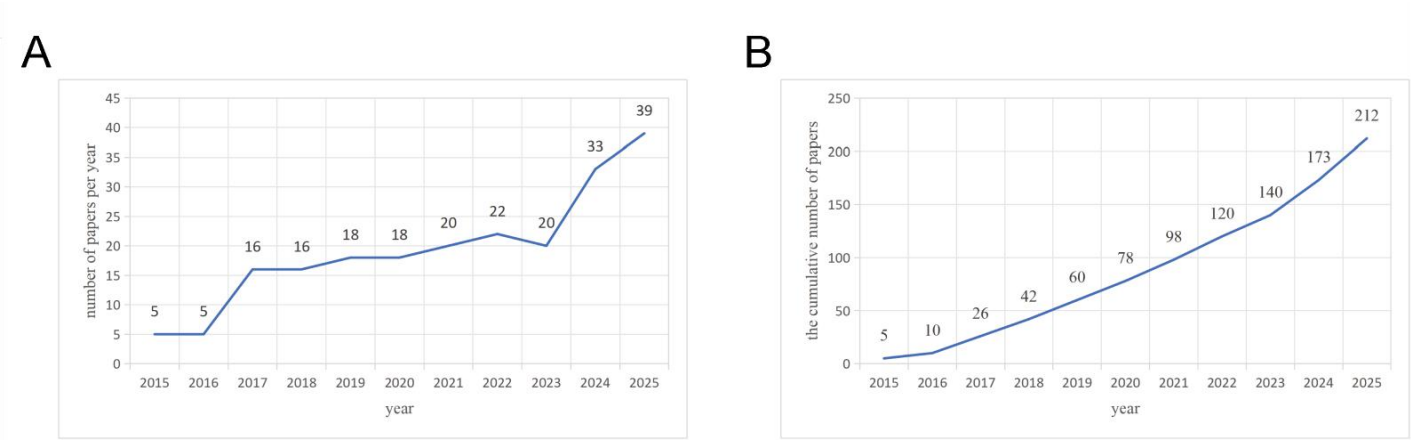

Figure 2. Annual and cumulative publication output in the 212-record corpus. (A) Annual publication count from 2015 to 2025. (B) Cumulative publication count, reaching 212 in 2025.

Disciplines and journals

The included publications span 32 disciplinary categories, among which oncology, biochemistry and molecular biology, and cell biology constitute the three core disciplines. Among these, biochemistry and molecular biology exhibit the highest betweenness centrality, indicating that it plays a pivotal bridging role in interdisciplinary integration (Figure 3). The records appeared in 126 journals, the top 10 journals by number of publications accounted for 21.69% of the total number of publications (Table 1). In the journal co-citation analysis, Cancer Research occupies a central position with the highest co-citation frequency (Figure 4).

Table 1. Top 10 journals by publication count and top 10 co-cited journals by citation count.

Rank	Journal	Count	IF/JCR	Rank	Cited Journal	Citations	Centrality	IF/JCR
1	Cancers	7	4.4/Q2	1	Cancer Research	158	0.03	16.6/Q1
2	Frontiers in Oncology	6	3.3/Q2	2	Oncogene	144	0.01	7.3/Q1
3	Cell Death & Disease	5	9.6/Q1	3	Clinical Cancer Research	116	0.03	10.2/Q1
4	International Journal of Molecular Sciences	4	4.9/Q1	4	Proceedings of the National Academy of Sciences of the United States of America (PNAS)	109	0.04	9.1/Q1
5	Cell Death Discovery	4	7.0/Q1	5	Oncotarget	108	0.02	5.1/Q2*
6	Oncotarget	4	5.1/Q2*	6	Journal of Biological Chemistry	99	0.02	3.9/Q2

Notes: The evaluation was based on the 2023 JCR. When multiple categories had inconsistent results in the JCR quartile, the result from the highest-ranked quartile was selected.

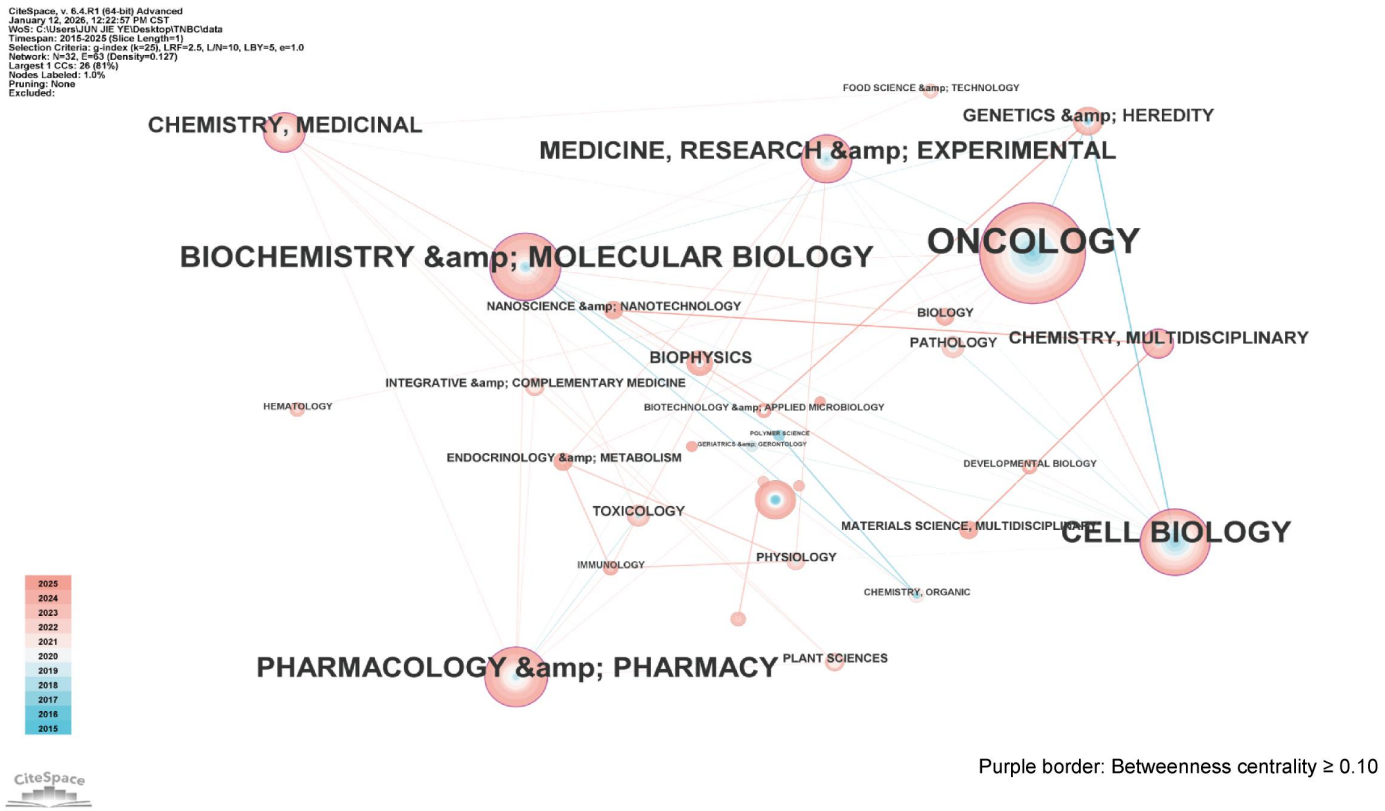

Figure 3. Co-occurrence network of discipline categories. Node size represents frequency, links represent co-occurrence or co-citation, and node colors indicate the year of occurrence.

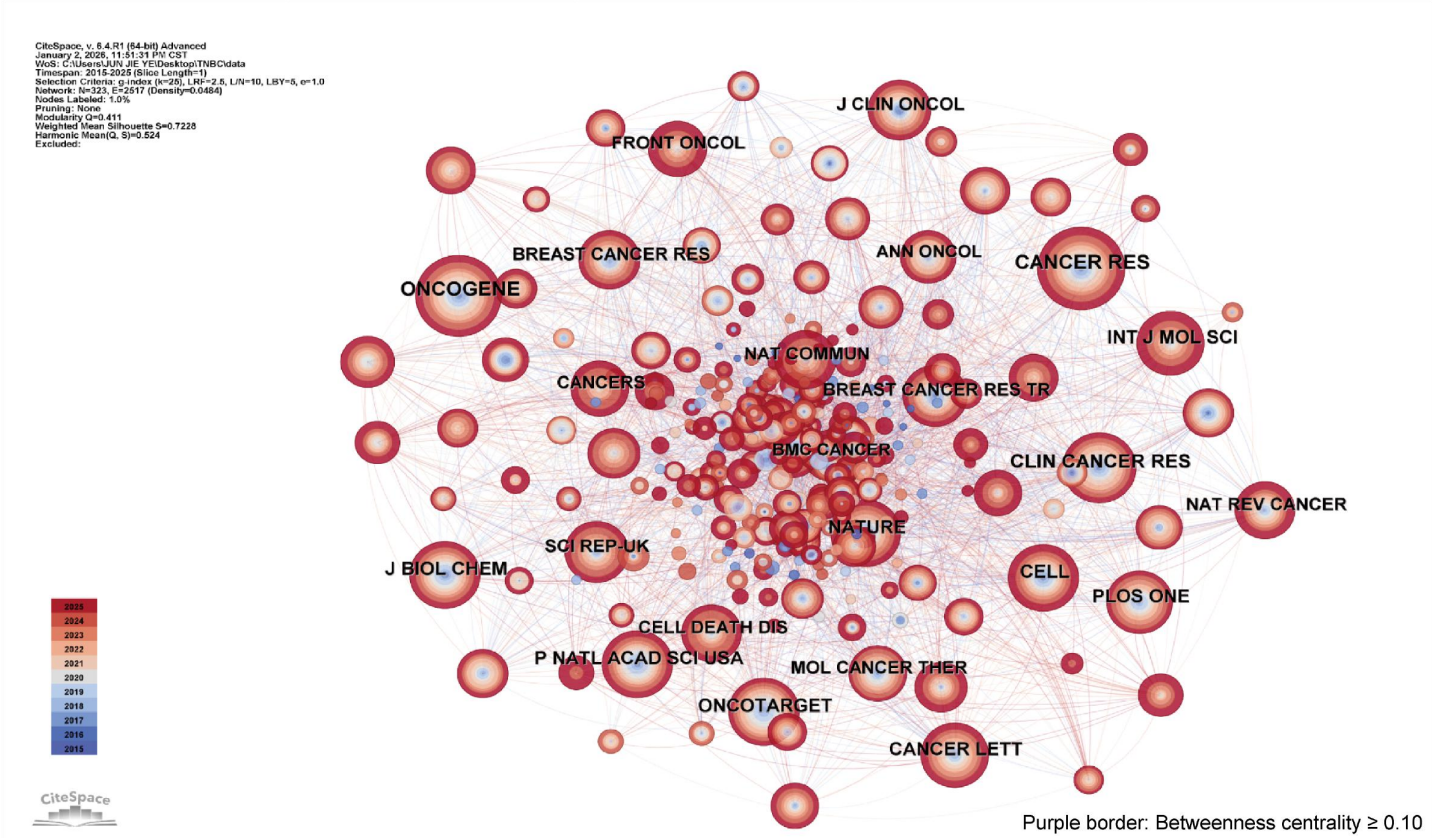

Figure 4. Journal co-citation network. Node size represents frequency, links represent co-occurrence or co-citation, and node colors indicate the year of occurrence.

Countries / Regions / Institutions / Authors / Collaborations

The 212 records included 1,724 authors from 422 institutional entries across 47 countries/regions. China contributed 98 records (46.23%), the United States 47 (22.17%), and India 17 (8.02%) (Table 2). Country/region labels were standardized for presentation; Taiwan is reported as Taiwan, China, while its counts and network metrics remain separate from those for mainland China because the original network was not rerun after geographic relabeling.

The country/region collaboration network contained 47 nodes and 92 links, with a density of 0.0851 (Figure 5). The United States (centrality 0.34), India (0.28), China (0.15), and England (0.12) had the highest betweenness centralities among the leading contributors (Table 3). China had the largest publication count, whereas the United States occupied the most central bridging position in the network.

Table 2. Top 10 countries/regions and authors by publication count.

Rank	Countries/regions	Count	Centrality	Rank	Authors	Count
1	China	98	0.15	1	Yaming Li	7
2	USA	47	0.34	2	Qifeng Yang	7
3	India	17	0.28	3	Wenjing Zhao	6
4	Italy	10	0.02	4	Yiran Liang	6
5	Canada	8	0.02	5	Dan Luo	5
6	Taiwan, China	7	0.00	6	Lijuan Wang	5
7	Germany	7	0.06	7	Bing Chen	4
8	Egypt	7	0.03	8	Dianwen Han	4
9	England	7	0.12	9	Shekhar, Malathy P	4
10	Spain	6	0.03	10	Yuhua Jin	2

Note: Taiwan is reported as Taiwan, China. Its publication count and centrality remain separate from mainland China because the original collaboration network was not recomputed after label standardization.

Table 3. Top 10 institutional entries by publication count.

Rank	Institutions	Count	Centrality
1	Chinese Academy of Sciences	6	0.00
2	Egyptian Knowledge Bank (EKB)	6	0.00
3	Harvard University	5	0.00
4	Central South University	5	0.00
5	Harbin Medical University	5	0.00
6	Barbara Ann Karmanos Cancer Institute	5	0.00
7	Fudan University	5	0.00
8	Harvard Medical School	4	0.00
9	Academia Sinica, Taiwan, China	4	0.00
10	Guangzhou University of Chinese Medicine	4	0.00

Note: Institutional names are shown as indexed in WoSCC. Affiliation variants, including Harvard University, Harvard Medical School, and Harvard University Medical Affiliates, were not merged; rankings and centrality values should therefore be interpreted as entry-level rather than organization-level metrics.

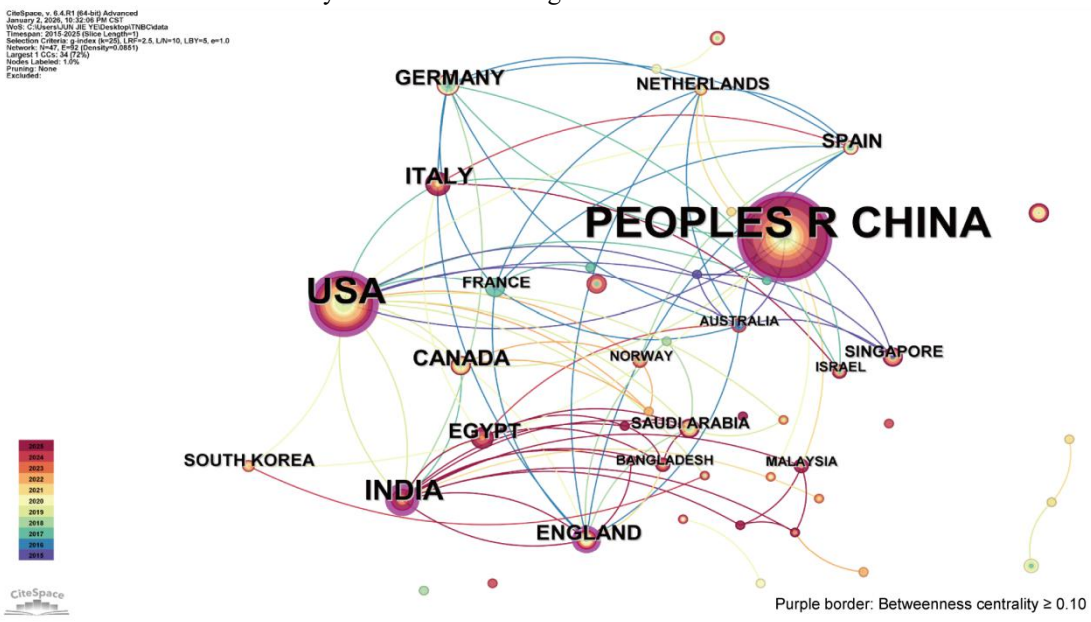

Figure 5. CiteSpace collaboration network. Node size represents publication count, links represent collaboration, colors indicate year, and purple rims denote betweenness centrality ≥0.10. Country/region names follow the normalized labels used in Table 3.

The largest bilateral publication count was observed between China and the United States (10 records, Figure 6). The network metrics describe connectivity but do not identify its causes. Nevertheless, the combination of high output and modest centrality suggests limited cross-network integration, which may reduce opportunities for independent replication, cross-population validation, and coordinated multicenter research.

At the institutional level, network density was 0.0163, and the 10 most productive institutional entries each had centrality reported as 0.00 (Table 3; Figure 7). These values do not support describing any institution as a coordinating hub. They may also be affected by unstandardized affiliation strings; for example, Harvard University, Harvard Medical School, and Harvard University Medical Affiliates appear as separate nodes.

The most productive institutional entries were the Chinese Academy of Sciences and Egyptian Knowledge Bank (EKB), with 6 records each (2.83%), followed by Harvard University, Central South University, and Harbin Medical University, with 5 records each (2.36%) (Table 3). These rankings reflect the affiliations as indexed in WoSCC and should not be interpreted as institution-level performance measures.

The most productive authors were Yaming Li and Qifeng Yang (7 records each; 3.30%), Wenjing Zhao and Yiran Liang (6 each; 2.83%), and Dan Luo and Lijuan Wang (5 each; 2.36%) (Table 2; Figure 8). Representative publications from these groups addressed noncoding RNA and endoplasmic-reticulum-stress mechanisms of chemoresistance [13,14]. The dispersed author network indicates that productivity was concentrated in small teams rather than a single field-wide collaboration hub.

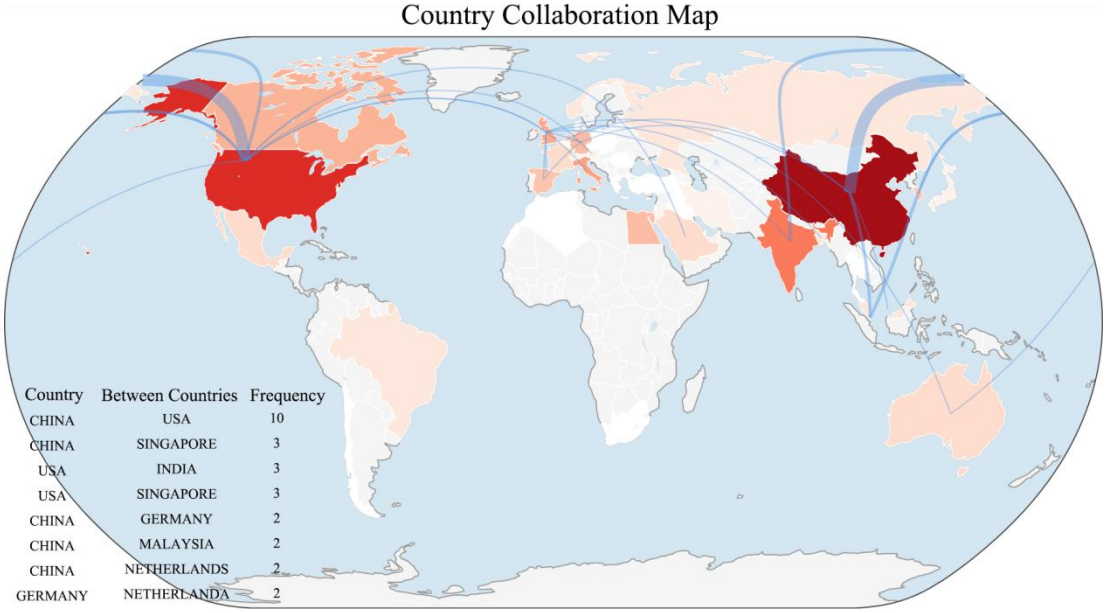

Figure 6. Geographic distribution of international collaboration.

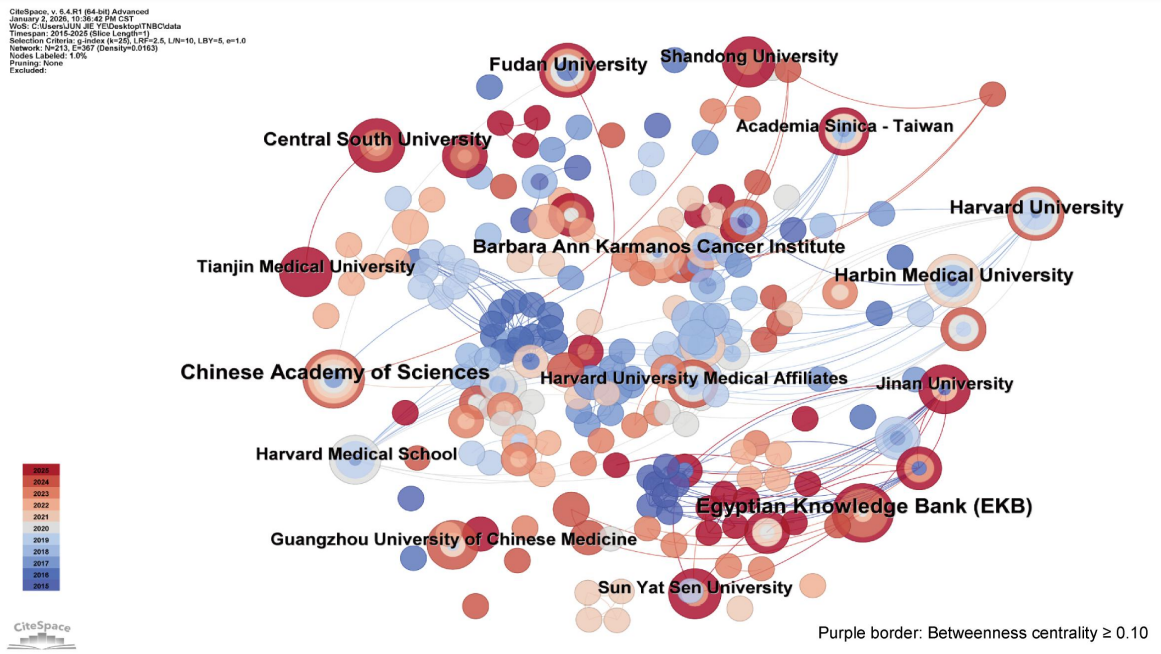

Figure 7. Institutional network based on affiliation entries as indexed in WoSCC. Institutional network based on affiliation entries as indexed in WoSCC.

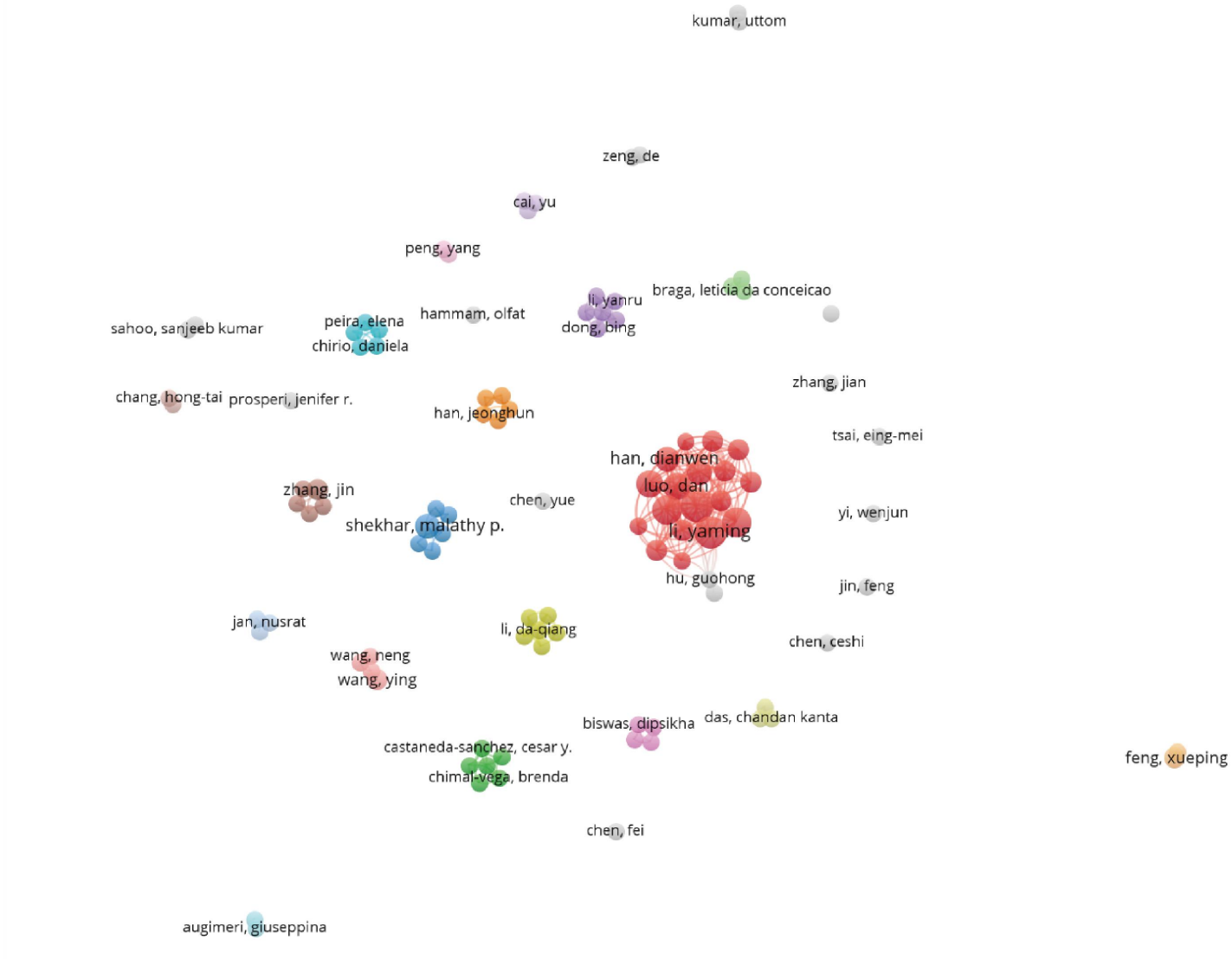

Figure 8. Author network.

Keyword analysis

The 30 most frequent keywords are listed in Table 4. The keywords revolve around disease phenotypes, chemotherapy resistance, and biological processes such as apoptosis, metastasis, and signaling pathway regulation. Ten keywords exhibited high centrality (≥ 0.10), forming the structural backbone of the research network (Table 4, Figure 9).

Ten keywords had betweenness centrality of at least 0.10: breast cancer (0.27), cells (0.19), drug resistance (0.18), chemoresistance (0.14), inhibition (0.14), apoptosis (0.13), pathway (0.11), metastasis (0.10), activation (0.10), and triple-negative breast cancer (0.10) (Figure 9). These values identify structurally connected terms within the corpus; they do not measure biological importance or therapeutic efficacy.

Table 4. Top 30 keywords by occurrence frequency.

Rank	Keywords	Count	Year	Centrality	Rank	Keywords	Count	Year	Centrality
1	expression	74	2015	0.07	16	doxorubicin	21	2018	0.09
2	TNBC	46	2018	0.09	17	pathway	20	2016	0.11
3	breast cancer	43	2015	0.27	18	therapy	17	2016	0.07
4	chemotherapy	41	2015	0.09	19	proliferation	14	2021	0.04
5	drug resistance	38	2015	0.18	20	multidrug resistance	14	2018	0.04
6	resistance	34	2017	0.08	21	stem cells	13	2016	0.02
7	cells	31	2015	0.19	22	paclitaxel	12	2017	0.06
8	apoptosis	30	2015	0.13	23	cisplatin resistance	12	2015	0.03
9	chemoresistance	27	2015	0.14	24	gene expression	11	2019	0.02
10	metastasis	26	2016	0.10	25	epithelial mesenchymal transition	11	2018	0.02
11	inhibition	26	2015	0.14	26	growth	11	2015	0.08
12	activation	26	2016	0.10	27	identification	9	2015	0.03
13	triple negative breast cancer	23	2017	0.10	28	phosphorylation	9	2017	0.02
14	survival	23	2015	0.06	29	in vitro	8	2015	0.03
15	mechanisms	21	2018	0.10	30	molecular mechanisms	8	2017	0.06

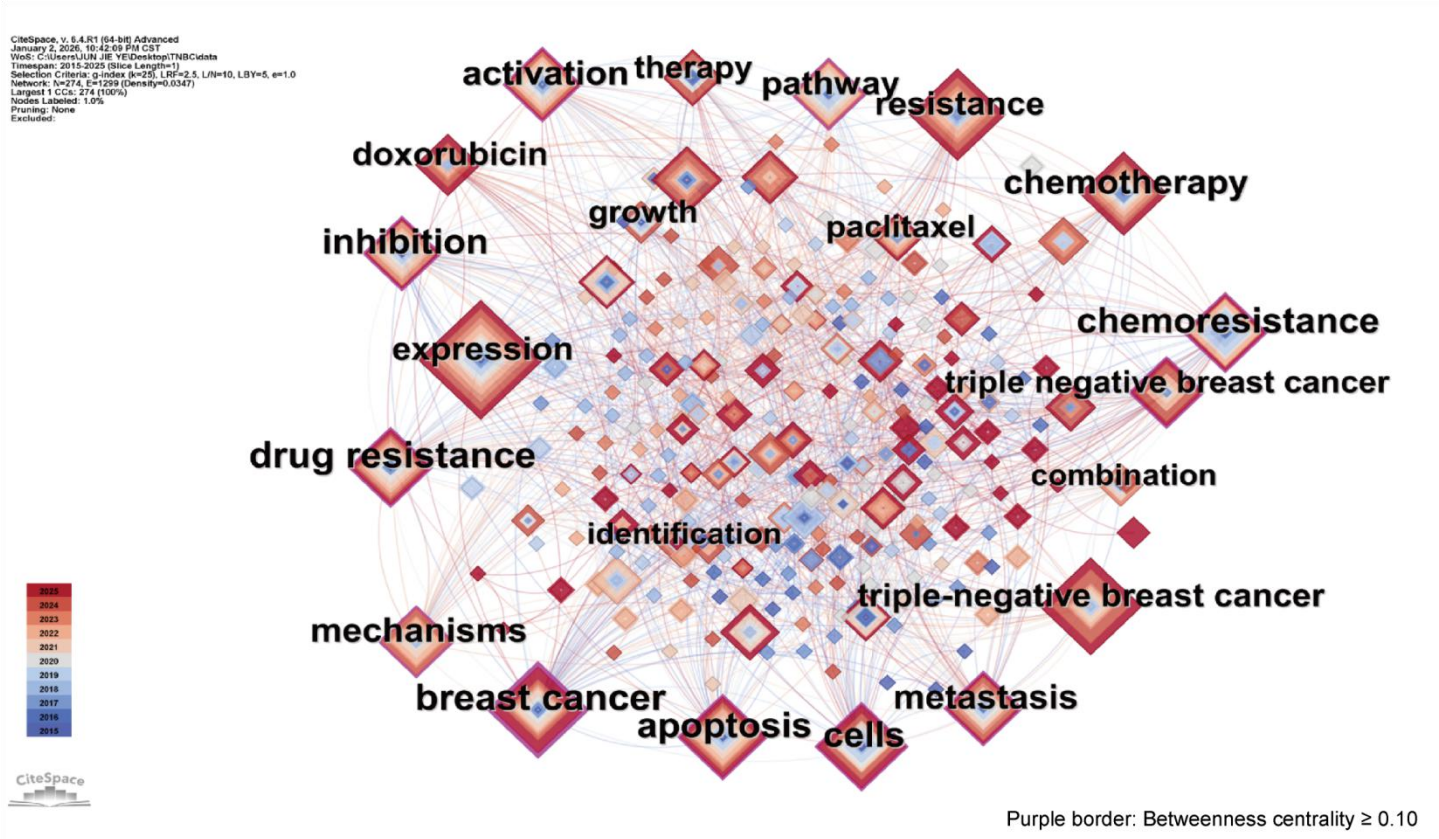

Figure 9. Keyword co-occurrence network.

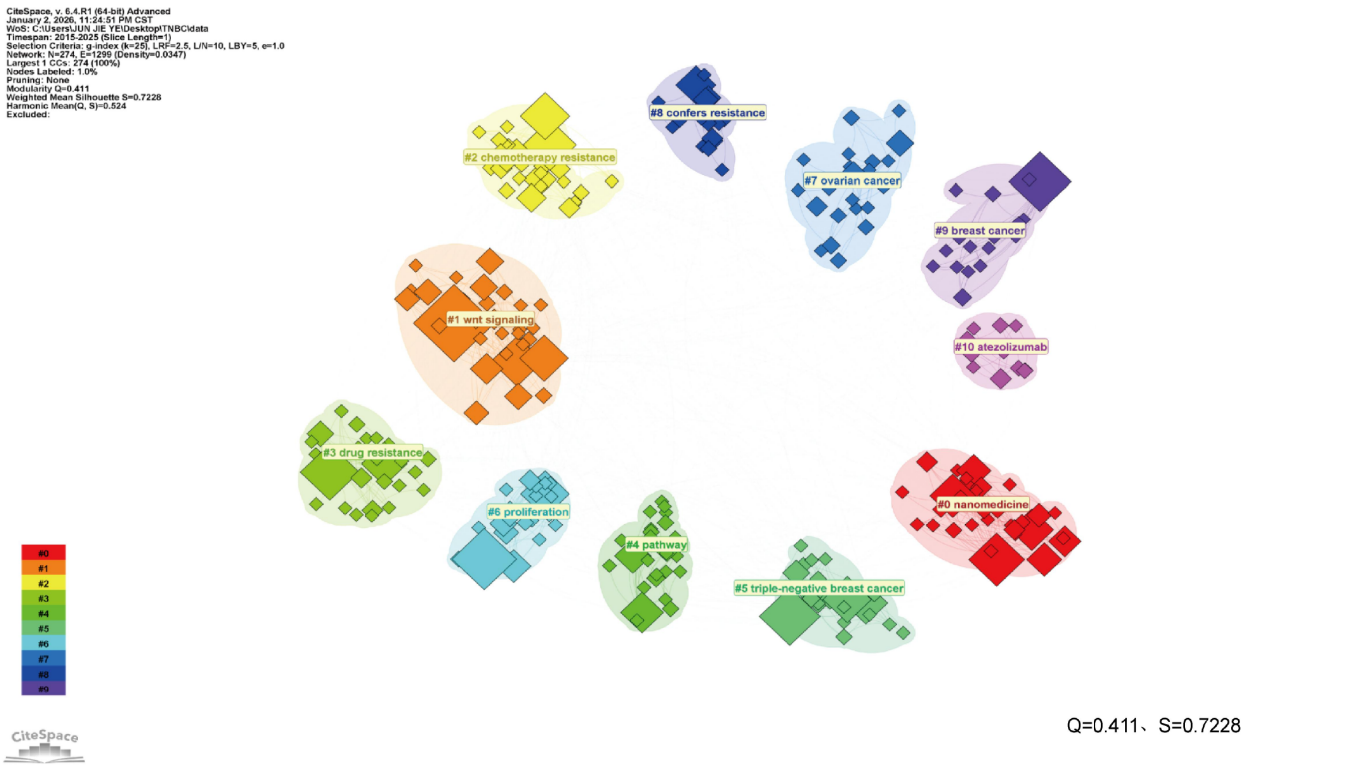

Figure 10. Eleven keyword clusters (#0–#10; modularity Q=0.411; weighted mean silhouette S=0.7228).

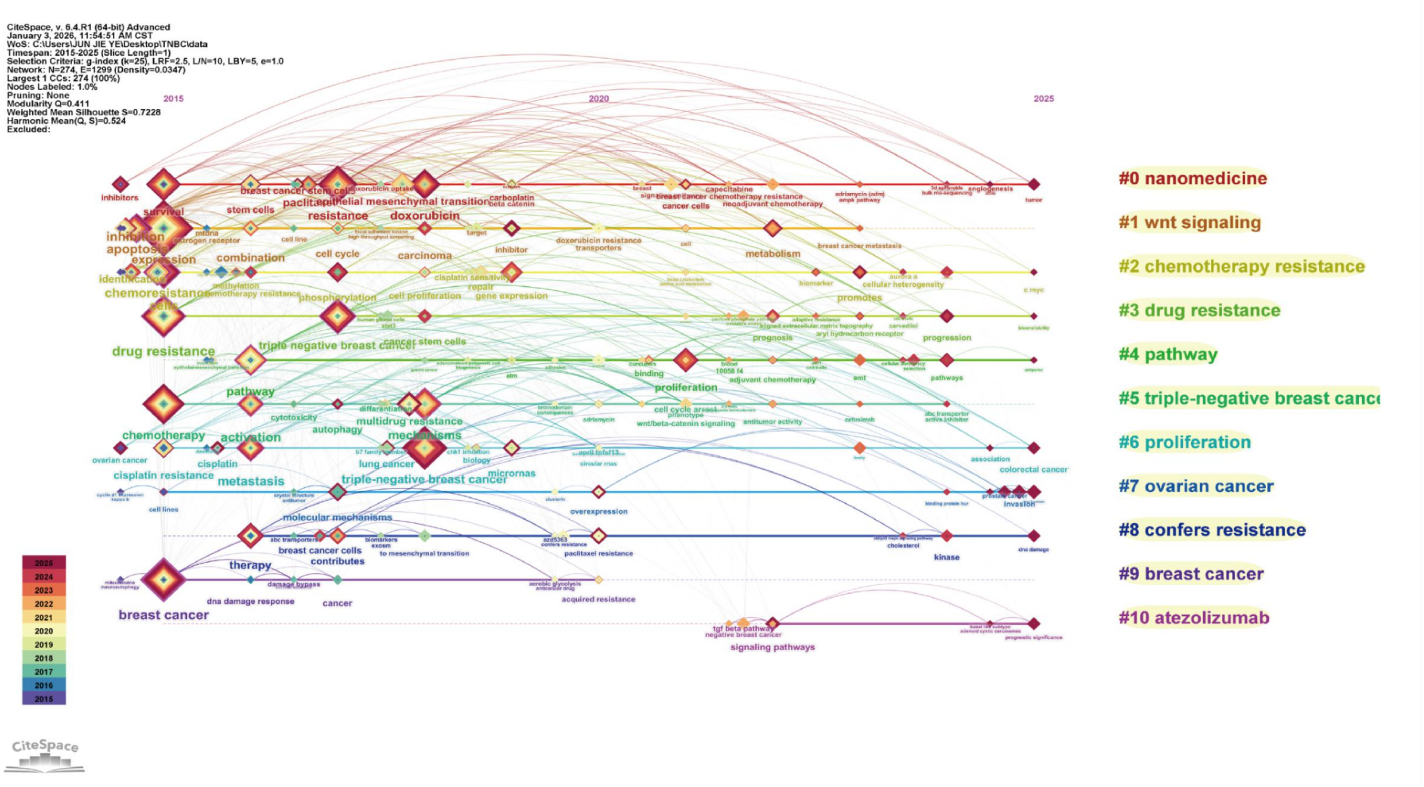

Figure 11. Keyword-cluster timeline.

CiteSpace identified 11 keyword clusters, labeled #0 through #10: nanomedicine (#0), Wnt signaling (#1), chemotherapy resistance (#2), drug resistance (#3), pathway (#4), triple-negative breast cancer (#5), proliferation (#6), ovarian cancer (#7), confers resistance (#8), breast cancer (#9), and atezolizumab (#10) (Figure 10). It is noteworthy that the atezolizumab cluster (#10) was derived from keyword co-occurrence analysis in the literature retrieved using a search strategy targeting four specified cytotoxic agents. Since no specialized immunotherapy-related search terms were included in the search strategy, this cluster solely reflects the intersection between immunotherapy-related literature and literature on chemotherapy resistance. Cluster quality was moderate (modularity Q=0.411) with acceptable within-cluster consistency (weighted mean silhouette S=0.7228).

The keyword timeline (Figure 11) shows persistent attention to chemotherapy, chemoresistance, drug resistance, and breast cancer across the study period. Mechanistic themes, including Wnt signaling, epithelial–mesenchymal transition, stem cells, metabolism, and phosphorylation, appeared alongside treatment-oriented themes such as nanomedicine and atezolizumab. The appearance of atezolizumab represents an adjacent immunotherapy topic within the retrieved corpus; because immune-checkpoint inhibitors were not dedicated search terms, the analysis cannot characterize the full literature on immunotherapy resistance.

Burst analysis (Figure 12) identified chemoresistance as the strongest burst term (strength 3.02; 2018−2019). Other notable bursts included multidrug resistance (2.84; 2020 − 2021), metabolism (2.79; 2022−2023), proliferation (2.63; 2022−2025), cisplatin resistance (2.46; 2015−2017), and mechanisms (2.22; 2020 − 2022). Terms with bursts continuing through 2025 included proliferation, gene expression (1.82), phosphorylation (1.60), carcinoma (1.07), identification (0.85), and survival (0.62).

The 2019 study by Echeverria et al. was the most cited article in the corpus (221 citations at data extraction) and described a reversible drug-tolerant state after neoadjuvant chemotherapy in TNBC[22]. In PDX models, pharmacologic inhibition of oxidative phosphorylation (OXPHOS) with IACS-010759 delayed residual-tumor regrowth; the study did not demonstrate clinical cure. A separate 2021 preclinical study identified OXPHOS as a metabolic vulnerability and reported tumor stabilization or enhanced activity of selected combinations in TNBC xenograft models [15].

Citation-burst strength quantifies a temporary increase in attention to a term or reference [16]. In this analysis, burst timing distinguishes earlier topics, such as cisplatin resistance and chemoresistance, from recent topics, such as proliferation, gene expression, and phosphorylation (Figure 12).

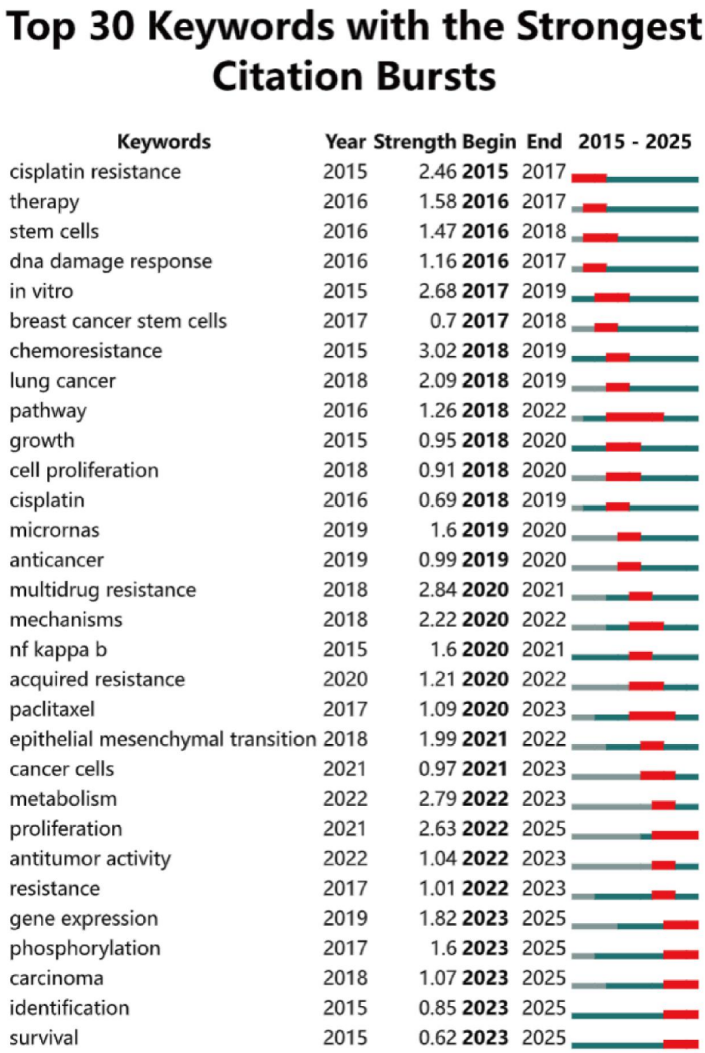

Figure 12. Top 30 keywords with the strongest citation bursts. CiteSpace settings were a 2015−2025 time span, 1-year slices, and g-index k=25.

These keyword patterns reflect shifts in research focus rather than clinically actionable evidence. Metabolism, nanomedicine, and phosphorylation emerged as key research hotspots in this literature analysis. The majority of studies addressing these topics were preclinical investigations, lacking robust clinical evidence; thus, further clinical trials are required for validation. This analysis cannot confirm their clinical translational value. Clinical utility would necessitate prospective validation, estimation of treatment-specific effects, safety assessments, and comparisons with established treatment regimens — outcomes that cannot be inferred from keyword frequency or term emergence.

Literature and reference analysis

The most highly cited article focuses on the reversible drug-tolerant state following neoadjuvant chemotherapy in TNBC, validated using PDX models and clinical samples [22]. Other high-impact studies have explored mechanisms such as tumor cell−macrophage crosstalk and ferroptosis [17], as well as summarized the signaling pathways in TNBC targeted by natural products [21] (Table 5). These high-impact studies delineate the core mechanistic themes in this field; however, their citation counts reflect academic interest rather than methodological rigor or the level of clinical evidence.

Within the co-citation reference network, two classic reviews on the mechanisms of chemotherapy resistance in TNBC exhibit the highest betweenness centrality, serving as pivotal knowledge bridges that connect diverse research domains (Table 6, Figure 13).

Table 5. Top 10 articles by citation count at data extraction.

Rank	Year	Title	Journal	First Author	Country	Citations
1	2019	Resistance to neoadjuvant chemotherapy in triple-negative breast cancer mediated by a reversible drug-tolerant state	Science Translational Medicine	Gloria V Echeverria	USA	221
2	2022	HLF regulates ferroptosis, development and chemoresistance of triple-negative breast cancer by activating tumor cell-macrophage crosstalk	Journal of Hematology & Oncology	Pinghua Li	China	201
3	2021	The signalling pathways and targets of traditional Chinese medicine and natural medicine in triple-negative breast cancer	Journal of Ethnopharmacology	Yang Z	China	186
4	2016	Mechanisms of Therapy Resistance in Patient-Derived Xenograft Models of BRCA1-Deficient Breast Cancer	Journal of the National Cancer Institute	Petra ter Brugge	Netherlands	162
5	2020	Targeting Glucose Metabolism to Overcome Resistance to Anticancer Chemotherapy in Breast Cancer	Cancers	Varghese, E	Qatar	161
6	2018	MiR-770 suppresses the chemo-resistance and metastasis of triple negative breast cancer via direct targeting of STMN1	Cell Death & Disease	Yaming Li	China	151
7	2022	Molecular Mechanisms, Biomarkers and Emerging Therapies for Chemotherapy Resistant TNBC	International Journal of Molecular Sciences	Paola Ferrari	Italy	140
8	2022	CircRNA-CREIT inhibits stress granule assembly and overcomes doxorubicin resistance in TNBC by destabilizing PKR	Journal of Hematology & Oncology	Xiaolong Wang	China	138
9	2020	Akt-targeted therapy as a promising strategy to overcome drug Resistance in breast cancer - A comprehensive review from chemotherapy to immunotherapy	Pharmacological Research	Parham Jabbarzadeh Kaboli	China	127
10	2018	Appraising the "entourage effect": Antitumour action of a pure cannabinoid versus a botanical drug preparation in preclinical models of breast cancer	Biochemical Pharmacology	Sandra Blasco-Benito	Spain	126

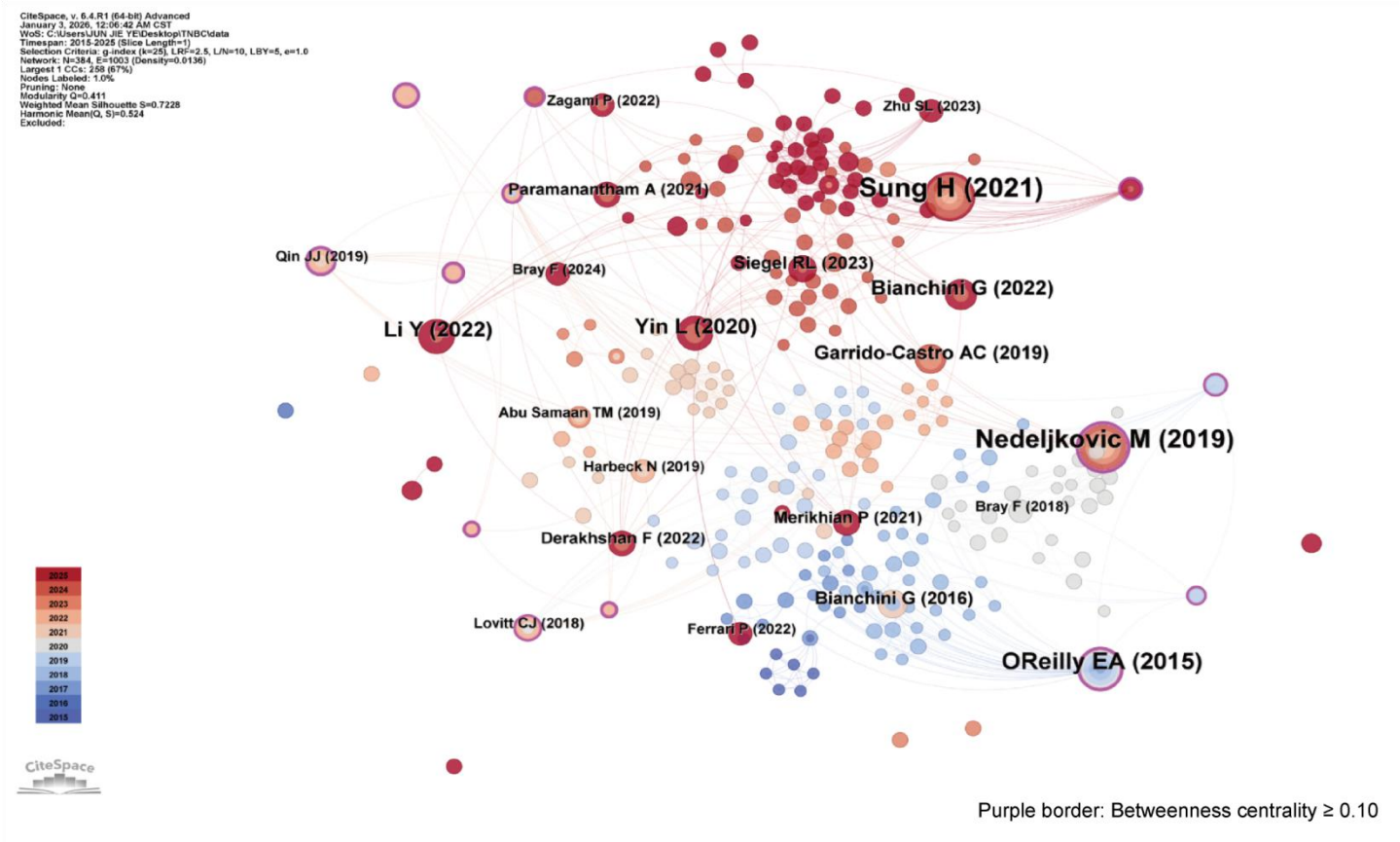

Figure 13. Reference co-citation network. Node size represents co-citation frequency, links represent co-citation relationships, and purple rims denote high betweenness centrality.

Table 6. Top 10 co-cited references by citation count.

Rank	Year	Title	Journal	First Author	Country	Citations	Centrality
1	2021	Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries.	CA: A Cancer Journal for Clinicians	Hyuna Sung	USA	19	0.04
2	2019	Mechanisms of Chemotherapy Resistance in TNBC-How We Can Rise to the Challenge	Cells	Milica Nedeljković	Serbia	16	0.41
3	2015	The fate of chemoresistance in triple negative breast cancer (TNBC)	BBA Clinical	Elma An O'Reilly	Ireland	13	0.41
4	2022	Recent advances in therapeutic strategies for TNBC	Journal of Hematology & Oncology	Yun Li	China	9	0.02
5	2020	TNBC molecular subtyping and treatment progress.	Breast Cancer Research	Yin Li	China	9	0.08
6	2022	Treatment landscape of TNBC - expanded options, evolving needs.	Nature Reviews Clinical Oncology	Giampaolo Bianchini	Italy	8	0.02
7	2019	Insights into Molecular Classifications of TNBC: Improving Patient Selection for Treatment.	Cancer Discovery	Ana C Garrido-Castro	USA	7	0.00
8	2023	Cancer statistics, 2023	CA: A Cancer Journal for Clinicians	Rebecca L Siegel	USA	6	0.00
9	2016	TNBC: challenges and opportunities of a heterogeneous disease	Nature Reviews Clinical Oncology	Giampaolo Bianchini	Italy	6	0.07

10	2021	Doxorubicin-Resistant TNBC Cells Exhibit Rapid Growth with Cancer Stem Cell-like Properties and EMT Phenotype, Which Can Be Transferred to Parental Cells through Autocrine Signalling	International Journal of Molecular Sciences	Anjugam Paramanantham	Korea	5	0.01

In the reference co-citation network (Figure 13), Nedeljković and Damjanović (2019) and O'Reilly et al. (2015) each had centrality of 0.41 among the top 10 references (Table 6). These works therefore combined frequent co-citation with bridging positions in the network.

Five references showed the strongest citation bursts (Figure 14): Sung et al. (strength 5.75; 2022–2025), O'Reilly et al. (5.20; 2017–2020), Nedeljković and Damjanović (4.66; 2021–2025), Garrido-Castro et al. (3.30; 2023–2025), and Qin et al. (2.06; 2021–2022). The reference timeline and cluster map are shown in Figure 15 and 16.

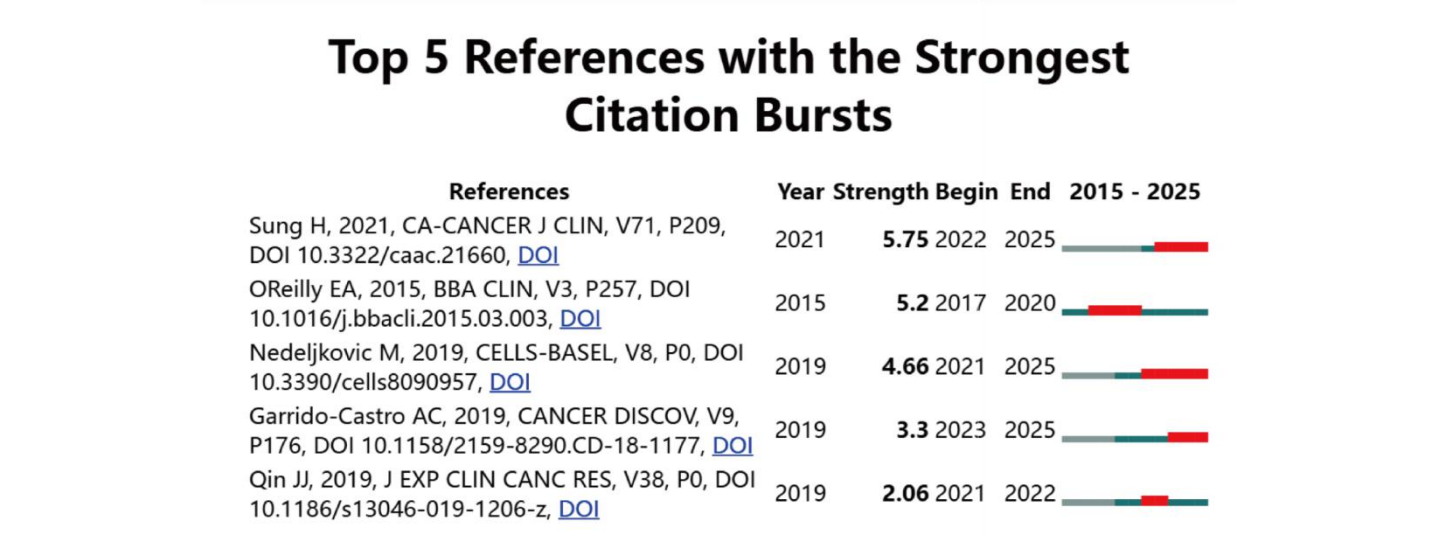

Figure 14. Five references with the strongest citation bursts.

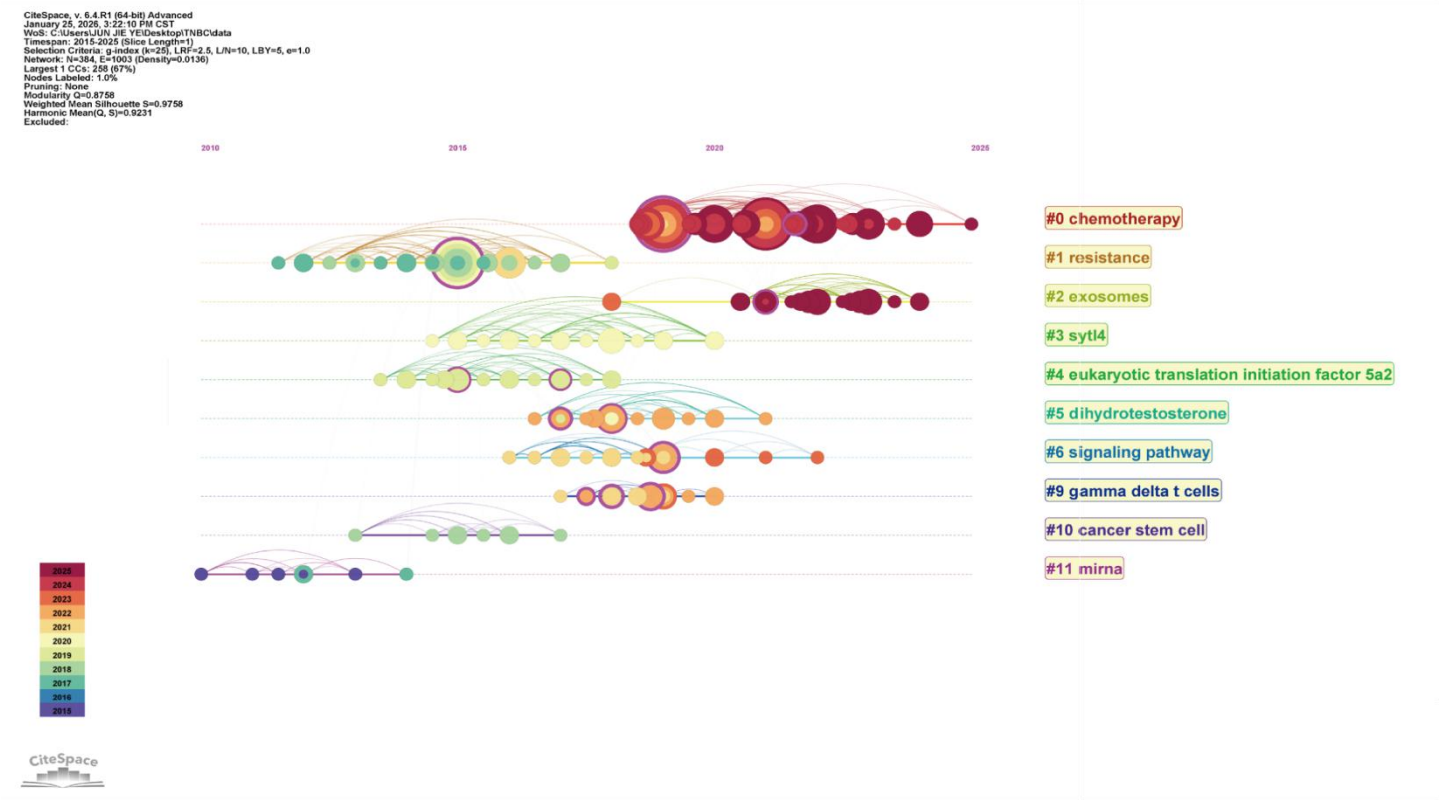

Figure 15. Reference-cluster timeline.

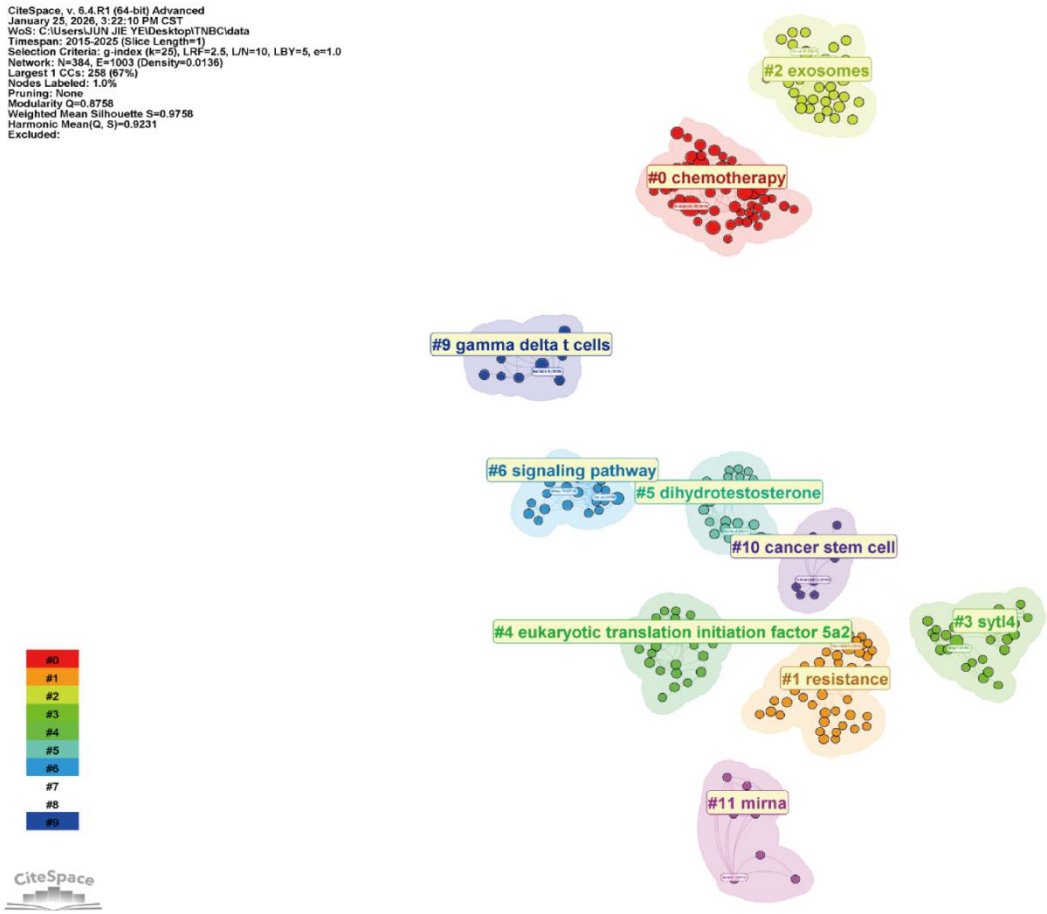

Figure 16. Reference-cluster map.

Discussion

Basic information

TNBC is clinically and molecularly heterogeneous, and cytotoxic chemotherapy remains central to treatment in both early and advanced disease, although contemporary care increasingly incorporates biomarker-directed agents [18,19,23]. Resistance is treatment- and context-specific; mechanisms identified for one drug, model, or disease stage should not be generalized without validation.

Across cancers, chemoresistance can involve altered drug transport and metabolism, enhanced DNA-damage repair, apoptosis avoidance, phenotypic plasticity, cancer stem-cell programs, and interactions with the tumor microenvironment [20]. Bibliometric analysis can identify which of these themes attract attention, but it cannot quantify their causal contribution or establish the effectiveness of an intervention.

Hotspots and frontiers

Research structure and collaboration

This study is not the first bibliometric analysis of TNBC. Hao et al. mapped 2000–2020 TNBC literature broadly [30], whereas the present analysis narrows the question to a 2015–2025 corpus retrieved with chemoresistance and four cytotoxic-drug terms. This narrower scope provides more specific information on chemoresistance-related themes but also reduces coverage and precludes claims about the entire TNBC treatment landscape.

The country network combined high output from China with greater bridging centrality for the United States and India. The bibliographic data cannot determine whether this pattern arose from language, funding, or scientific priorities. A cautious interpretation is that the field remains partitioned across national and institutional groups. More transparent data sharing, harmonized experimental definitions, and cross-site validation would reduce duplicated effort and improve the generalizability of mechanistic findings.

The most visible mechanistic contributions in the corpus included noncoding-RNA regulation [13,24,25], endoplasmic-reticulum stress [14], ferroptosis and macrophage crosstalk [17], reversible drug tolerance and OXPHOS [15,22], stromal remodeling and cancer stem-cell plasticity [26], and EMT in doxorubicin-resistant cells [27]. The co-citation prominence of the reviews by Nedeljković and Damjanović and O'Reilly et al. further indicates sustained attention to multifactorial chemoresistance [28,29]. These themes are consistent with the keyword clusters, but most supporting studies are preclinical.

Hotspots, mechanistic themes, and translational limits

The bibliometric results support three connected themes. First, the chemotherapy-resistance and drug-resistance clusters (#2 and #3) form the clinical problem around which the network is organized. Second, Wnt signaling, pathway, proliferation, apoptosis, EMT, and cancer stem cells (CSCs) represent mechanistic work on tumor-cell survival and plasticity. Third,

nanomedicine and atezolizumab represent treatment-oriented extensions. This structure links the discussion directly to the cluster, timeline, and burst results.

Experimental studies illustrate the mechanistic theme but also its evidentiary limits. Stromal Hedgehog signaling promoted a chemoresistant CSC phenotype in TNBC models, and stromal targeting sensitized xenografts to docetaxel [26]. Doxorubicin-resistant TNBC cells acquired EMT and CSC-like features in a single-cell-line model[27]. Paclitaxel-induced extracellular vesicle signaling was associated with reduced chemosensitivity in experimental breast-cancer systems [32]. These findings are biologically coherent with the keyword network, but they do not establish population-level benefit or a standard clinical strategy.

Immune-evasion and tumor-microenvironment literature intersects with chemoresistance because immune and stromal cells can alter tumor survival and drug exposure [33–36]. However, immune-checkpoint inhibitor resistance is a distinct clinical question with dedicated biomarkers and treatment-specific evidence[38]. The atezolizumab cluster should therefore be interpreted as an adjacent topic in this corpus.

Nanomedicine is the most prominent keyword cluster (#0), indicating ongoing publication activity in the areas of drug delivery and chemotherapy resistance research. The majority of studies incorporating nanomedicine are preclinical investigations, lacking robust clinical evidence; therefore, further clinical trials are required for validation. This analysis cannot confirm its clinical translational value. Previous reviews have described strategies targeting CSCs, optimizing drug delivery, and reducing systemic exposure [31,37]; however, these reviews primarily encompass preclinical and early translational studies. The prominence of a keyword does not substantiate clinical efficacy, safety, manufacturability, or cost-effectiveness; thus, claims of clinical applicability should not be made based on this evidence alone.

Implications and future research

The results support methodological priorities rather than treatment recommendations. Future studies should prespecify drug-specific resistance definitions, distinguish intrinsic from acquired resistance, report TNBC molecular subtype and disease stage, and connect laboratory models to prospectively collected clinical samples. International and interinstitutional collaborations could facilitate external validation and multicenter replication. Notably, treatment-oriented themes—including metabolic inhibition, biomarkers, and nanomedicine—represent research hotspots identified in this literature review analysis; however, these areas still lack robust clinical validation and should be advanced through staged preclinical validation and properly designed clinical trials.

Methodological context and comparison with prior bibliometric work

Bibliometric methods describe the structure and evolution of a literature base through publication, citation, and network data [10–12,16]. They complement systematic reviews but do not synthesize intervention effects or grade clinical evidence.

The most closely related prior work is the panoramic bibliometric mapping of the entire TNBC research field conducted by Hao et al. [30], which analyzed 1904 publications retrieved from WoSCC between 2000 and 2020. To elucidate the incremental contributions and scope boundaries of this study, we systematically compared these two works along their core dimensions, as summarized in Table 7.

Regarding specific differences, previous studies have provided a comprehensive overview of the field of TNBC research, whereas this study specifically narrows its scope to the chemoresistance mechanisms of four conventional cytotoxic drugs, thereby offering a more focused presentation of the thematic characteristics of this specialized subfield. Furthermore, this study extends the observation window by five years, up to 2025, capturing recent research trends and emerging focal points—including proliferation, gene expression, and phosphorylation—which were not sufficiently evident in earlier datasets spanning 2000–2020. The thematic structure identified in this study centers on drug resistance and its underlying mechanistic pathways, distinguishing it from the broader cluster sets identified in the comprehensive field analysis. Correspondingly, this narrower search scope means that these findings do not represent the full spectrum of TNBC research across all subtypes, treatment modalities, and clinical settings. However, the consistent national-level patterns observed across both studies—namely, the highest number of publications in China and the highest network centrality in the United States—indicate that these patterns constitute a stable structural feature within the broader TNBC research ecosystem.

Journal impact factors and quartiles provide journal-level context but do not measure the quality of individual studies [39,40]. Similarly, citation counts are time-dependent and may favor older publications. Accordingly, journal and citation rankings in this study are descriptive indicators only.

Table 7. Comparison between this study and the broad TNBC bibliometric analysis by Hao et al. (2022).

Dimension	Hao et al. (2022)	This study
Core research scope	Entire TNBC research field (all topics)	Chemoresistance mechanisms of four specified cytotoxic agents
Time span	2000–2020	2015–2025
Number of included publications	1904	212
Database source	Web of Science Core Collection	Web of Science Core Collection
Analytical tools	CiteSpace, VOSviewer	CiteSpace, VOSviewer, bibliometrix
Core thematic clusters	Metastasis, EGFR, lncRNA, immunotherapy, targeted therapy	Nanomedicine, Wnt signaling, chemotherapy resistance, drug resistance, proliferation
Country-level pattern	China ranked first in output; USA had highest betweenness centrality	China ranked first in output; USA had highest betweenness centrality
Key emerging topics (by end of study period)	Immunotherapy, liquid biopsy, ferroptosis	Proliferation, gene expression, phosphorylation, metabolism

Limitations

This study has several limitations. First, it used only WoSCC and included only English-language articles and reviews; relevant records indexed exclusively in PubMed, Scopus, Embase, or non-English sources may have been missed. Second, the query specified cisplatin, paclitaxel, doxorubicin, and gemcitabine and did not include other clinically used agents or emerging treatment classes as dedicated terms. The findings therefore apply to the retrieved corpus rather than the complete literature on TNBC treatment resistance. In addition, all network analyses in this study directly used the original indexed affiliation fields exported from the WoSCC. The affiliation names were not standardized, so the affiliation-related results should be interpreted with caution.

Third, no alternative-query, date-window, or database sensitivity analysis was performed. Fourth, institution and author names were analyzed as indexed; affiliation variants may have split a single organization into multiple nodes and contributed to the centrality values of 0.00 in Table 3. Fifth, citation counts, impact factors, and network topology are time-dependent and sensitive to database coverage and parameter settings. Finally, keyword frequency, clustering, and burst detection measure research attention, not causal importance, treatment efficacy, clinical maturity, or cost-effectiveness. Notably, this study did not perform stratified analyses according to the molecular subtypes of TNBC, individual drug types, experimental versus clinical studies, disease stages, or clinical trial outcomes, so it is difficult to provide targeted clinical guidance.

Conclusion

As an exploratory bibliometric analysis based on 212 publications retrieved from the WoSCC, this study delineates the research landscape of chemotherapy resistance mechanisms in TNBC within a specific search scope; however, it does not represent the entirety of the literature on TNBC chemotherapy resistance. Publication activity in this field has increased substantially from 2015 to 2025, with a marked acceleration in recent years. Within the 212-record WoSCC corpus captured by the prespecified English-language, four-drug search, publication activity on TNBC chemoresistance increased substantially from 2015 to 2025. China contributed the largest number of records, whereas the United States had the highest country-level betweenness centrality; institutional centrality remained low. This article addresses chemotherapy resistance, signaling pathways, apoptosis, proliferation, and cancer cell plasticity; more recently, it has also focused on gene expression, phosphorylation, metabolism, and nanomedicine. Notably, phosphorylation, metabolism, and nanomedicine have been identified as research hotspots in this literature analysis. Regarding the inclusion of these topics in existing studies, the majority involve preclinical research, lacking robust clinical evidence; therefore, further clinical trials are needed for validation. This analysis cannot confirm their clinical translational value. These findings systematically delineate the current research activities and unmet needs in this field, yet they do not establish clinical efficacy. Broader multi-database searches, drug- and subtype-specific analyses, normalized affiliation data, sensitivity analyses, and clinical validation are required before therapeutic or healthcare recommendations can be made.

Author Contributions

Conceptualization, Yifei Chen; Methodology, Junjie Ye; Software, Junjie Ye; Formal analysis, Yifei Chen; Data curation, Yifei Chen; Writing ─ original draft preparation, Yifei Chen; Writing ─ review and editing, Yifei Chen, Jia Lu, Junjie Ye, Xi Deng and Qiyan Zeng; Article polishing, Jia Lu; Supervision, Yifei Chen and Qiyan Zeng; Funding acquisition, Qiyan Zeng.

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Data availability statement

The data used in this study were retrieved from the Web of Science database using publicly available search terms. All bibliographic data analyzed are available from Web of Science (https://www.webofscience.com, accessed on December 8, 2025) and were processed using VOSviewer software (version 1.6.20) and CiteSpace (version 6.4. R1) and Bibliometrix (version 5.2.1). No additional datasets were generated or analyzed during the study.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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