ACCSCIENCE PUBLISHING

Cancer Plus

REVIEW ARTICLE

Quantitative bibliometric insights into cisplatin resistance in breast cancer (2010–2024): Implications for drug development

Jiawei Kang[1], Nan Jiang[1], Munire Shataer[2], and Tayier Tuersong[3]*

[1]The First College of Clinical Medicine, Xinjiang Medical University, Ürümqi, Xinjiang, China

[2]Department of Histology and Embryology, Basic Medical College, Xinjiang Medical University, Ürümqi, Xinjiang, China

[3]Department of Pharmacy, Xinjiang Key Laboratory of Neurological Diseases, Xinjiang Clinical Research Center for Nervous System Diseases, Second Affiliated Hospital of Xinjiang Medical University, Ürümqi, Xinjiang, China

Abstract

This study presents an extensive bibliometric analysis of cisplatin resistance (CR) in breast cancer (BC) from 2010 to 2024, elucidating global research trends, collaboration networks, and prospective research directions. Particular attention is given to novel therapeutic strategies, such as multi-target drug design and biomarker-guided treatments, aimed at overcoming challenges associated with drug resistance. This study utilizes the PubMed database and employs a topic search strategy, integrating the R package "bibliometrix" to conduct an in-depth analysis of the number of published documents, patterns of collaboration, journal impact, author contributions, institutional outputs, national collaboration networks, as well as keyword co-occurrences and citation networks. China and the United States are the principal contributors to research in this domain, with the Islamic Azad University and the journal *Cancers* serving as the primary platforms for academic dissemination. Notable researchers in this field include Wang, B. and Chekhun, V. F. Furthermore, the study highlights three particularly significant publications. Research hotspots include CR, triple-negative BC, BRCA1, DNA repair, microRNA, prostate cancer, ceRNA, LINCRNA, and prognosis, while trending topics comprise CR, triple-negative BC, BRCA1, autophagy, cytotoxicity, and DNA damage. This study provides actionable insights into research trends and translational opportunities in BC CR, emphasizing the integration of microRNA regulation, autophagy mechanisms, and multi-target drug design in clinical applications. Collaborative efforts between leading countries and institutions are pivotal to advancing therapeutic strategies and improving patient outcomes.

Keywords: Breast cancer; Bibliometrics; Research trends; Cisplatin resistance; Multi-target drug design; Precision oncology; Therapeutic strategies; Translational medicine

***Corresponding author:**
Tayier Tuersong
(tayiertuersong@163.com)

Citation: Kang J, Jiang N, Shataer M, and Tuersong T. Quantitative bibliometric insights into cisplatin resistance in breast cancer (2010–2024): Implications for drug development. *Cancer Plus*. 2025;7(3):1-19.
doi: 10.36922/CP025220037

Received: May 29, 2025

Revised: June 22, 2025

Accepted: July 1, 2025

Published online: July 30, 2025

1. Introduction

Breast cancer (BC) is characterized by considerable molecular heterogeneity. Despite substantial advancements in early screening and therapeutic interventions in recent years, the efficacy of treatment remains influenced by a multitude of factors.[1] Cisplatin,

a chemotherapy agent extensively utilized across various cancer types, demonstrates limited effectiveness in the treatment of BC.[2] Cisplatin primarily exerts its therapeutic effects through the formation of DNA adducts, leading to cell death. Nevertheless, a significant number of BC patients exhibit acquired resistance to cisplatin following treatment, thereby substantially diminishing its clinical efficacy.[3]

Cisplatin resistance (CR) constitutes a multifactorial phenomenon characterized by mechanisms such as genetic alterations and augmented DNA repair processes, which collectively diminish its therapeutic efficacy.[4] Research has demonstrated that the tumor microenvironment, the expression of intracellular drug efflux pumps, and the enhancement of DNA repair mechanisms are critical contributors to CR.[5] Consequently, a comprehensive investigation into the mechanisms underlying BC resistance to cisplatin is essential not only for elucidating the biological foundations of this resistance but also for establishing a theoretical framework to inform the development of novel therapeutic strategies.[6]

Furthermore, research on CR underscores the critical importance of personalized treatment strategies. By employing molecular signature analysis, it is possible to distinguish between patients who are either sensitive or resistant to cisplatin, thus enabling the optimization of treatment regimens and enhancing therapeutic outcomes.[7] Despite significant advancements in chemotherapy, resistance to cisplatin remains a formidable challenge in the treatment of BC. Dysfunction in BC susceptibility gene 1 (BRCA1), a crucial determinant of cellular sensitivity, alongside the regulation of autophagy, has emerged as a potential therapeutic target. Conducting a comprehensive analysis of current research trends could provide valuable insights for guiding translational studies and the development of innovative drug designs.[8]

Bibliometrics is a field dedicated to the quantitative study of scientific publications. It has become an essential instrument for revealing research trends, identifying knowledge gaps in research fields, and assessing the influence of scientific research results.[9] In addition, analyzing models and collaboration networks enables researchers to better understand the interconnections between disciplines and the contributions of various countries in specific research fields.[10]

The objective of this research is to conduct an in-depth bibliometric analysis of the literature concerning cisplatin chemoresistance in BC, published from 2010 to 2024. This analysis focuses on trends in publications, patterns of collaboration, and identification of leading contributors to the field, including countries, institutions, journals, and authors. Furthermore, this research looks into significant research topics and new development trends within the field, intending to offer guidance and insights for future research directions and clinical practices.

2. Methods

2.1. Data origins and search strategy

PubMed served as the principal data repository, providing access to an extensive database of biomedical literature.[11] Pertinent studies were identified through the following search strategy: ("breast cancer" OR "mammary carcinoma" OR "breast neoplasms") AND ("cisplatin" OR "DDP") AND ("drug resistance" OR "cisplatin resistance" OR "chemoresistance" OR "resistant") in title/abstract, with restrictions applied to the title/abstract fields. The dataset was acquired on September 9, 2024, and included comprehensive metadata exported through PubMed's "export file" functionality.[12]

2.2. Data analysis

The primary tool used in this study for bibliometric analysis is the R package version 4.2.3 of "bibliometrix,"[13] which was accessed at https://www.bibliometrix.org. R code was used alongside the Bibliometrix package for data analysis (R version 4.2.0).[14,15] The Bibliometrix package included the "biblioAnalysis()" command and the "summary()" function,[16] which aided in the initial interpretation of data. The "metaTagExtraction" and "Biblionetwork" commands were used to analyze collaboration networks, and the "Networkplot" command was then employed for graphical representation. Moreover, the "Biblioshiny()" function was utilized to examine national scientific partnerships, networks of institutional collaborations, keyword analysis, co-occurrence networks, and thematic map analysis.

3. Results

3.1. Exploring and analyzing literature

A comprehensive examination of the literature revealed 640 relevant articles, with Figure 1 clearly outlining the methodology.

3.2. Analysis of publication and citation trends

As depicted in Figure 2A, the annual volume of publications exhibited an upward trend from 2010 to 2020, followed by a subsequent decline from 2021 to 2024. Since 2010, the average annual citation frequency has exhibited a declining trend; potential reasons may encompass citation lag time, the emergence of alternative therapies, among other factors.

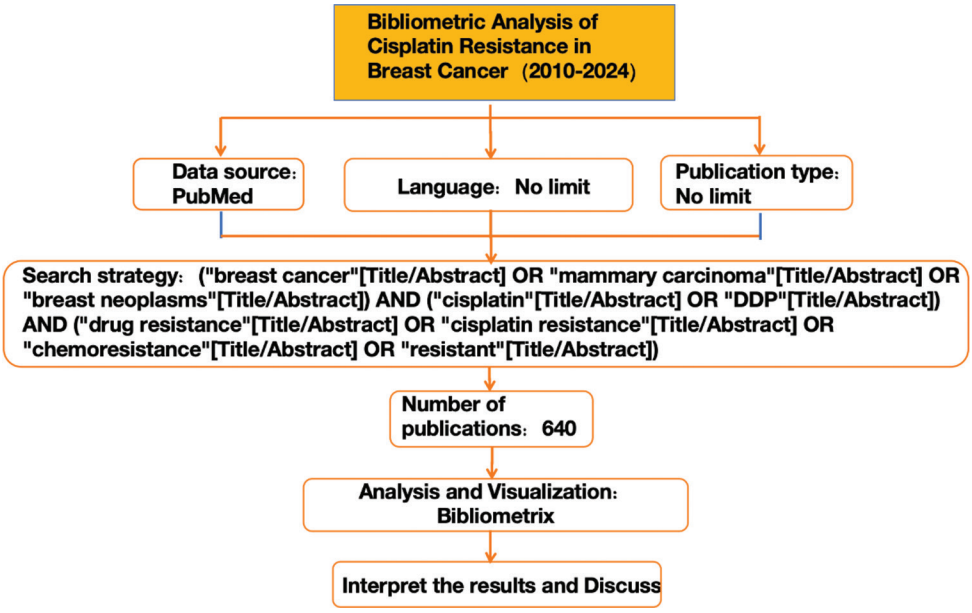

Figure 1. Study flow diagram

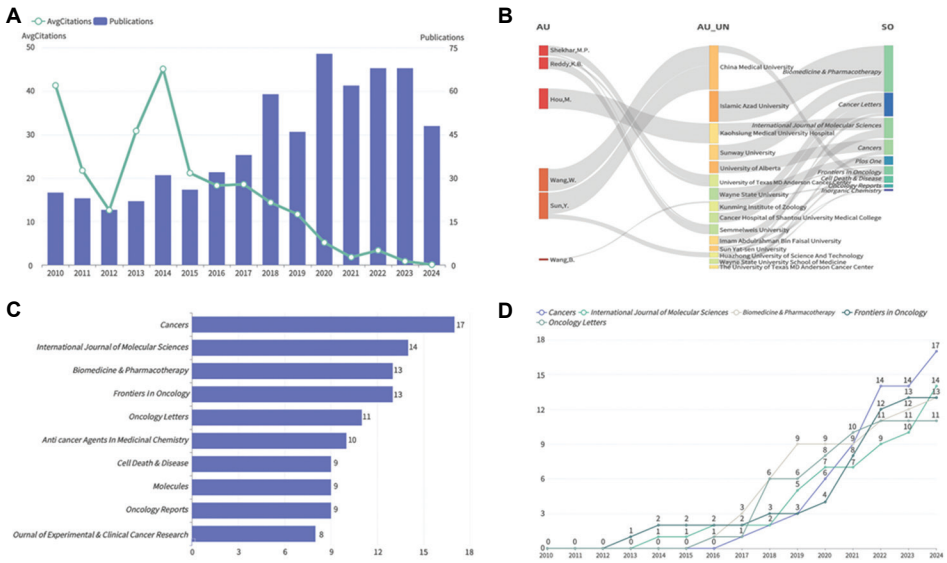

Figure 2. Publication-related data. (A) Trends in yearly publications and their average citations. (B) Three-field system (Left field: Author name; Middle field: Affiliation; Right field: Source). (C) Bar graph showing the distribution of literature sources. (D) The cumulative publication volume of the five top journals over the years.

3.3. Three-field system

Figure 2B illustrates the collaborative networks among authors, institutions, and publications.

3.4. Journal analysis

Figure 2C presents the ten journals with the highest number of publications, with *Cancers* ranking first ($n = 17$), followed by the *International Journal of Molecular Sciences* ($n = 14$), and *Biomedicine and Pharmacotherapy* ($n = 13$) in third position. Meanwhile, Figure 2D illustrates the annual publication trends, indicating an overall upward trajectory for all categories. Notably, the journal *Cancers* demonstrates the most rapid growth, whereas the others exhibit a more stable increase.

3.5. Author analysis

Figure 3A identifies the top 10 authors based on publication volume, with Chekhun, V. F. ($n = 8$) leading

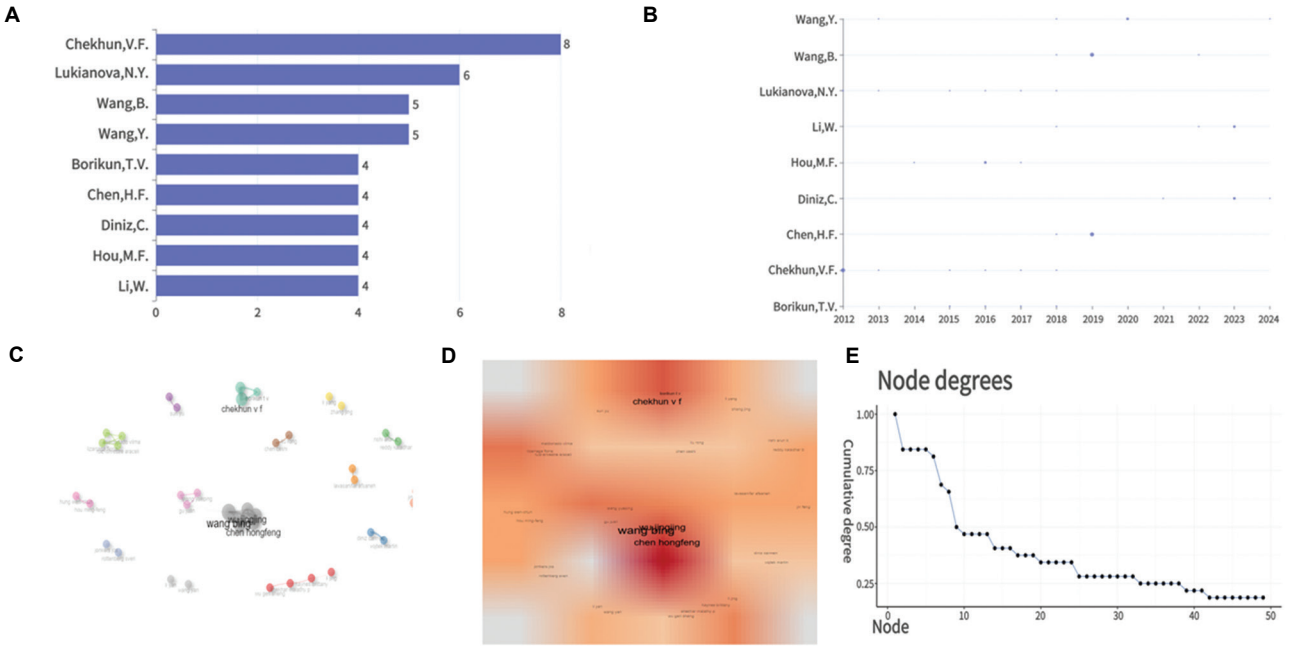

Figure 3. Analysis of core authors and their collaboration networks. (A) The top 9 highly relevant authors. (B) A review of the productivity trends of the top 10 authors over time. (C–E) Maps showing collaboration networks and their density: (C) map of collaboration networks, (D) map of density, and (E) the number of links associated with each node.

the list. Lukianova, N. Y. (n = 6) is tied for second place, while Wang, B. (n = 5) and Wang, Y. (n = 5) share the third position. Figure 3B illustrates the annual publication trends, revealing that most authors typically published one paper per year. Notably, Chekhun, V. F. published three papers in 2012, Hou, M. published two in 2016, and Wang, B. published three in 2019, demonstrating their heightened research activity during these years. Figures 3C–E depict the co-authorship network, where lines between nodes signify collaborative efforts, and highlighted connections denote frequent collaborations among highly prolific authors. Significantly, Wang, B. (Cluster = 8; Betweenness = 15; Closeness = 0.125; PageRank = 0.0344), Chen, H. (Cluster = 8; Betweenness = 0; Closeness = 0.0909; PageRank = 0.0279), Wu, J. (Cluster = 8; Betweenness = 0; Closeness = 0.0909; PageRank = 0.0279), and Chekhun, V. F. (Cluster = 9; Betweenness = 0; Closeness = 0.5; PageRank = 0.0266) are distinguished in the network analysis. The inclusion of Wang, B., Chen, H., and Wu, J. within the same cluster indicates potential shared research interests or collaborative efforts, with Wang, B. emerging as the most influential researcher based on the given metrics. Chekhun, V. F. holds a pivotal role within the network, promoting collaborations with fellow researchers.

3.6. Institutional analysis

Figure 4A presents the top 10 institutions ranked by publication volume. Islamic Azad University leads with 30 publications, followed by a tie for second place between Harvard Medical School and University of Alberta, each with 17 publications. China Medical University and Sun Yat-sen University are tied for third place, each contributing 15 publications. Figure 4B provides a detailed analysis of the annual publication trends, indicating a general upward trajectory. The University of Alberta demonstrates a consistent level of output, while Islamic Azad University exhibits a marked increase in publication volume following the year 2022.

3.7. Country analysis

Figure 5A shows a list of countries ranked according to the number of publications by corresponding authors, with China occupying the foremost position (total publications [P] = 209; single-country publications [SCP] = 186; and multi-country publications [MCP] = 23). Next is the United States (USA, P = 66; SCP = 51; MCP = 15) and India (P = 26; SCP = 22; MCP = 4). China's research output in this domain substantially surpasses that of other nations, characterized by frequent international collaborations. While most countries participate in multi-country collaborations, Portugal (P = 6; SCP = 6; MCP = 0) and Turkey (P = 6; SCP = 6; MCP = 0) exhibit a notable absence of such cooperative efforts.

The analysis in this study covers publications from 59 countries and regions globally, as shown in Figure 5B, with

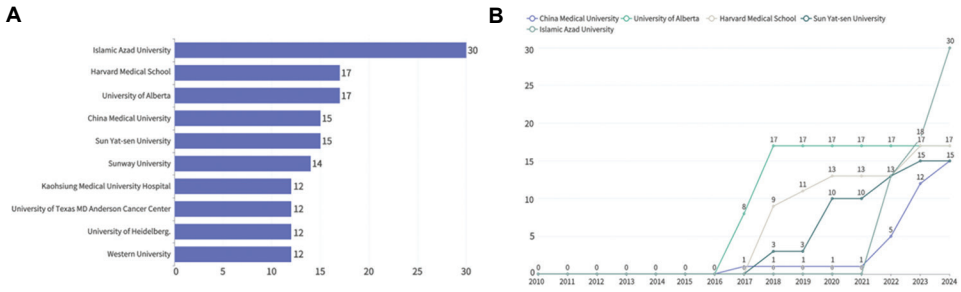

Figure 4. Analysis of core institutions and their research output. (A) The top 10 most relevant affiliations. (B) Production over time for the top five affiliations.

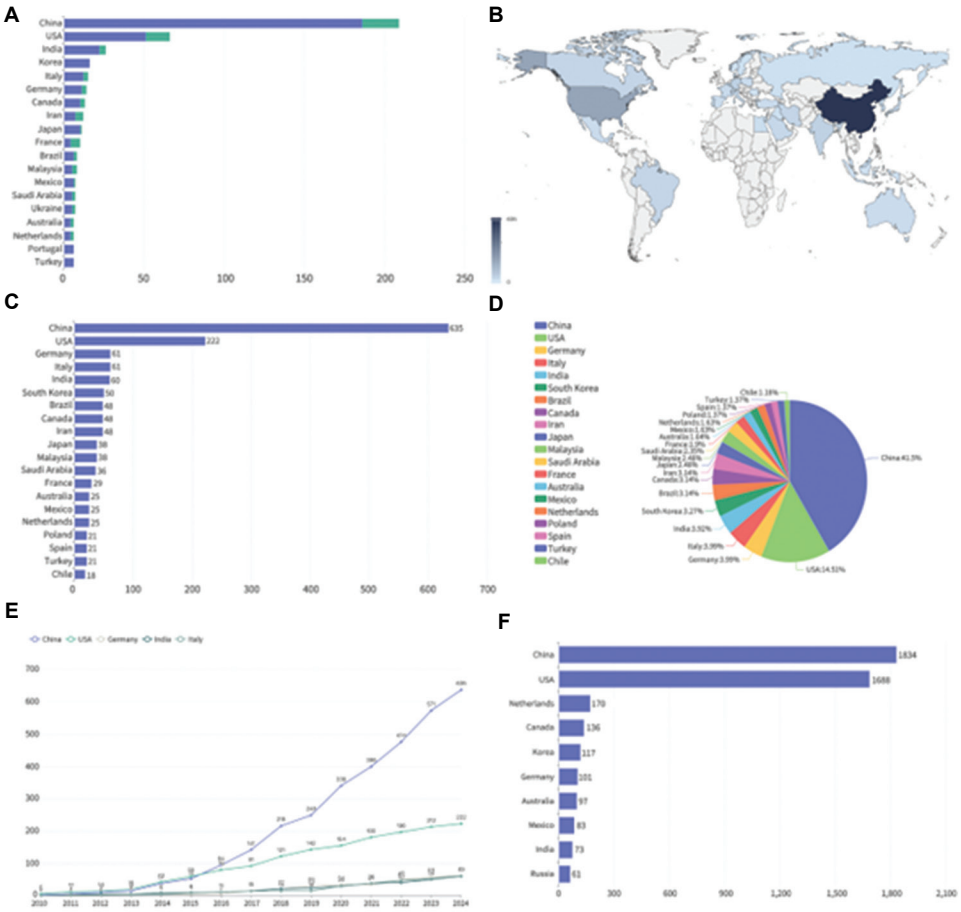

Figure 5. Analysis of publication characteristics and performance at the national level. (A) The ranking of publications by the countries of corresponding authors and the percentage of international collaboration (blue represents single-country publications, green represents multi-country publications). (B) The number of publications published in each country. (C) The 20 leading countries in terms of publication numbers. (D) Percentage of publications in the leading 20 countries. (E) Publication numbers and their growth trends in the top five nations. (F) Number of articles cited in the country with the most publications.

Figure 5C and D illustrating the geographical spread of these publications, highlighting the top 20 countries and regions. China leads in publication numbers with 635 entries (41.5%), followed by the USA with 222 entries (14.51%), and Germany with 61 entries (3.99%).

Figure 5E illustrates the annual publication trends of the top five countries by volume, highlighting overall growth. China and the USA show particularly rapid increases, while Germany has seen a significant rise in publications since 2017.

Meanwhile, Figure 5F presents the top 10 nations ordered by total citations (TC), highlighting that China (TC = 1834) and the USA (TC = 1688) possess significantly higher citation counts compared to other countries, underscoring their considerable international influence in scientific output.

3.8. Map of global collaboration among countries

The network for international research collaboration, involving 52 countries and regions, is depicted in Figure 6. The USA and China have the highest collaboration frequency, partnering 17 times. In addition, the USA, China, Italy, and Germany show notable activity and diversity in their international research partnerships, as reflected in their extensive collaborations with various countries and regions. Future collaboration between translational medicine teams in China and the USA has the potential to accelerate the clinical application of these findings, thereby facilitating the development of multicenter clinical trials focused on therapies for CR.

3.9. Outstanding literature

This section reviews the ten most influential papers in the research field, assessed through international rankings based on citations (Figure 7A and Table 1) and rankings by impact factor (Table 2). The paper titled "Identification of distinct basal and luminal subtypes of muscle-invasive bladder cancer with different sensitivities to frontline chemotherapy" has been cited 789 times, highlighting its significant influence. In addition, the studies "Overexpression of BLM enhances DNA damage and sensitivity to platinum salts in triple-negative breast and serous ovarian cancers" and "Approaches to treat triple-negative metastatic breast cancer: Individualized targeted treatments or chemosensitization?" are also notable, distinguished by a high impact factor of 56.7, establishing them as benchmarks in the domain.

3.10. Network of co-citations

The literature's co-citation network is illustrated in Figure 7B-D, highlighting "Galluzzi L, 2011" (Cluster = 1; Betweenness = 296.277; Closeness = 0.0056; PageRank = 0.0841) and "Dasari S, 2014" (Cluster = 1; Betweenness = 275.6006; Closeness = 0.0056; PageRank = 0.0723) as pivotal documents in the research domain. Their inclusion in the same cluster indicates a thematic linkage and a common research focus among the scholarly community.

3.11. Keyword analysis

Figures 8A-C present the ten most common keywords in the field's literature, with "Breast cancer" (n = 142) and "Cisplatin" (n = 119) being the most frequent, far exceeding others. Other notable keywords include "Drug resistance" (n = 49), "Chemoresistance" (n = 43), "Apoptosis" (n = 40), "Triple-negative breast cancer (TNBC)" (n = 32), "Cisplatin resistance" (n = 28), "Chemotherapy" (n = 24), "Cancer" (n = 22), and "Resistance" (n = 18). These results are consistent with the word cloud, underscoring their importance in the field. Figure 8D shows the annual trends of these keywords, indicating a steady increase, especially for "Breast cancer" and "Cisplatin," which suggests rising interest. The growing frequency of terms such as "Drug

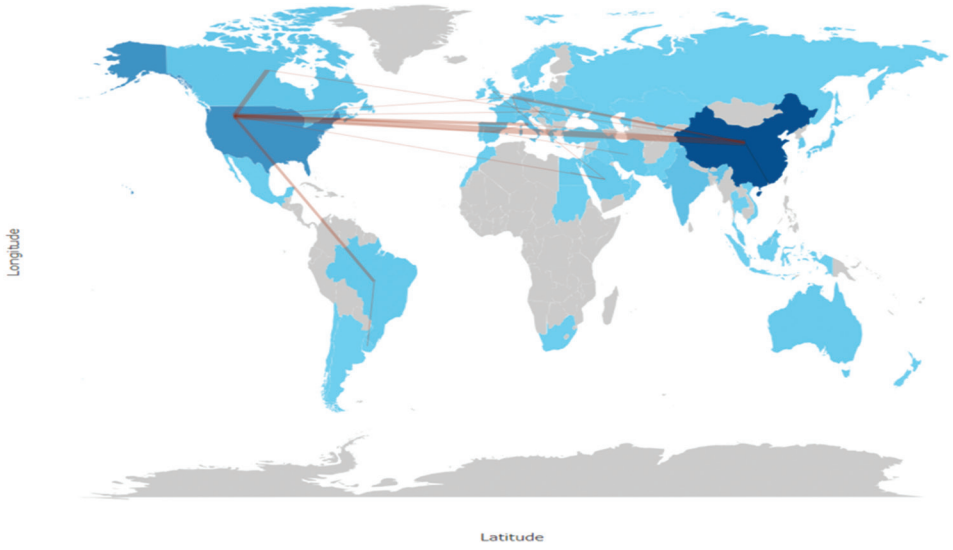

Figure 6. A map showing collaborative networks among countries around the world

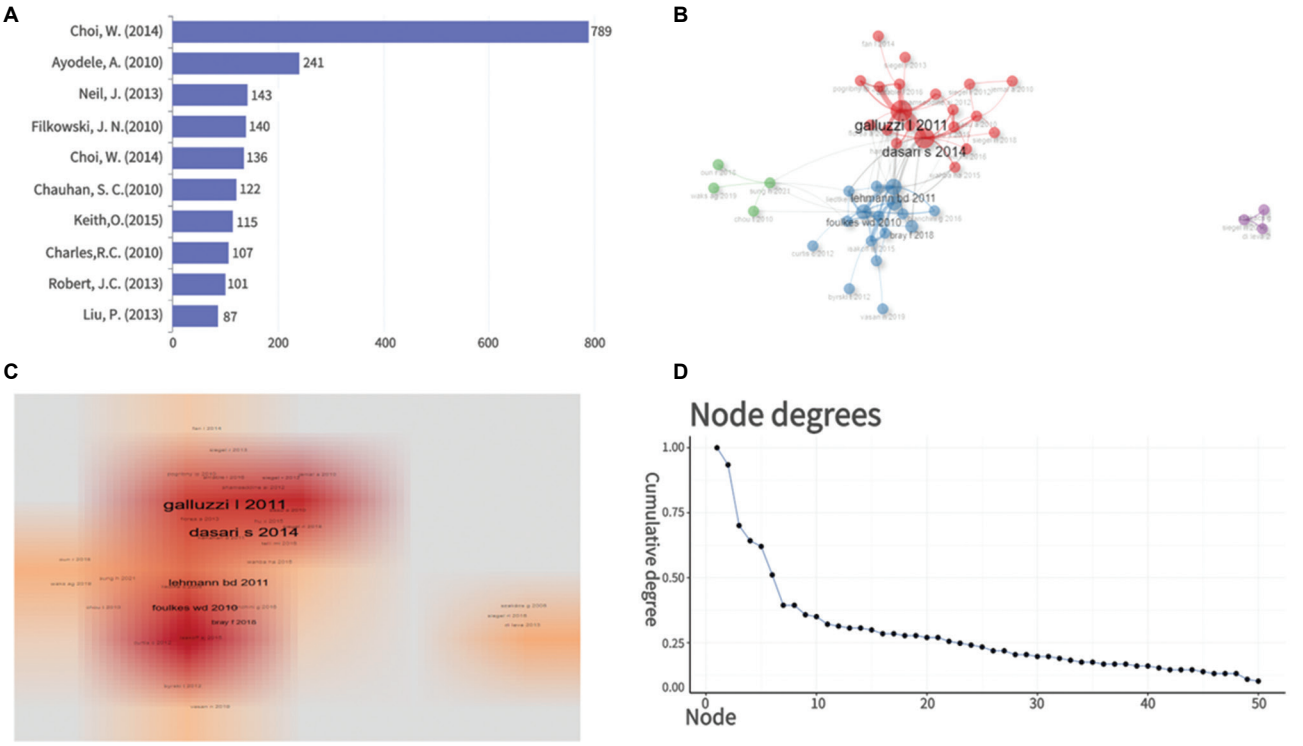

Figure 7. Analysis of literature citation characteristics and co-citation networks. (A) An overview of the top 10 most cited manuscripts on a global scale. (B) Visualization of the literature co-citation network. (C) The density of co-citations in literature. (D) The number of connections between nodes.

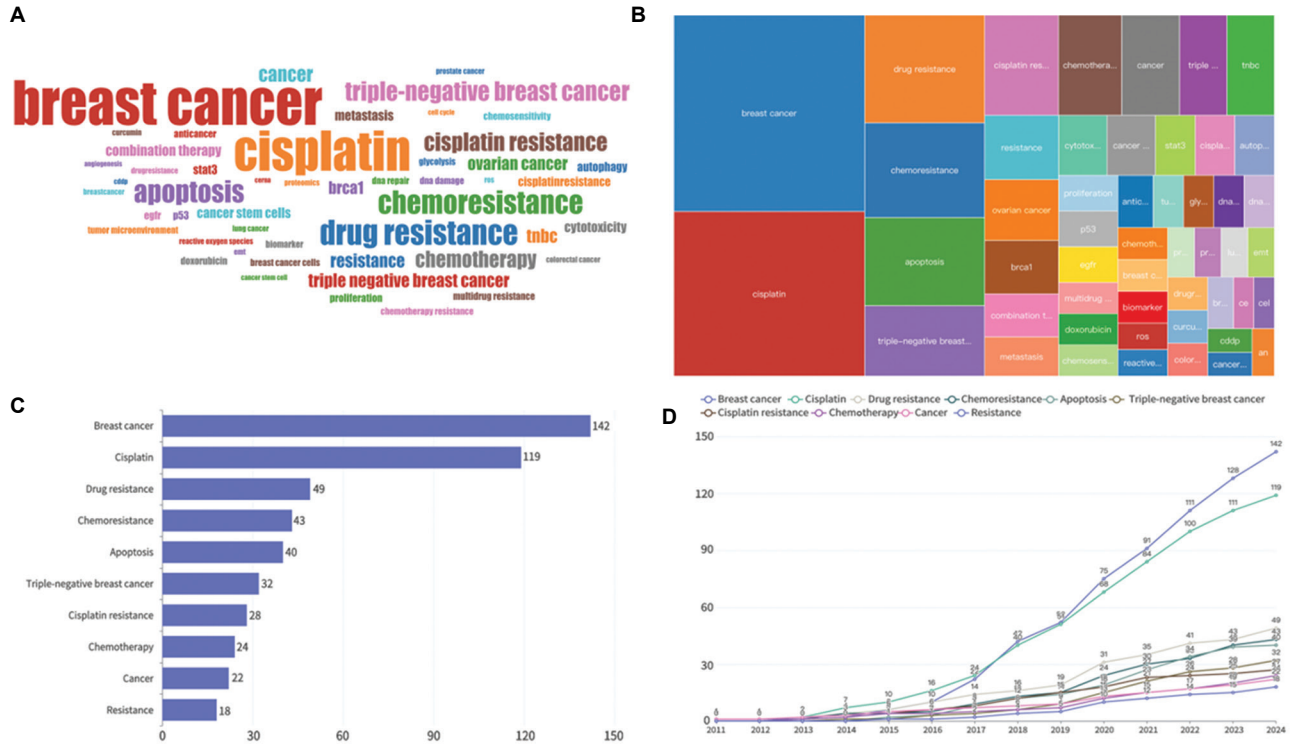

Figure 8. Analysis of keyword characteristics and evolution. (A) Word cloud for the pertinent terms. (B) Diagram of related words in a tree structure. (C) Top 10 most frequently occurring words. (D) The occurrence of the top 10 keywords throughout different periods.

Table 1. Literature with a high citation rate

Title	Published date	Periodical	IF	Quoted
Identification of distinct basal and luminal subtypes of muscle-invasive bladder cancer with different sensitivities to frontline chemotherapy.	February 2014, 15	*Cancer Cell*	48.8	789
R428, a selective small molecule inhibitor of Axl kinase, blocks tumor spread and prolongs survival in models of metastatic breast cancer.	February 2010, 11	*Cancer Research*	12.5	241
Stabilization of mutant BRCA1 protein confers PARP inhibitor and platinum resistance.	October 2013, 3	*Proceedings of the National Academy of Sciences of the United States of America*	9.4	143
Alterations of microRNAs and their targets are associated with acquired resistance of MCF-7 breast cancer cells to cisplatin.	January 2010, 26	*International Journal of Cancer*	5.7	140
Intrinsic basal and luminal subtypes of muscle-invasive bladder cancer.	June 2014, 25	*Nature Reviews Urology*	12.1	136
Fabrication of curcumin encapsulated PLGA nanoparticles for improved therapeutic effects in metastatic cancer cells.	July 2010, 15	*Journal of Colloid and Interface Science*	9.4	122
miR-134 in extracellular vesicles reduces triple-negative breast cancer aggression and increases drug sensitivity.	September 2015, 30	*Oncotarget*	0	115
FOXM1 confers acquired cisplatin resistance in breast cancer cells.	January 2010, 14	*Molecular Cancer Research*	4.1	107
Proteomic markers of DNA repair and PI3K pathway activation predict response to the PARP inhibitor BMN 673 in small cell lung cancer.	October 2013, 1	*Clinical Cancer Research*	10	101
Disulfiram targets cancer stem-like cells and reverses resistance and cross-resistance in acquired paclitaxel-resistant triple-negative breast cancer cells.	September 2013, 7	*British Journal of Cancer*	6.4	87

Abbreviations: BRCA1: Breast cancer susceptibility gene 1; FOXM1: Forkhead box proten M1; IF: Impact factor; PARP: Poly-ADP-ribose polymerase; PLGA: Poly (lactic-co-glycolic acid).

Table 2. Literature that received high scores

Title	Published date	Periodical	IF	Quoted
Overexpression of BLM promotes DNA damage and increased sensitivity to platinum salts in triple-negative breast and serous ovarian cancers.	February 2018, 17	*Annals of Oncology*	56.7	27
Treatment of triple-negative metastatic breast cancer: toward individualized targeted treatments or chemosensitization?	October 2010, 15	*Annals of Oncology*	56.7	50
Clonal fitness inferred from time-series modelling of single-cell cancer genomes	June 2021, 24	*Nature*	50.5	5
Identification of distinct basal and luminal subtypes of muscle-invasive bladder cancer with different sensitivities to frontline chemotherapy.	February 2014, 15	*Cancer Cell*	48.8	789
Multicenter Phase II study of lurbinectedin in BRCA-mutated and unselected metastatic advanced breast cancer and biomarker assessment substudy.	September 2018, 22	*Journal of Clinical Oncology*	42.1	25
A novel lncRNA ROPM-mediated lipid metabolism governs breast cancer stem cell properties.	October 2021, 30	*Journal of Hematology and Oncology*	29.5	6
HLF regulates ferroptosis, development and chemoresistance of triple-negative breast cancer by activating tumor cell-macrophage crosstalk.	January 2022, 7	*Journal of Hematology and Oncology*	29.5	3
Micro-RNA expression in cisplatin resistant germ cell tumor cell lines.	May 2011, 18	*Molecular Cancer*	27.7	49
Interferon regulatory factor 4 binding protein is a novel p53 target gene and suppresses cisplatin-induced apoptosis of breast cancer cells.	August 2012, 15	*Molecular Cancer*	27.7	15
The tumor proteasome as a novel target for gold (III) complexes: implications for breast cancer therapy.	January 2010, 5	*Coordination Chemistry Reviews*	20.3	19

Abbreviations: BLM: Bloom helicase; HLF: Hepatic leukemia factor; lncRNA: Long non-coding RNA; ROPM: Regulator of phospholipid metabolism.

resistance," "Chemoresistance," "Cisplatin resistance," "Chemotherapy," and "Resistance" highlights a focus on overcoming CR in BC treatment.

3.12. Thematic co-occurrence network analysis

Figures 9A-C facilitate the visualization of keywords pertinent to this domain. By analyzing these network

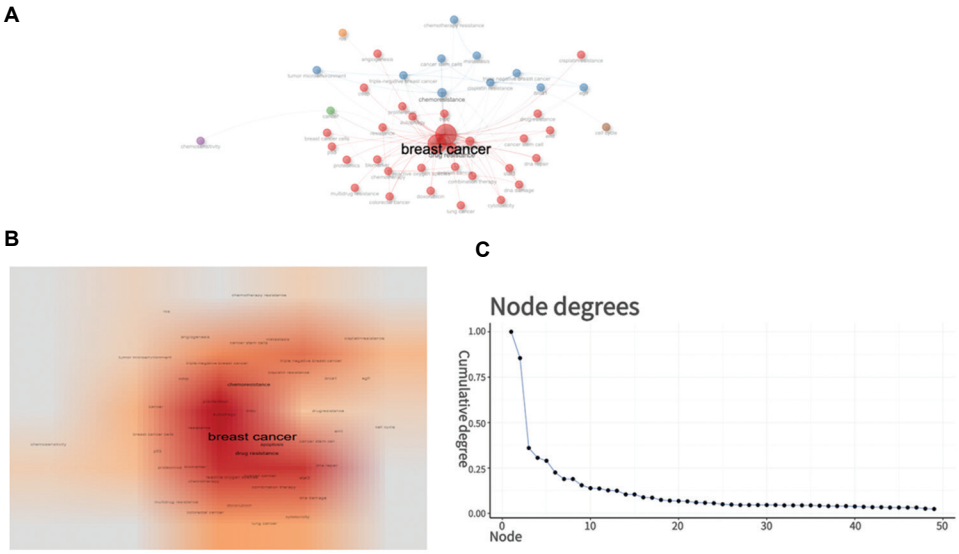

Figure 9. Analysis of keyword clustering and co-occurrence relationships. (A) Keyword analysis-based clustering diagram. The circle size corresponds to the number of occurrences, while the color indicates cluster diversity. (B) The darker areas indicate greater co-occurrence frequencies or stronger relationships. (C) The number of connections between nodes.

indicators, it is possible to discern research hotspots and key concepts, along with their respective positions and significance within the research network. We classified the keywords into six distinct clusters and observed that "Breast cancer" (Cluster 1; Betweenness centrality = 557.6428; Closeness centrality = 0.0185; and PageRank = 0.2057) holds a pivotal position in the research landscape. Similarly, "Cisplatin" (Cluster 1; Betweenness centrality = 299.9237; Closeness centrality=0.0161;andPageRank=0.1631),"Chemoresistance" (Cluster 2; Betweenness centrality = 51.8449; Closeness centrality = 0.013; and PageRank = 0.0528), and "Cisplatin resistance" (Cluster 2; Betweenness centrality = 45.25; Closeness centrality = 0.0116; and PageRank = 0.0294) exhibit significant betweenness centrality within their respective clusters. This underscores the extensive scholarly focus on CR. Keywords such as "Cytotoxicity," "Autophagy," and "DNA damage," characterized by low betweenness centrality and PageRank values, show reduced co-occurrence frequencies compared to other keywords. Keywords such as "Cytotoxicity" (Betweenness = 0, Closeness = 0.0116, and PageRank = 0.0126), "Autophagy" (Betweenness = 0, Closeness = 0.0118, and PageRank = 0.0128), and "DNA damage" (Betweenness = 0, Closeness = 0.0108, and PageRank = 0.0085) within Cluster 1 may indicate potential research avenues. The identification of "Ovarian cancer" (Cluster = 1; Betweenness = 0.3532; Closeness = 0.0122; and PageRank = 0.0228), "Colorectal cancer" (Cluster = 1; Betweenness = 0; Closeness = 0.0116; and PageRank = 0.0101), and "Lung cancer" (Cluster = 1; Betweenness = 0; Closeness = 0.0096; and PageRank = 0.005) suggests that researchers are investigating CR across various cancer types, not limited to BC. In addition, the significant roles of "Cancer stem cells" (Cluster = 2; Betweenness = 0.1834; Closeness = 0.0112; and PageRank = 0.0129) and "Metastasis" (Cluster = 2; Betweenness = 1.2243; Closeness = 0.0111; and PageRank = 0.0138) are emphasized in the progression of BC and the development of CR.

3.13. Trend analysis and thematic mapping

Figure 10 presents the frequency of emergence of several key research themes across different years. Notably, "Breast cancer" (Cluster 1) and "Cisplatin" (Cluster 1) are the most frequently appearing themes in the literature, with occurrences of 142 and 119, respectively. The median annual occurrence for these themes is 2020, reflecting sustained scholarly attention since 2018 and a peak in research activity in 2020, thereby indicating their status as persistent focal points. Furthermore, the topics of "Cancer stem cells" (Cluster 2) and "Metastasis" (Cluster 2), although less frequently addressed, have median annual occurrences in 2019 and 2021, respectively, signifying continued research interest. The terms "Drug resistance" (Cluster 1) and "Chemoresistance" (Cluster 2) are mentioned 49 and 43 times, respectively, with a median annual occurrence in 2020, highlighting an increasing concern regarding drug resistance in recent years. The terms "Triple-negative breast cancer" (Cluster 2) and "TNBC" (Cluster 1) exhibited median annual occurrences in 2021 and 2022, respectively, reflecting a growing scholarly interest in this research domain. Similarly,

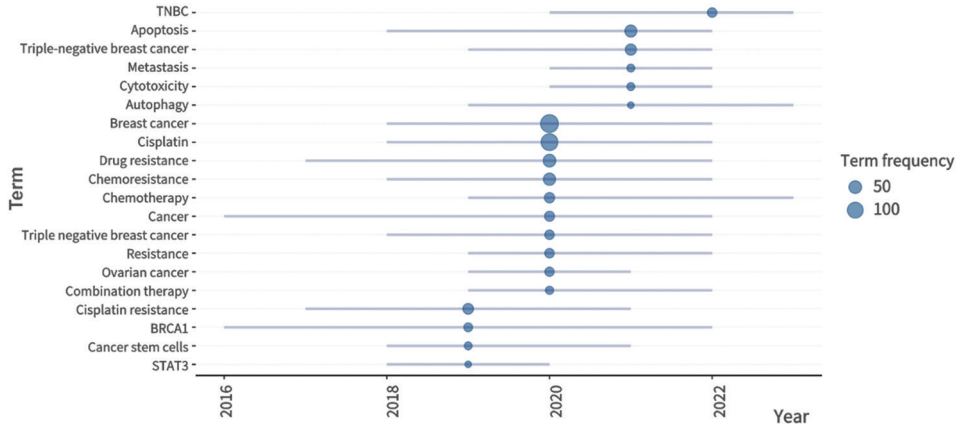

Figure 10. Keywords associated with trending topics

"Autophagy" (Cluster 1) and "Cytotoxicity" (Cluster 1) demonstrated median annual occurrences in 2021 and 2022, respectively, highlighting an increasing focus on these biological processes as potential therapeutic targets in cancer research. These trends may suggest emerging directions for future research.

This study seeks to identify key research themes in the field, acknowledging the difficulty of predicting future research paths. To address this, we utilized the thematic map module (Figure 11) to examine significant topics and potential research directions. In the first quadrant, clusters include "DNA repair," "MicroRNA," and "Prostate cancer," as well as "Competing endogenous RNA" (ceRNA), "Long intergenic non-coding RNA" (LINCRNA), and "Prognosis." The fourth quadrant features clusters of "Breast cancer," "Cisplatin," and "Drug resistance," which are central to this study. "Cytotoxicity" and "DNA damage" are associated with anticancer and multi-drug resistance within the same quadrant. Clusters of "CR," "TNBC," and "BRCA1" are in the first and fourth quadrants, emphasizing their role as both current research hotspots and developing trends. Our analyses suggest that addressing CR in BC is a major focus of current research. The analysis indicates that current research primarily concentrates on CR, TNBC, BRCA1, DNA repair, microRNA, prostate cancer, ceRNA, LINCRNA, and prognosis. Future research is expected to focus on CR, TNBC, BRCA1, autophagy, cytotoxicity, and DNA damage. CR, TNBC, and BRCA1 are central to current research and are expected to remain key areas of focus in future studies. The findings indicate that future research should prioritize the investigation of BRCA1-mediated DNA repair mechanisms and the regulation of autophagy as crucial pathways for the development of multi-target therapeutic strategies.

4. Discussion

4.1. Review and in-depth interpretation of bibliometric results

4.1.1. Review of current research status

The period from 2010 to 2024 has witnessed a general upward trajectory in the number of publications within this field; however, a downturn has been observed since 2021. This suggests that research activity may have reached its zenith in 2020, followed by a subsequent decline. The persistent decrease in citation counts could indicate a possible decrease in the quality of published papers or highlight the challenges associated with achieving significant breakthroughs in this area of research. Notably, the journal *Cancers* has emerged as the primary publication venue for research in this field, consistently demonstrating an increase in the number of articles published annually. Authors including Chekhun, V. F., Lukianova, N. Y., and Wang, B. exhibit a prolific publication record. Analysis of their collaborative network reveals a strong cooperative dynamic among researchers, with Wang, B. and Chekhun, V. F. occupying central roles. Their prominence underscores their significance within this academic domain. Since 2022, Islamic Azad University has initiated the publication of research in this domain, rapidly establishing itself as the leading institution in terms of publications from 2010 to 2024. This achievement underscores the university's robust academic standing and highlights its significant focus on the issue of BC resistance to cisplatin chemotherapy in recent years. Furthermore, China and the USA occupy the first and second positions, respectively, in terms of the number of publications and citations. This indicates their substantial lead over other countries in this field and suggests a high level of collaboration between them. Notably, China Medical University and Sun Yat-sen University, both

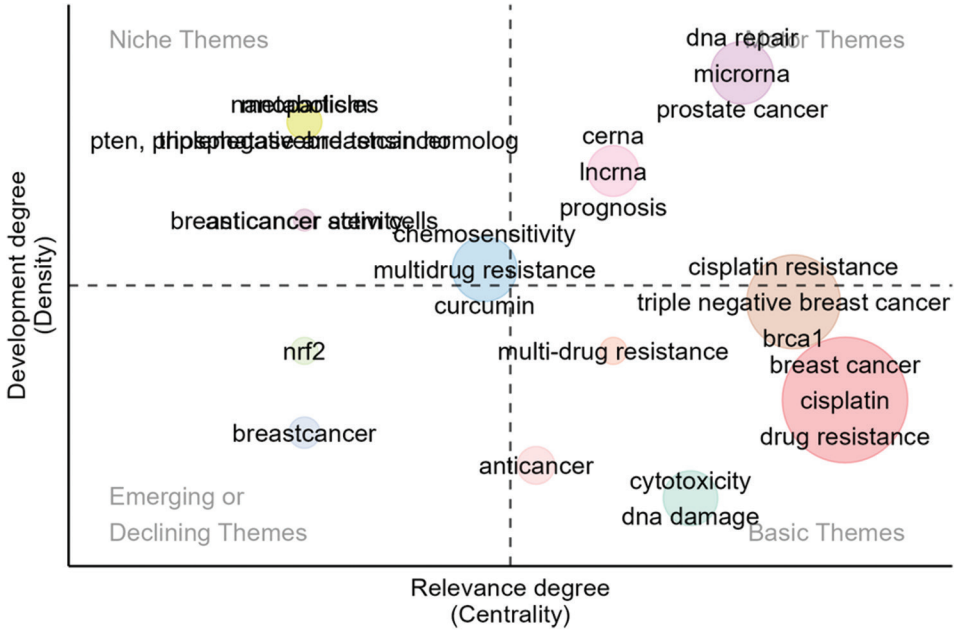

Figure 11. Thematic map: Centrality is represented on the horizontal axis, showing the topic's relevance to the field, while density is represented on the vertical axis, showing how developed the topic is. Four quadrants are plotted accordingly: motor themes, niche themes, emerging or declining themes, and basic themes.

of which are ranked third in terms of publication output, along with prominent authors such as Wang, B., Chen, H., and Wu, J., are all affiliated with Chinese institutions. This concentration of leading researchers and institutions justifies the forefront position where the China's research outcomes in this field have occupied currently on the global scale. The paper titled "Identification of distinct basal and luminal subtypes of muscle-invasive bladder cancer with different sensitivities to frontline chemotherapy"[17] has been cited 789 times. In addition, the articles "Overexpression of BLM promotes DNA damage and increased sensitivity to platinum salts in triple-negative breast and serous ovarian cancers"[18] and "Treatment of triple-negative metastatic breast cancer: toward individualized targeted treatments or chemosensitization?"[19] possess an impact factor as high as 56.7. These works have provided significant insights and have substantially advanced the development of the field. In the co-citation network analysis of the literature, it was observed that the works of Galluzzi *et al.*[20] and Dasari and Tchounwou[21] exhibit a significant interrelation in terms of research topics, concepts, or methodologies, and have been extensively cited in subsequent studies. A keyword analysis identified the central themes of this research to include "Breast cancer," "Cisplatin," and "Drug resistance." Through an examination of the topic co-occurrence network, trend topics, and topic maps, this study identifies "Cisplatin resistance," "Triple-negative breast cancer (TNBC)," "BRCA1," "DNA repair," "MicroRNA," "Prostate cancer," "ceRNA," "LINCRNA," and "Prognosis" as prominent areas of current research interest. Furthermore, it anticipates that "Cisplatin resistance," "TNBC," "BRCA1," "Autophagy," "Cytotoxicity," and "DNA damage" will emerge as significant topics in future research endeavors. Recent findings indicate that concurrently targeting BRCA1-mediated DNA repair mechanisms and autophagy regulation could provide a dual-faceted strategy to address CR. This methodology shows potential for the development of novel multi-target therapeutics.

4.1.2. Hotspots and trends in research

A bibliometric analysis reveals that the terms "Cisplatin resistance," "BRCA1," and "TNBC" have consistently emerged as prominent and central keywords from 2010 to 2024. Investigations concerning BRCA1 are poised to offer significant insights into the mechanisms underlying CR. In patients with TNBC, BRCA1 mutations not only influence the sensitivity to cisplatin therapy but may also initiate novel mechanisms of drug resistance through modulation of the DNA repair pathway.[22-27] Research indicates that tumor cells deficient in BRCA1 demonstrate heightened sensitivity to DNA-damaging agents like cisplatin, offering novel insights for targeted therapeutic strategies.[22,24] However, there are notable limitations in the current research on this topic. Nevertheless, during the course of treatment, tumor cells can develop resistance to these drugs through multiple mechanisms, such as the

reactivation of DNA repair pathways.[23,24] For instance, the loss of BRCA1 function may compel tumor cells to depend on alternative DNA repair mechanisms, consequently diminishing their sensitivity to cisplatin.[26,27] It's crucial to recognize that studies exploring these resistance mechanisms often rely on simplified models, which might not fully represent the complexities of resistance evolution in patients. Furthermore, a substantial correlation exists between BRCA1 expression levels and CR, indicating the necessity of considering BRCA1 status to optimize treatment strategies in clinical practice.[22,24,25] Incorporating BRCA1 mutation screening into clinical practice has the potential to stratify patients effectively and inform the administration of cisplatin in conjunction with poly ADP-ribose polymerase (PARP) inhibitors, thereby enhancing therapeutic outcomes. Nonetheless, the application of BRCA1 expression as a predictive biomarker is complicated by technical variability in assessment methods and considerable intra- and inter-tumoral heterogeneity. These precision oncology strategies may prove crucial in overcoming the resistance challenges associated with TNBC.

4.1.3. Future directions in hotspot interdisciplinary areas

(A). Regulatory role of microRNA

In contrast to prior investigations, this study combines bibliometric analysis with trend prediction to elucidate novel intersections between BRCA1 dysfunction and microRNA regulation. As a gene regulatory factor, microRNA may substantially influence CR by targeting *BRCA1* or autophagy-related genes, such as *BECN1*. Otherwise, studies have shown that microRNA-21 (miR-21) enhances the chemoresistance of gastric cancer cells by inhibiting autophagy, a process mediated through the PI3K/Akt/mTOR signaling pathway.[28] Furthermore, miR-223 has been identified as a regulator of autophagy through its targeting of F-box and WD repeat domain-containing protein 7 in non-small cell lung cancer, which subsequently impacts sensitivity to cisplatin.[29] In the context of ovarian cancer, the expression of miR-1301 has been correlated with CR, potentially influencing this resistance by modulating autophagy and epithelial-mesenchymal transition.[30] In addition, recent studies have demonstrated that NIMA-related kinase 2 promotes autophagy by stabilizing the Beclin-1 protein, which contributes to the development of resistance to bortezomib in multiple myeloma cells.[31] In small cell lung cancer, miR-199a-5p has been identified as a potential mediator of CR through its regulation of the interaction between the *p62* gene and autophagy.[32] In addition, miR-4486 has been found to inhibit autophagy by targeting autophagy-related gene 7, thereby reversing CR in colon cancer cells.[33] The main shortcomings of these initial studies are their focus on single miR-target interactions, overlooking the study of combined regulatory networks. Moreover, there is a significant absence of *in vivo* validation in the context of BRCA-mutated TNBC, which is the group most relevant to the mechanisms of CR. Further investigation into the roles of these and other miRs, particularly in relation to BRCA1, could elucidate additional regulatory mechanisms associated with CR in BC. Such insights may facilitate the development of targeted therapeutic strategies. Future clinical trials ought to prioritize the stratification of patients according to BRCA1 and microRNA profiles to improve the precision and efficacy of cisplatin-based treatment regimens.

(B). Connection between autophagy and TNBC resistance

Although prior research has elucidated the influence of *BRCA1* mutations on the sensitivity to platinum-based chemotherapeutics, the interaction with autophagy-related pathways remains insufficiently investigated. The role of autophagy in cancer is multifaceted, as it can either facilitate tumor cell survival or induce cell death.[34] It is plausible that a relationship exists between autophagy and drug resistance in BRCA1-deficient TNBC, wherein the modulation of autophagy may impact tumor progression and therapeutic response. For example, under hypoxic or nutrient-deficient conditions, the activation of autophagy can facilitate the survival of tumor cells in adverse microenvironments.[35] Furthermore, aberrant autophagy activation is significantly associated with chemoresistance, particularly in the context of BRCA1 deficiency.[36] Research suggests that therapeutic strategies aimed at modulating autophagy may effectively mitigate drug resistance in TNBC, especially in conjunction with targeted therapies.[37] However, there remains a considerable gap in translation. While altering autophagy shows promise in preclinical models, often using genetic silencing methods, achieving targeted and safe pharmacological control of autophagy dynamics in human tumors is still challenging. This challenge arises due to the risks of systemic toxicity and the triggering of compensatory pathways. Autophagy-related genes, including *BECN1* and *MAP1LC3A*, and their expression levels may impact patients' responses to chemotherapy.[38] Nonetheless, it's crucial to be exercise caution: while there are correlative findings

between autophagy gene expression and prognosis, these do not establish causality and frequently fail to account for confounding factors, such as tumor stage heterogeneity or prior treatment exposures among study cohorts. In addition, studies have demonstrated that autophagy within the tumor microenvironment can influence tumor progression by modulating the infiltration of immune cells.[39] Consequently, an enhanced comprehension of the mechanisms underlying autophagy in BRCA1-deficient TNBC will establish a critical foundation for addressing CR in this cancer subtype. Moreover, the intricate dual roles of autophagy, encompassing "pro-survival" and "pro-death" aspects, are heavily reliant on the surrounding circumstances. Existing models often overlook patient-specific variables, such as metabolic conditions or immune microenvironment variations, which play a key role in influencing autophagic outcomes. Simultaneously, advancing research on the dual role of autophagy-related molecules is essential for the development of novel therapeutic strategies.[40,41]

(C). Systematic drug design

Research has demonstrated that resistance to cisplatin is linked to multiple mechanisms, involving DNA repair, evading programmed cell death, and regulating autophagy.[37,42,43] Targeting the DNA repair pathway, specifically the *BRCA1* gene, has the potential to increase the sensitivity of tumor cells to cisplatin.[43] Furthermore, autophagy is a critical factor in the survival and drug resistance of tumor cells; thus, modulating autophagy may significantly influence the response of these cells to chemotherapeutic agents.[44] In TNBC, mutations in the *BRCA1* gene result in a diminished capacity for DNA repair, thereby rendering these cells more susceptible to DNA-damaging agents such as cisplatin.[45] Nonetheless, as treatment advances, tumor cells may develop resistance to the drug through mechanisms such as the activation of autophagy.[46] Consequently, integrating research on the ceRNA mechanism may facilitate the identification of key molecules that regulate both autophagy and DNA repair, offering novel targets for drug development.[47] Nevertheless, due to the well-documented context-dependency of ceRNA networks and the frequent compensatory activation of alternative resistance pathways in clinical settings, these targets require extensive validation. The development of pharmacological agents that simultaneously target both BRCA1 and the autophagy pathway has the potential to mitigate CR and enhance therapeutic outcomes. This multi-targeted approach may not only augment the antitumor efficacy of cisplatin but also diminish the emergence of drug resistance.[48] Future investigations should prioritize the effective integration of these mechanisms to optimize clinical efficacy.[49]

4.2. In-depth analysis of drug resistance mechanisms

4.2.1. Multiple functions of BRCA1

The function of BRCA1 extends beyond its involvement in DNA homologous recombination repair; it plays a critical role in the broader context of drug resistance mechanisms. Specifically, BRCA1 contributes to genomic stability by facilitating the repair of cisplatin-induced DNA double-strand breaks. However, mutations in BRCA1 can compromise its repair capabilities, resulting in increased cellular sensitivity to cisplatin.[23,26] Notably, some studies have indicated that tumor cells may regain drug resistance through the occurrence of "reversion mutations" in BRCA1.[50-52] Moreover, BRCA1 is linked to the PI3K/Akt and KEAP1-Nrf2 pathways, with aberrant activation of these pathways potentially facilitating drug resistance through mechanisms such as oxidative stress or augmented survival signaling.[53-58] Future studies should undertake a systematic analysis of the interactions among these signaling networks.

4.2.2. The twofold function of autophagy

As previously discussed, autophagy exhibits a dual role in tumor cell survival, functioning to both promote and inhibit this process.[34] It is also recognized that in drug-resistant cells, autophagy facilitates cell survival by mitigating metabolic toxicity induced by cisplatin, notably through the overexpression of Beclin-1, a critical regulator of autophagic activity in these cells.[38] Moreover, excessive activation of autophagy has the potential to counteract drug resistance by triggering mitochondrial dysfunction and apoptosis. For example, research has demonstrated that the concurrent use of cisplatin and autophagy inducers can substantially increase apoptosis rates.[59]

4.2.3. Combined treatment strategies

(A). Targeting DNA repair

PARP inhibitors have been demonstrated to effectively impede the DNA repair mechanisms in cells deficient in BRCA1. Research indicates that the concurrent administration of cisplatin and PARP inhibitors not only augments the incidence of DNA double-strand breaks but also enhances therapeutic efficacy by promoting apoptosis, thereby significantly

improving the treatment response rate in patients with TNBC.[60-63]

(B). Regulating autophagy activity

Future research endeavors may focus on developing combined pharmacological strategies that target autophagy-related molecules. Empirical evidence suggests that autophagy inhibitors, such as chloroquine and hydroxychloroquine, when administered alongside chemotherapeutic agents in various cancer types, augment the cytotoxic effects of cisplatin on tumor cells by disrupting autophagic flux, thereby significantly enhancing therapeutic efficacy.[64,65] Furthermore, studies have demonstrated that the integration of autophagy inhibitors with cisplatin can effectively surmount drug resistance in tumor cells, thereby enhancing patient prognosis.[66] Subsequent research should aim to identify and target critical molecules within the autophagy pathway, concentrate on the precise regulation of autophagy-related genes, and refine drug combination strategies to offer novel approaches for the treatment of TNBC.[59]

4.3. Optimization and development of international cooperation

China and the USA are markedly leading other nations in research within this domain, often engaging in collaborative efforts. The literature suggests that joint publications between China and the USA generally demonstrate a higher academic impact. A joint study conducted by Harvard Medical School in the USA and Sun Yat-sen University in China has introduced an innovative approach for the extraction of literature information, thereby advancing BC research and enhancing the efficiency of medical professionals and researchers.[67] In resource-constrained environments, academic collaboration can significantly improve the sustainability and efficacy of research endeavors.[68] Cancer Core Europe exemplifies this by amalgamating the expertise and resources of seven premier cancer research institutions, thereby advancing research and development in the field of precision oncology.[69] Furthermore, international cooperation has been pivotal in BC-related lymphedema research, as global collaborative networks facilitate the sharing of data and resources among researchers, thereby expediting research progress.[70] In the future, integrating China's high-yield research teams with translational medicine teams in the USA has the potential to generate more impactful research outcomes and facilitate the clinical application of research findings. Establishing a comprehensive network for multicenter studies can significantly enhance the generalizability and applicability of research outcomes, potentially expediting the global approval process for innovative therapies targeting CR.

4.4. Clinical translation and therapeutic prospects

4.4.1. Implementation of personalized treatment

Individualized treatment strategies for TNBC that incorporate BRCA1 genetic testing have demonstrated considerable clinical potential. By identifying BRCA1-deficient patients through genetic screening and subsequently administering a regimen of cisplatin and PARP inhibitors, therapeutic efficacy can be markedly enhanced.[71,72] This approach presents promising prospects for TNBC patients and merits further advancement and investigation in future clinical practice.[73,74]

4.4.2. Potential of novel drug development

(A). MicroRNA therapy

The exploration of microRNA mimics or inhibitors, including miR-152-3p mimics, is underway to modulate the expression of BRCA1 and autophagy-related molecules.

(B). Multi-target combination therapy

As previously discussed, the integration of DNA repair inhibition with autophagy regulation in drug design has the potential to inform the development of therapeutic strategies that address a range of drug resistance mechanisms.

4.4.3. Translational implications

The study of CR in BC reveals complex translational implications. Multi-target drug design and combination therapy are essential in treatment strategies. CR involves various mechanisms, and drugs targeting both the BRCA1-mediated DNA repair pathway and the autophagy pathway, such as combining PARP inhibitors with cisplatin, can enhance treatment response rates in patients with TNBC. Using autophagy inhibitors alongside cisplatin can increase cytotoxicity and help overcome resistance. Personalized treatment for TNBC based on BRCA1 genetic testing shows significant potential. Identifying patients with BRCA1 deficiencies through genetic screening and treating them with a combination of cisplatin and PARP inhibitors can greatly improve efficacy. Meanwhile, recent research has introduced deep learning models that could serve as a technical foundation for integrating BRCA1 and other genetic data, thereby enhancing the accuracy of stratification and the prediction of drug resistance in BC imaging detection.[75,76] In addition, advancements in novel drug development, including microRNA therapy, can regulate related molecular expressions, and multi-target combination therapy shows promise in addressing various drug resistance mechanisms. However, translational research faces challenges, including drug resistance heterogeneity and recurrence, necessitating the

development of more adaptable combination treatment strategies and sustainable treatment plans. As research advances, it is anticipated that patient prognosis will improve in the future.

4.4.4. Limitations

The data utilized in this study are exclusively derived from the PubMed database, potentially introducing publication bias and limiting the retrieval of all pertinent literature. Furthermore, the statistical cutoff date for this study is set at September 9, 2024, which may result in incomplete data for publications from that year and consequently impact the reported findings, including the potential limitations associated with the identification of emerging topics, among others.

5. Conclusion

This study elucidates significant research trajectories and collaborative networks concerning CR in BC, with a particular focus on BRCA1 dysfunction and the regulation of autophagy as crucial domains for therapeutic advancement. It is recommended that future research endeavors prioritize translational studies and the development of multi-targeted pharmacological interventions to address the clinical challenges associated with treatment resistance.

Acknowledgments

None.

Funding

This study was supported by the Natural Science Foundation of Xinjiang Uyghur Autonomous Region–Youth Science Foundation (2022D01C277), China.

Conflict of interest

The authors declare that they have no competing interests.

Author contributions

Conceptualization: Jiawei Kang, Tayier Tuersong
Visualization: Jiawei Kang, Nan Jiang, Munire Shataer
Writing – original draft: Jiawei Kang
Writing – review & editing: Jiawei Kang

Ethics approval and consent to participate

This study utilized publicly available datasets with comprehensive patient informed consent.

Consent for publication

Not applicable.

Availability of data

Data supporting the findings of this study are available from the corresponding author on reasonable request.

References

1. Cox K, Alford B, Soliman H. Emerging therapeutic strategies in breast cancer. *South Med J*. 2017;110(10):632-637.

   doi: 10.14423/SMJ.0000000000000709

2. Vasan N, Baselga J, Hyman DM. A view on drug resistance in cancer. *Nature*. 2019;575(7782):299-309.

   doi: 10.1038/s41586-019-1730-1

3. Haider T, Pandey V, Banjare N, Gupta PN, Soni V. Drug resistance in cancer: mechanisms and tackling strategies. *Pharmacol Rep*. 2020;72(5):1125-1151.

   doi: 10.1007/s43440-020-00138-7

4. Duan M, Ulibarri J, Liu KJ, Mao P. Role of nucleotide excision repair in cisplatin resistance. *Int J Mol Sci*. 2020;21(23):9248.

   doi: 10.3390/ijms21239248

5. Ji X, Lu Y, Tian H, Meng X, Wei M, Cho WC. Chemoresistance mechanisms of breast cancer and their countermeasures. *Biomed Pharmacother*. 2019;114:108800.

   doi: 10.1016/j.biopha.2019.108800

6. Zhou J, Kang Y, Chen L, *et al*. The drug-resistance mechanisms of five platinum-based antitumor agents. *Front Pharmacol*. 2020;11:343.

   doi: 10.3389/fphar.2020.00343

7. Wang S, Li MY, Liu Y, *et al*. The role of microRNA in cisplatin resistance or sensitivity. *Expert Opin Ther Targets*. 2020;24(9):885-897.

   doi: 10.1080/14728222.2020.1785431

8. Tan Q, Joshua AM, Wang M, *et al*. Up-regulation of autophagy is a mechanism of resistance to chemotherapy and can be inhibited by pantoprazole to increase drug sensitivity. *Cancer Chemother Pharmacol*. 2017;79(5):959-969.

   doi: 10.1007/s00280-017-3298-5

9. Koerniadi MMU, Tadjoedin FM, Hutomo DI, Tadjoedin ESS, Rizal MI, Sulijaya B. Bibliometric network analysis and visualization of research trends in gingivectomy. *Clin Cosmet Investig Dent*. 2024;16:209-218.

   doi: 10.2147/CCIDE.S470234

10. Chou W, Chow JC. Identifying authorial roles in research: A Kano model-based bibliometric analysis for the Journal of Medicine (Baltimore) 2023. *Medicine* (*Baltimore*). 2024;103(35):e39234.

    doi: 10.1097/MD.0000000000039234

11. Rae AR, Mork JG, Demner-Fushman D. The NLM indexer assignment dataset: a new large-scale dataset for reviewer

assignment research. *J Assoc Inf Sci Technol*. 2023;74(2):205-218.

doi: 10.1002/asi.24722

12. D'Souza J, Ng V. Classifying temporal relations in clinical data: A hybrid, knowledge-rich approach. *J Biomed Inform*. 2013;46 Suppl(0):S29-S39.

doi: 10.1016/j.jbi.2013.08.003

13. Aria M, Cuccurullo C. Bibliometrix: An R-tool for comprehensive science mapping analysis. *J Informetr*. 2017;11(4):959-975.

doi: 10.1016/j.joi.2017.04.002

14. Ogunsakin RE, Ebenezer O, Ginindza TG. A bibliometric analysis of the literature on norovirus disease from 1991-2021. *Int J Environ Res Public Health*. 2022;19(5):2508.

doi: 10.3390/ijerph19052508

15. Musa HH, Musa TH. A systematic and thematic analysis of the top 100 cited articles on mRNA vaccine indexed in Scopus database. *Hum Vaccin Immunother*. 2022;18(6):2135927.

doi: 10.1080/21645515.2022.2135927

16. Volpe S, Mastroleo F, Krengli M, Jereczek-Fossa BA. Quo vadis Radiomics? Bibliometric analysis of 10-year Radiomics journey. *Eur Radiol*. 2023;33(10):6736-6745.

doi: 10.1007/s00330-023-09645-6

17. Choi W, Porten S, Kim S, *et al*. Identification of distinct basal and luminal subtypes of muscle-invasive bladder cancer with different sensitivities to frontline chemotherapy. *Cancer Cell*. 2014;25(2):152-165.

doi: 10.1016/j.ccr.2014.01.009

18. Birkbak NJ, Li Y, Pathania S, *et al*. Overexpression of BLM promotes DNA damage and increased sensitivity to platinum salts in triple-negative breast and serous ovarian cancers. *Ann Oncol*. 2018;29(4):903-909.

doi: 10.1093/annonc/mdy049

19. Berrada N, Delaloge S, Andre F. Treatment of triple-negative metastatic breast cancer: Toward individualized targeted treatments or chemosensitization? *Ann Oncol*. 2010;21 Suppl 7:vii30-vii35.

doi: 10.1093/annonc/mdq279

20. Galluzzi L, Senovilla L, Vitale I, *et al*. Molecular mechanisms of cisplatin resistance. *Oncogene*. 2012;31(15):1869-1883.

doi: 10.1038/onc.2011.384

21. Dasari S, Tchounwou PB. Cisplatin in cancer therapy: Molecular mechanisms of action. *Eur J Pharmacol*. 2014;740:364-378.

doi: 10.1016/j.ejphar.2014.07.025

22. Imyanitov EN. Cytotoxic and targeted therapy for BRCA1/2-driven cancers. *Hered Cancer Clin Pract*. 2021;19(1):36.

doi: 10.1186/s13053-021-00193-y

23. Janysek DC, Kim J, Duijf PHG, Dray E. Clinical use and mechanisms of resistance for PARP inhibitors in homologous recombination-deficient cancers. *Transl Oncol*. 2021;14(3):101012.

doi: 10.1016/j.tranon.2021.101012

24. Raimundo L, Calheiros J, Saraiva L. Exploiting DNA damage repair in precision cancer therapy: BRCA1 as a prime therapeutic target. *Cancers* (*Basel*). 2021;13(14):3438.

doi: 10.3390/cancers13143438

25. Kalra M, Tong Y, Jones DR, *et al*. Cisplatin +/- rucaparib after preoperative chemotherapy in patients with triple-negative or BRCA mutated breast cancer. *NPJ Breast Cancer*. 2021;7(1):29.

doi: 10.1038/s41523-021-00240-w

26. Cai C. A novel mechanism to induce BRCAness in cancer cells. *Cancer Res*. 2020;80(14):2977-2978.

doi: 10.1158/0008-5472.CAN-20-1451

27. Murakami M, Izumi H, Kurita T, Koi C, Morimoto Y, Yoshino K. UBE2L6 is involved in cisplatin resistance by regulating the transcription of ABCB6. *Anticancer Agents Med Chem*. 2020;20(12):1487-1496.

doi: 10.2174/1871520620666200424130934

28. Gu Y, Fei Z, Zhu R. miR-21 modulates cisplatin resistance of gastric cancer cells by inhibiting autophagy via the PI3K/Akt/mTOR pathway. *Anticancer Drugs*. 2020;31(4):385-393.

doi: 10.1097/CAD.0000000000000886

29. Wang H, Chen J, Zhang S, *et al*. MiR-223 regulates autophagy associated with cisplatin resistance by targeting FBXW7 in human non-small cell lung cancer. *Cancer Cell Int*. 2020;20:258.

doi: 10.1186/s12935-020-01284-x

30. Yu JL, Gao X. MicroRNA 1301 inhibits cisplatin resistance in human ovarian cancer cells by regulating EMT and autophagy. *Eur Rev Med Pharmacol Sci*. 2020;24(4):1688-1696.

doi: 10.26355/eurrev_202002_20343

31. Xia J, He Y, Meng B, *et al*. NEK2 induces autophagy-mediated bortezomib resistance by stabilizing Beclin-1 in multiple myeloma. *Mol Oncol*. 2020;14(4):763-778.

doi: 10.1002/1878-0261.12641

32. Liu X, Wang X, Chai B, *et al*. miR-199a-3p/5p regulate tumorgenesis via targeting Rheb in non-small cell lung cancer [published correction appears in Int J Biol Sci. 2023 Jul 27;19(12):3830. doi: 10.7150/ijbs.86344.]. *Int J Biol Sci*. 2022;18(10):4187-4202.

doi: 10.7150/ijbs.70312

33. Wang W, Chen L, Zhu W, *et al*. miR-4486 reverses cisplatin-resistance of colon cancer cells via targeting ATG7 to

inhibiting autophagy. *Exp Ther Med.* 2021;22(6):1465.

doi: 10.3892/etm.2021.10900

34. Ahmadi-Dehlaghi F, Mohammadi P, Valipour E, Pournaghi P, Kiani S, Mansouri K. Autophagy: A challengeable paradox in cancer treatment. *Cancer Med*. 2023;12(10):11542-11569.

doi: 10.1002/cam4.5577

35. Chen Y, Gibson SB. Three dimensions of autophagy in regulating tumor growth: Cell survival/death, cell proliferation, and tumor dormancy. *Biochim Biophys Acta Mol Basis Dis*. 2021;1867(12):166265.

doi: 10.1016/j.bbadis.2021.166265

36. Noguchi M, Hirata N, Tanaka T, Suizu F, Nakajima H, Chiorini JA. Autophagy as a modulator of cell death machinery. *Cell Death Dis.* 2020;11(7):517.

doi: 10.1038/s41419-020-2724-5

37. Cocco S, Leone A, Roca MS, *et al*. Inhibition of autophagy by chloroquine prevents resistance to PI3K/AKT inhibitors and potentiates their antitumor effect in combination with paclitaxel in triple negative breast cancer models. *J Transl Med*. 2022;20(1):290.

doi: 10.1186/s12967-022-03462-z

38. Usman RM, Razzaq F, Akbar A, *et al*. Role and mechanism of autophagy-regulating factors in tumorigenesis and drug resistance. *Asia Pac J Clin Oncol*. 2021;17(3):193-208.

doi: 10.1111/ajco.13449

39. de Souza ASC, Gonçalves LB, Lepique AP, de Araujo-Souza PS. The role of autophagy in tumor immunology-complex mechanisms that may be explored therapeutically. *Front Oncol*. 2020;10:603661.

doi: 10.3389/fonc.2020.603661

40. Chen C, Gao H, Su X. Autophagy-related signaling pathways are involved in cancer (Review). *Exp Ther Med*. 2021;22(1):710.

doi: 10.3892/etm.2021.10142

41. Silva VR, Neves SP, Santos LS, Dias RB, Bezerra DP. Challenges and therapeutic opportunities of autophagy in cancer therapy. *Cancers* (*Basel*). 2020;12(11):3461.

doi: 10.3390/cancers12113461

42. Panaretakis T. Cisplatin-induced apoptosis and development of resistance are transcriptionally distinct processes. *Cell Cycle*. 2012;11(20):3723.

doi: 10.4161/cc.22114

43. Zhu Y, Zhang C, Yin Q, Xu W, Luo Y, Ou J. FOXO4 suppresses cisplatin resistance of triple-negative breast cancer by inhibiting autophagy. *Am J Med Sci*. 2025;369(2):252-263.

doi: 10.1016/j.amjms.2024.08.012

44. Lu H, Tong W, Jiang M, *et al*. Mitochondria-targeted multifunctional nanoprodrugs by inhibiting metabolic reprogramming for combating cisplatin-resistant lung cancer. *ACS Nano.* 2024;18(32):21156-21170.

doi: 10.1021/acsnano.4c04024

45. Tazzite A, Jouhadi H, Benider A, Nadifi S. BRCA mutational status is a promising predictive biomarker for platinum- based chemotherapy in triple-negative breast cancer. *Curr Drug Targets.* 2020;21(10):962-973.

doi: 10.2174/1389450121666200203162541

46. Varol A, Boulos JC, Jin C, Klauck SM, Zhitkovich A, Efferth T. Inhibition of MSH6 augments the antineoplastic efficacy of cisplatin in non-small cell lung cancer as autophagy modulator. *Chem Biol Interact*. 2024;402:111193.

doi: 10.1016/j.cbi.2024.111193

47. Ghazy S, Oktay L, Durdağı S. A novel algorithm for the virtual screening of extensive small molecule libraries against ERCC1/XPF protein-protein interaction for the identification of resistance-bypassing potential anticancer molecules. *Turk J Biol.* 2024;48(2):91-111.

doi: 10.55730/1300-0152.2686

48. Yue P, Han B, Zhao Y. Focus on the molecular mechanisms of cisplatin resistance based on multi-omics approaches. *Mol Omics*. 2023;19(4):297-307.

doi: 10.1039/d2mo00220e

49. Wang B, Zhang R, Wang Y, *et al*. Targeting Rab26 to conquer cisplatin-resistant lung cancer with self-assembled DNA nanomaterials. *Biomacromolecules*. 2023;24(5):2063-2074.

doi: 10.1021/acs.biomac.2c01493

50. Loehr A, Hussain A, Patnaik A, *et al*. Emergence of BRCA reversion mutations in patients with metastatic castration-resistant prostate cancer after treatment with rucaparib. *Eur Urol*. 2023;83(3):200-209.

doi: 10.1016/j.eururo.2022.09.010

51. Imyanitov E, Sokolenko A. Mechanisms of acquired resistance of BRCA1/2-driven tumors to platinum compounds and PARP inhibitors. *World J Clin Oncol.* 2021;12(7):544-556.

doi: 10.5306/wjco.v12.i7.544

52. Pettitt SJ, Frankum JR, Punta M, *et al*. Clinical BRCA1/2 reversion analysis identifies hotspot mutations and predicted neoantigens associated with therapy resistance. *Cancer Discov.* 2020;10(10):1475-1488.

doi: 10.1158/2159-8290.CD-19-1485

53. DeNicola GM, Karreth FA, Humpton TJ, *et al.* Oncogene-induced Nrf2 transcription promotes ROS detoxification and tumorigenesis. *Nature*. 2011;475(7354):106-109.

doi: 10.1038/nature10189

54. Li D, Hong X, Zhao F, Ci X, Zhang S. Targeting Nrf2 may

reverse the drug resistance in ovarian cancer. *Cancer Cell Int*. 2021;21(1):116.

doi: 10.1186/s12935-021-01822-1

55. Telkoparan-Akillilar P, Panieri E, Cevik D, Suzen S, Saso L. Therapeutic targeting of the NRF2 signaling pathway in cancer. *Molecules*. 2021;26(5):1417.

doi: 10.3390/molecules26051417

56. He F, Antonucci L, Karin M. NRF2 as a regulator of cell metabolism and inflammation in cancer. *Carcinogenesis*. 2020;41(4):405-416.

doi: 10.1093/carcin/bgaa039

57. Smolkova K, Miko E, Kovacs T, Leguina-Ruzzi A, Sipos A, Bai P. Nuclear factor erythroid 2-related factor 2 in regulating cancer metabolism. *Antioxid Redox Signal*. 2020;33(13):966-997.

doi: 10.1089/ars.2020.8024

58. Jasek-Gajda E, Jurkowska H, Jasińska M, Lis GJ. Targeting the MAPK/ERK and PI3K/AKT signaling pathways affects NRF2, Trx and GSH antioxidant systems in leukemia cells. *Antioxidants* (*Basel*). 2020;9(7):633.

doi: 10.3390/antiox9070633

59. Yang Y, Liu L, Tian Y, *et al*. Autophagy-driven regulation of cisplatin response in human cancers: Exploring molecular and cell death dynamics. *Cancer Lett.* 2024;587:216659.

doi: 10.1016/j.canlet.2024.216659

60. Lin KY, Kraus WL. PARP inhibitors for cancer therapy. *Cell*. 2017;169(2):183.

doi: 10.1016/j.cell.2017.03.034

61. Huang YZ, Sang MY, Xi PW, *et al*. FANCI inhibition induces PARP1 redistribution to enhance the efficacy of PARP inhibitors in breast cancer. *Cancer Res*. 2024;84(20):3447-3463.

doi: 10.1158/0008-5472.CAN-23-2738

62. Li Y, Miao W, Yuan C, *et al*. PARP inhibitor boost the efficacy of photothermal therapy to TNBC through enhanced DNA damage and inhibited homologous recombination repair. *Drug Deliv Transl Res*. 2025;15(3):955-967.

doi: 10.1007/s13346-024-01650-6

63. Sakogawa K, Aoki Y, Misumi K, *et al*. Involvement of homologous recombination in the synergism between cisplatin and poly (ADP-ribose) polymerase inhibition. *Cancer Sci*. 2013;104(12):1593-1599.

doi: 10.1111/cas.12281

64. Skrzeszewski M, Maciejewska M, Kobza D, Gawrylak A, Kieda C, Was H. Risk factors of using late-autophagy inhibitors: Aspects to consider when combined with anticancer therapies. *Biochem Pharmacol*. 2024;225:116277.

doi: 10.1016/j.bcp.2024.116277

65. Hassan AMIA, Zhao Y, Chen X, He C. Blockage of autophagy for cancer therapy: A comprehensive review. *Int J Mol Sci*. 2024;25(13):7459.

doi: 10.3390/ijms25137459

66. Wu Y, Wang A, Feng G, *et al*. Autophagy modulation in cancer therapy: Challenges coexist with opportunities. *Eur J Med Chem*. 2024;276:116688.

doi: 10.1016/j.ejmech.2024.116688

67. Hughes KS, Zhou J, Bao Y, Singh P, Wang J, Yin K. Natural language processing to facilitate breast cancer research and management. *Breast J*. 2020;26(1):92-99.

doi: 10.1111/tbj.13718

68. Hasan W, Simeon-Dubach D, Tumilasci V, Sebbel P, Orth S. Challenges and opportunities for collaboration between academic biobanks and industry: Results of an international survey of academic biobanks. *Biopreserv Biobank*. 2024.

doi: 10.1089/bio.2023.0156

69. Carmona J, Chavarria E, Donoghue K, *et al*. Cancer core Europe: Leveraging institutional synergies to advance oncology research and care globally. *Cancer Discov.* 2024;14(7):1147-1153.

doi: 10.1158/2159-8290.CD-24-0377

70. Huang J, Li J, Li Y, *et al*. Bibliometric analysis of breast cancer-related lymphedema research trends over the last 2 decades. *Front Oncol*. 2024;14:1360899.

doi: 10.3389/fonc.2024.1360899

71. Xie Y, Xiao D, Li D, *et al*. Combined strategies with PARP inhibitors for the treatment of BRCA wide type cancer. *Front Oncol*. 2024;14:1441222.

doi: 10.3389/fonc.2024.1441222

72. Rodler E, Sharma P, Barlow WE, *et al*. Cisplatin with veliparib or placebo in metastatic triple-negative breast cancer and BRCA mutation-associated breast cancer (S1416): A randomised, double-blind, placebo-controlled, phase 2 trial. *Lancet Oncol*. 2023;24(2):162-174.

doi: 10.1016/S1470-2045(22)00739-2

73. Guney Eskiler G, Ozman Z, Haciefendi A, Cansaran-Duman D. Novel combination treatment of CDK 4/6 inhibitors with PARP inhibitors in triple negative breast cancer cells. *Naunyn Schmiedebergs Arch Pharmacol.* 2023;396(5):1031-1041.

doi: 10.1007/s00210-022-02375-4

74. Macchini M, Centonze F, Peretti U, *et al*. Treatment opportunities and future perspectives for pancreatic cancer patients with germline BRCA1-2 pathogenic variants. *Cancer Treat Rev*. 2021;100:102262.

doi: 10.1016/j.ctrv.2021.102262

75. Qian L, Bai J, Huang Y, Zeebaree DQ, Saffari A, Zebari DA. Breast cancer diagnosis using evolving deep convolutional neural network based on hybrid extreme learning machine technique and improved chimp optimization algorithm. *Biomed Signal Process Control*. 2024;87(A):105492.

doi: 10.1016/j.bspc.2023.105492

76. Cao J, Zeebaree DQ, Chen Q, Zebari DA. Breast cancer diagnosis using hybrid AlexNet-ELM and chimp optimization algorithm evolved by Nelder-Mead simplex approach. *Biomed Signal Process Control*. 2023;85:105053.

doi: 10.1016/j.bspc.2023.105053