FUTURE SCIENCE OA
2025, VOL. 11, NO. 1, 2484159
https://doi.org/10.1080/20565623.2025.2484159

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RESEARCH ARTICLE

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Unraveling the anoikis-cancer nexus: a bibliometric analysis of research trends and mechanisms

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ABSTRACT

Background: Cancer, influenced by genetics and the environment, involves anoikis, a cell death mechanism upon extracellular matrix detachment crucial for metastasis. Understanding this relationship is key for therapy. We analyze cancer and anoikis trends using bibliometrics.
Methods: A search was conducted from Web of Science Core, PubMed, Scopus and non-English databases such as the CNKI (inception- 21 December 2024). Data analysis employed Microsoft Excel, VOSviewer, CiteSpace, R software, and the online platform (https://bibliometric.com/).
Results: 2510 publications were retrieved, with a significant increase in the last decade. China led, the University of Texas system was productive, and the Oncogene Journal was popular. Breast, and colorectal cancers were frequently studied. Among them, representative tumor-related mechanisms were identified, commonalities such as (EMT, ECM, autophagy) and respective specific mechanisms were summarized.
Conclusion: This bibliometric analysis highlights rapid advances in anoikis research in cancer, emphasizing EMT and FAK pathways' translational potential, guiding targeted therapies, and improving cancer treatment outcomes.

ARTICLE HIGHLIGHTS

- Anoikis is a cell death mode that involves detachment from the extracellular matrix and is closely related to cancer. We used VOSviewer, CiteSpace, R studio, and online platforms to conduct a bibliometric analysis of cancer and anoikis.
- The publications and citations of anoikis-related research have grown steadily, with a significant surge in publication volume observed in 2023 and a notable spike in citation volume occurring in 2019.
- China and the United States are the leading contributors, with the University of Texas system ranking as the most prolific institution.
- Chanvorachote P and Zhang Y are top authors, while co-cited references reveal critical insights into tumor progression and therapeutic targets.
- Emerging trends focus on metabolism, statistics, microenvironment, tumor microenvironment, promoting anoikis and discovery, with thematic evolution showing interest in biomarkers and cancer metastasis.

ARTICLE HISTORY
Received 24 September 2024
Accepted 12 March 2025

KEYWORDS
Anoikis; Cancer; Bibliometric analysis; VOSviewer; CiteSpace

1. Introduction

Cancer is a complex disease characterized by the uncontrolled growth and spread of abnormal cells. Various factors, including genetics and environmental exposures, contribute to cancer development, making early detection and treatment critical for improving outcomes [1]. Anoikis is a crucial form of programmed cell death that transpires

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Supplemental data for this article can be accessed online at https://doi.org/10.1080/20565623.2025.2484159.

when cells detach from the extracellular matrix (ECM) or neighboring cells. It plays a vital role in preserving tissue homeostasis and preventing the metastasis of cancer. Anoikis is indispensable for normal development and tissue remodeling as it ensures that cells are accurately positioned and anchored to the ECM [2]. The development and progression of cancers frequently entail the evasion of anoikis, a process that enables cancer cells to survive and flourish in circumstances where typical cells undergo programmed cell death. To evade anoikis, cancer cells acquire various adaptations and molecular alterations, which provide them with a survival advantage and promote their ability to invade surrounding tissues and metastasize to distant locations [3]. Cancer cells often develop resistance to anoikis, attributed to various mechanisms such as the dysregulation of cell adhesion molecules, changes in signaling pathways related to cell survival and apoptosis, activation of pro-survival signaling pathways, and the expression of anti-apoptotic proteins [4,5]. Furthermore, genetic and epigenetic changes can also contribute to the acquisition of anoikis resistance, leading to further cancer progression and metastasis [6–8].

Bibliometric analysis involves a quantitative examination of publication patterns and citation records with the aim of identifying key publications, influential authors, research networks, and emerging research topics [9]. The integration of bibliometrics with machine learning techniques enhances the capacity to extract insights from scholarly data and uncover latent relationships within the scientific literature [10]. This approach offers a holistic comprehension of the research landscape while facilitating the identification of research gaps and opportunities for future investigation [11].

To the best of our knowledge, no bibliometric studies have been conducted in the field of anoikis in cancers. This paper introduced a machine learning-based bibliometric analysis with the objective of visualizing and exploring the association between anoikis and cancer through a comprehensive analysis of relevant scientific literature. Through an analysis of publications that discuss the relationship between anoikis and various facets of cancer, including cancer development, metastasis, and therapeutic intervention, we extracted valuable information such as keywords, author relationships, and citation patterns. Furthermore, we identify influential publications and emerging research topics, which serve as valuable resources for researchers, clinicians, and policymakers, aiding in the identification of potential avenues for further research and the development of treatment strategies. Additionally, we employed advanced data visualization techniques to elucidate patterns, trends, and connections, thereby enhancing our understanding of the intricate interplay between anoikis and cancer. This research holds the potential to catalyze advancements in cancer biology, therapeutics, and patient care, ultimately leading to improved outcomes for individuals affected by cancer.

2. Material and methods

2.1. Source database and data collection

The database source is the Web of Science Core Collection (WoSCC) Bibliographic Database Scientific Citation Index Extended Edition (SCIE), PubMed Database, Scopus Database, and non-English databases such as the CNKI Database, which are used to retrieve a total of 2672 documents on 22 December 2024, to avoid deviation. Publication time span is set to start from the database until 21 December 2024. Search terms include anoikis and cancer, etc., see the appendix for details. Then, two independent researchers (NS and JJ) downloaded all eligible data at the same time and selected the most core literature from the subject articles and comments, and excluded unrelated duplicates and literature, including conference abstracts, early stages. Visit, withdraw research, book chapters, conference papers, and data protocols. Any dispute between the two authors will be submitted to a third party (CD) to resolve the unresolved agreement. Finally, 2510 papers were included in the final data for further analysis. The detailed screening procedure is shown in Supplementary Figure 1.

2.2. Data extraction and analysis

Eligible data and recorded information of analyzed documents were retrieved to import several software for research. The Microsoft Excel 2019, VOSviewer (v.1.6.17), CiteSpace (v.6.2.R2), R software (v.3.6.1), and online platform (https://bibliometric.com/) were used to analyze the characteristic information of publications [12,13]. All associated data with annual publishment trends, countries/regions, journals and prolific institutions were imported into Excel for quantitative and dynamics trends. In Trend Topics analysis, the Word Minimum Frequency is set to 10. The parameters of Factorial Analysis are set to Number of terms: 50, N. of Clusters: 2, Num. of documents: 5. Meanwhile, VOSviewer was used to analyze the cooperation among countries, institutions, authors, and keywords. While

CiteSpace aimed to definite the dual-map overlay of journals, knowledge map, and timeline view of references, top references and keywords with the strongest citation bursts. And the parameters were set as: link retaining factor (LRF) = 3(LRF controls the number of links retained in the co-citation network and affects the sparsity of the graph. LRF = 3 means that in each time slice, each node retains at most 3 strongest links. This parameter can balance information integrity and readability), e for top N (e=1)(This parameter controls the number of high-impact papers included in the analysis in each time segment, with e=1 selecting the most cited papers in each year to ensure that the study focuses on high-impact papers), time interval (beginning–2024), years per slice (1), look back years (LBY = 5), links (strength: cosine, scope: within slices), selection criteria (g-index: k=5) (This is the criterion for determining high-impact literature to be included in the analysis. g-index=k×h-index, k=5 means that when selecting high-impact literature, the g-index is allowed to be 5 times the h-index to ensure that the most important papers are not underestimated), and minimum duration (MD = 1) [14]. The quality of authors and journals was evaluated via the H-index. Journal Citation Reports and impact factor of journals were referred to the online website (https://jcr.clarivate.com/). This study was designed in strict accordance with the guidelines for bibliometric research [15]. In order to compare the differences in the number of publications between China and the United States at 26 consecutive time points, this study used the Wilcoxon Signed-Rank Test to analyze the significant differences.

3. Results

3.1. Annual growth trend of publications and citations

This article confirmed a total of 2510 documents including 2171 articles and 339 reviews based on the search strategy. The number of annual articles published and the citations per year maintained steady growth over time in Figure 1. Among them, the year with the highest number of paper publications and citations was 2023, with over 200 documents published and more than 10,000 citations. Additionally, the publications of the recent 10 years all exceeded 120, and research in this area has shown explosive growth in the past two years, indicating the high attention paid to this type of research.

3.2. Countries/regions and institutions analysis

The bibliometric analysis included 2510 papers from 68 different countries/regions and 2322 institutions. The publications column diagram of the top 20 productive countries was demonstrated in Figure 2A, showing single-country publications with a green bar and multiple country publications with a red bar. The China ranked first in the list of total documents (N=763), followed by the United States (N=594) and Japan (N=172) in Table 1. Meanwhile, a geographic visualization map in Figure 2B showed typical country distribution characteristics

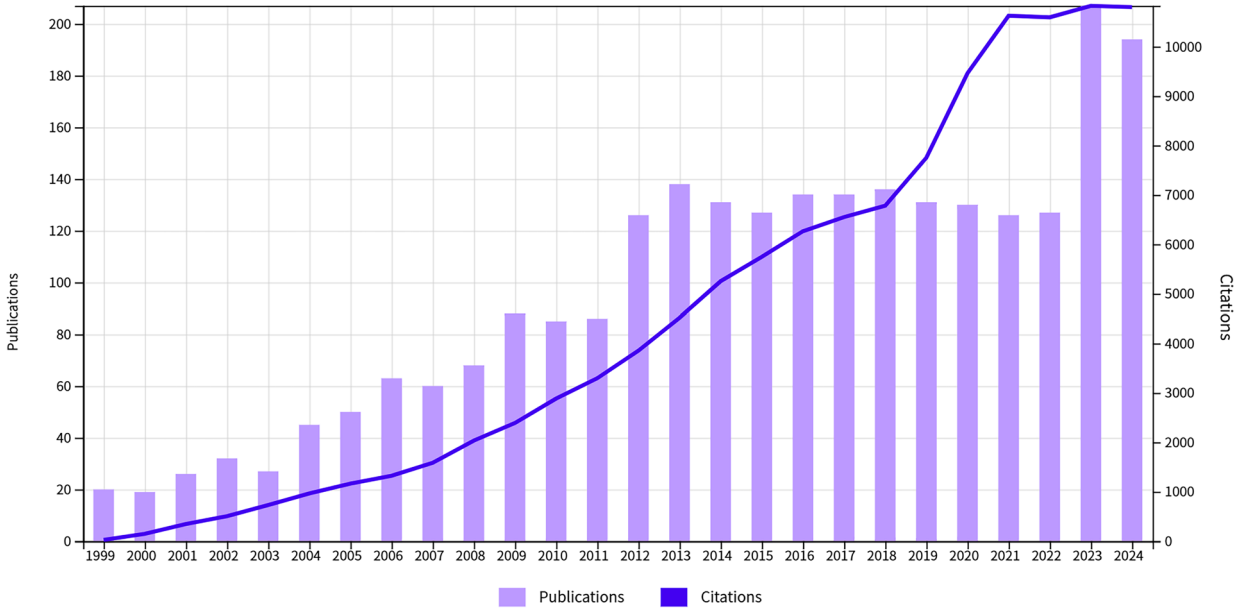

Figure 1. Trends in the annual publications and citations from 1999 to 21 December 2024.

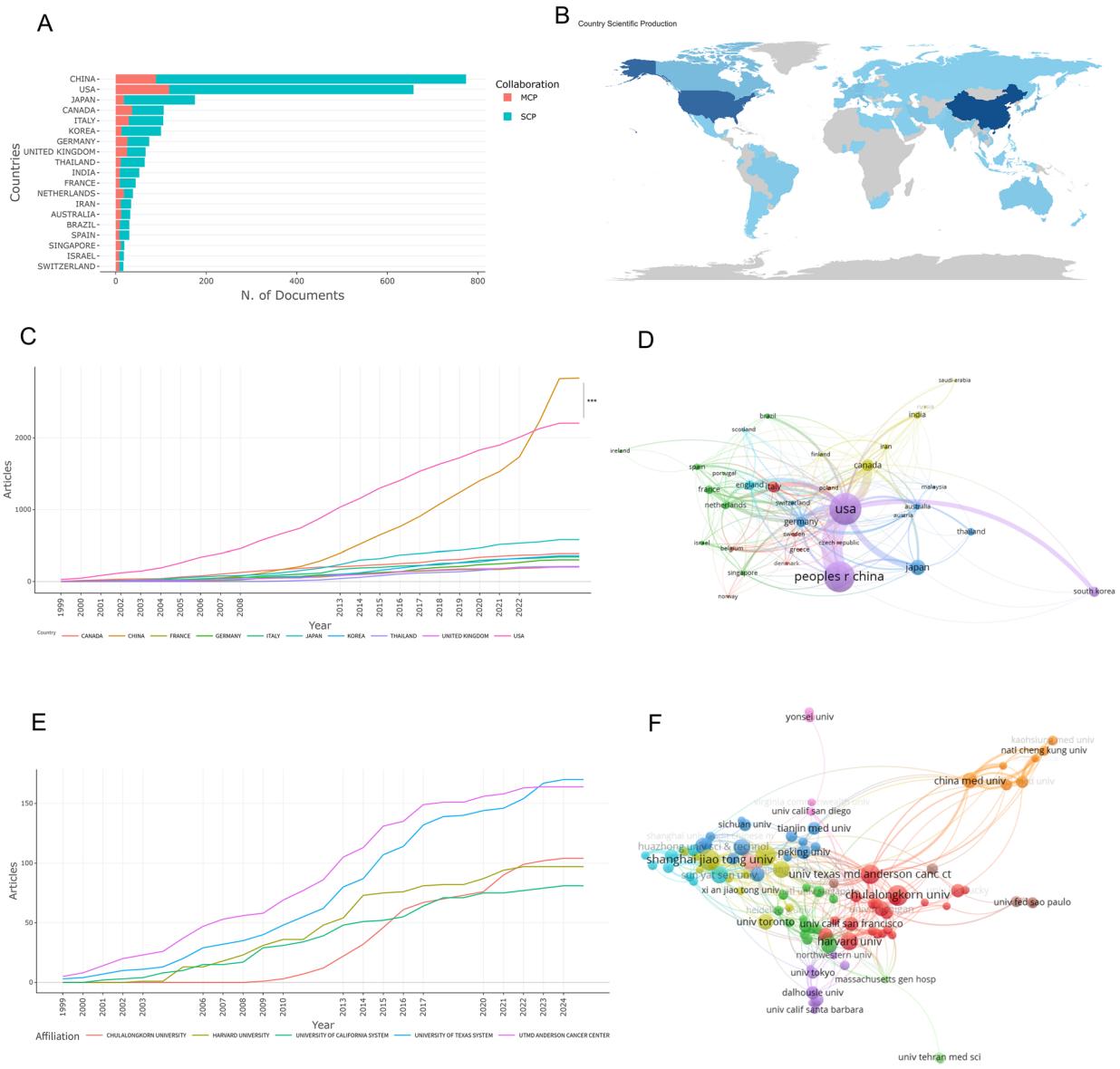

Figure 2. Analysis of publications from different countries/regions and institutions. **(A)** Top 20 productive countries about single country publications and multiple country publications. **(B)** Geographic distribution map from different countries/regions about published documents. **(C)** Top 10 productive countries based on the annual publications over time. **(D)** The national/regional output network visualization map (T ≥ 9, N = 34). **(E)** Top 5 productive institutions based on the annual publications over time. **(F)** The institutions output network visualization map (T ≥ 10, N = 104). ***$p < 0.001$.

Table 1. Top 10 most productive countries and institutions.

Rank	Country	Documents	SCP	MCP	Per citations	Institutions	Documents
1	CHINA	763	676	87	25.4	UNIVERSITY OF TEXAS SYSTEM (The United States, North America)	170
2	USA	594	481	113	72.40	UTMD ANDERSON CANCER CENTER (The United States, North America)	164
3	JAPAN	172	154	18	28.7	CHULALONGKORN UNIVERSITY (Thailand, Asia)	104
4	CANADA	105	69	36	54.6	HARVARD UNIVERSITY (The United States, North America)	97
5	ITALY	105	76	29	60.4	UNIVERSITY OF CALIFORNIA SYSTEM (The United States, North America)	81
6	KOREA	94	81	13	37.6	SUN YAT SEN UNIVERSITY (China, Asia)	72
7	GERMANY	73	48	25	71.9	UNIVERSITY OF MICHIGAN (The United States, North America)	68
8	THAILAND	64	53	11	22.7	UNIVERSITY OF TORONTO (Canada, North America)	68
9	UNITED KINGDOM	64	39	25	68.9	CENTRAL SOUTH UNIVERSITY (China, Asia)	67
10	INDIA	50	41	9	26.1	HARVARD MEDICAL SCHOOL (The United States, North America)	67

SCP: Single country publications, MCP: Multiple country publications.

with dense distributions in East Asia and North America. And the dynamic of top 10 productive countries in Figure 2C manifested the continuity of a high publications ratio about the United States and China in this field. The Wilcoxon signed-rank test shows that there is a highly significant difference in the number of publications between China and the United States at 26 time points ($Z = -4.36$, $p < 0.001$), with an effect size of $r = 0.85$, indicating that the difference is highly practical. Specifically, the United States published more papers than China at 24 time points (92.3%) (positive rank sum $W^+ = 324$), while China only surpassed the United States at the last two time points (negative rank sum $W^- = 3$). The temporal trend of the number of publications of the two countries is shown in Figure 2C. The United States had a clear advantage in the early stage, but China has shown explosive growth since 2022. Among the top ten countries in terms of total number of publications, as shown in the data in Table 1, the United States (N = 72.40), Germany (N = 71.9), and the United Kingdom (N = 68.9) have the top three positions per citation, indicating that the quality of the papers is relatively high. As shown in Figure 2D, the main coauthorship network map was established with 34 countries/regions (34/68, 50%) whose publication numbers were more than 9. The width of links between different countries or regions nodes suggested that the cooperations among China, the United States, Japan, Canada and Germany were much closer. Figure 2E shows the dynamic of the top 5 prolific institutions from 1999 to 2024 and the progress of the various institutions changed markedly in 2009, followed by a rapid growth after that. Notably, The University of Texas system from America ranked first (N = 170) in Table 1, followed by UTM D Anderson Cancer Center (N = 134), Chulalongkorn University from Thailand (N = 109), while Central South University also entered the top ten research units in the world, of which 6 of the top 10 productive institutions are from the United States, 3 are from China, and the remaining 1 is from Thailand. Meanwhile, the three institutions discussed before had the most collaborative relationship in 104 displayed countries (N ≥ 10) nodes in Figure 2F.

3.3. Authors and co-cited authors

A total of 12,772 authors had published the related research, with the top 3 productive scholars: Chanvorachote P (N = 51), Zhang Y (N = 34) and Li J (N = 25). And H-index refers to the researcher who published more than H papers with at least H citations [16], evaluating the individual scholarship level or the publication output. As shown in Table 2, among them, Chanvorachote P is not only a prolific scholar but also a high H-index scholar in this field. Meanwhile, Chiarugi P (N = 839), Giannoni E (N = 829) and Brugge JS (N = 470) were confirmed as the top 3 citation authors, and Chanvorachote P was selected as the most H-index in the list of co-cited authors. In addition, Lotka's law was used to evaluate the author's productivity, demonstrating the number of authors against the number of contributions made by each author. The mathematical formula for Lotka's law is: $A(n)=A(1)/n^2$. (A (n) is the number of scholars with n papers published and A (1) is the number of scholars with only one paper). In Supplementary Figure 2A, Lotka's law was used to calculate author productivity, showing the number of authors decreased as the number of articles published increased. In Supplementary Figure 2B it is shown that Wang Y published the most articles in 2024, and he is also the researcher with the most total citations for publications in each year.

3.4. Journals and co-cited academic journals

A total of 606 academic journals and 5537 co-cited journals were concerned to have been published in this field, with *Oncogene* (N = 108, Q1/8.0, H-index = 51) ranking first, followed by *Cancer Research* (N = 85, Q1/11.2, H-index = 54) and *PLoS One* (N = 65, Q2/3.7, H-index = 29) in Table 3. Interestingly, among cited sources, *Cancer*

Table 2. Top 10 most productive relevant and locally cited authors.

Rank	Relevant authors	Documents	H-index	Local cited authors	Citations	H-index
1	CHANVORACHOTE P	51	24	CHIARUGI P	839	10
2	ZHANG Y	34	16	GIANNONI E	829	9
3	LI J	25	18	BRUGGE JS	470	10
4	WANG Y	25	12	PEEPER DS	444	10
5	ZHANG X	25	18	SCHAFER ZT	440	14
6	KYPRIANOU N	24	19	SCHIMMER AD	430	6
7	TANAKA K	21	17	DEBNATH J	419	13
8	LIU Y	20	9	PAOLI P	388	1
9	ZHANG J	19	10	SIMPSON CD	365	5
10	CHEN Y	18	10	CHANVORACHOTE P	333	24

Table 3. Top 10 most productive relevant and cited sources.

Rank	Relevant sources	Documents	JCR/iF*	H-index	Cited sources	Citations	JCR/iF*	H-index
1	ONCOGENE	108	Q1/8.0	51	Cancer Research	7108	Q1/11.2	54
2	CANCER RESEARCH	85	Q1/11.2	54	Journal of Biological Chemistry	5658	Q2/4.8	39
3	PLOS ONE	65	Q2/3.7	29	Oncogene	4797	Q1/8.0	51
4	JOURNAL OF BIOLOGICAL CHEMISTRY	61	Q2/4.8	39	Cell	3910	Q1/64.5	1
5	ONCOTARGET	59	Q1/5.2	27	Nature	3414	Q1/64.8	5
6	SCIENTIFIC REPORTS	50	Q2/4.6	17	PNAS	3308	Q1/11.1	10
7	CANCERS	46	Q2/5.2	17	Journal of Cell Biology	2797	Q1/7.8	4
8	CELL DEATH & DISEASE	45	Q1/9.0	27	Nature Reviews Cancer	2337	Q1/78.5	3
9	ANTICANCER RESEARCH	40	Q4/2.0	17	Clinical Cancer Research	2111	Q1/11.5	16
10	INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES	34	Q2/5.6	15	Science	2027	Q1/56.9	0

JCR/IF*: JCR/IF2022, PNAS: Proceedings of The National Academy of Sciences of The United States of America.

Research (N = 7108) had the most citations, followed by *Journal of Biological Chemistry* (N = 5658) and *Oncogene* (N = 4797), whose citations all exceeded 4000. Meanwhile, in terms of dynamic sources (Supplementary Figure 3A), the number of publications from *Oncogene* and *Cancer Research* has been taking up the largest proportions in this field. And around 2009 and 2011, the documents from other sources began to increase dramatically, consistent with the characteristic of countries and institutions analysis. In addition, according to Bradford's law, all source areas were divided into three zones including zone 1 (core journals), zone 2, and zone 3, with a similar number of papers and an increasing number of journal and we used the Bradford's law to assess almost 20 journals as the source clustering, such as *Oncogene*, *Cancer Research* and *PLoS One* in Supplementary Figure 3C. Notably, the analysis from the visualization map of journals and co-cited journals density (Supplementary Figure 3B and 3D) by VOSviewer further demonstrated the collaborative relationships between diverse journals. Nodes density represented total link strengths (TLS), which confirmed *Oncogene* and *Cancer Research* as the most collaborative sources in the list of journals and co-cited journals, due to more darker nodes. In Figure 3, the topic distribution of the journals is presented by biplot overlay via Citespace. (The left side represented citing journals; the right side represented cited journals, and the links between the two sides were on behalf of the citation route [17]. There was only one main pathway from molecular, biology, immunology to molecular, biology, genetics (z = 8.130946, f = 47,998), which also predicted the hot topic and trend of anoikis and cancer.

3.5. Analysis of Co-cited references

Co-cited references refer to studies in which two or more references are cited together by other publications [18]. Table 4 shows the top 10 co-cited references published from 2009 to 2018 in this field. For instance, the review titled "Mechanism and medical implications of mammalian autophagy" in *Nature Reviews Molecular Cell Biology* occupied the first rank with a total of 1951 citations and 34.92 normalized total citations, which detailly discussed autophagy as a promisingly therapeutic approach to modulate pathology process including cancer and neurodegeneration. The published journals of all the top 10 co-cited references are authoritative in this field, such as *Nature*, *Cancer Research,* etc. After a comprehensive analysis of the foci of these co-cited references, literature hotspots laid on the relationship between anoikis related molecules and tumor progression or metastasis, upregulation and downregulation of transcription factors associated with anoikis, the role of antioxidant and oncogene prevention. Besides, emergent terms were identified based on temporal metrics and citation burstiness in Supplementary Figure 4, showing the top 20 references with the strongest citation bursts. Among them, the review with the most strength titled Anoikis molecular pathways and its role in cancer progression" published on *Biochimica et Biophysica Acta*, explores the mechanisms of anoikis resistance in cancer cells, highlighting its role in metastasis and identifying potential therapeutic targets for anti-metastatic treatments.

3.6. Analysis of keywords

Keywords could show the focus of the literature and help scholars find current research hotspots and future trends, along with co-cited references. A total of accumulatively most used 50 keywords were demonstrated with the research tree map in Figure 4A, among which expression 740(9%) ranked first, followed by metastasis 415(5%) and apoptosis 363(4%). Notably, the results also include some related cancer terms such as breast

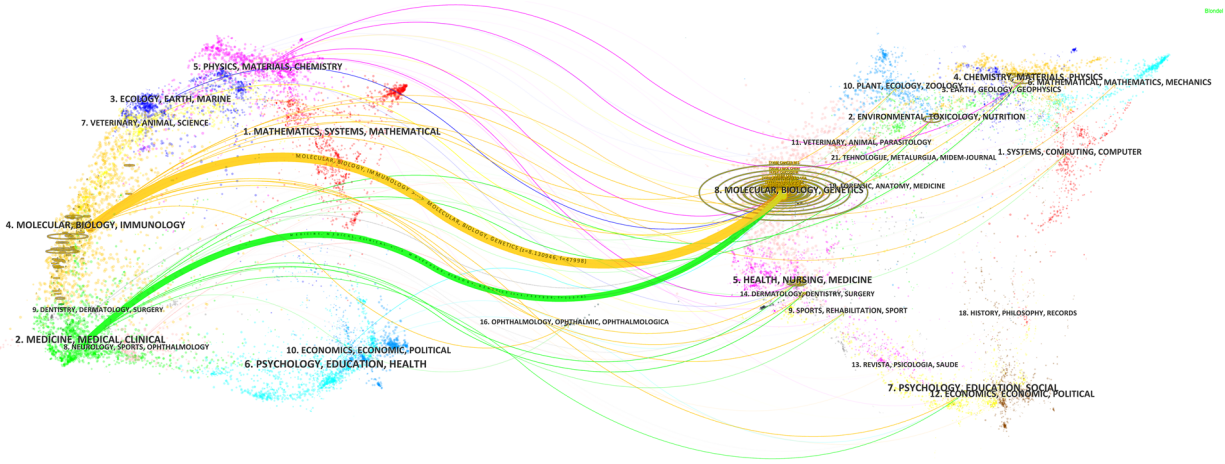

Figure 3. A biplot overlay of journals related to anoikis and cancer.

Table 4. Top 10 co-cited references related to anoikis and cancer.

References	Journal	Publication year	Citations	TC per year	Normalized TC
Mechanism and medical implications of mammalian autophagy	Nature Reviews Molecular Cell Biology	2018	1951	278.71	34.92
Ovarian cancer development and metastasis	The American Journal of Pathology	2010	1242	82.80	15.80
Loss of E-cadherin promotes metastasis via multiple downstream transcriptional pathways	Cancer Res	2008	1193	70.18	11.23
Whole-genome sequencing and comprehensive molecular profiling identify new driver mutations in gastric cancer	Nature Genetics	2014	837	76.09	18.08
Anoikis molecular pathways and its role in cancer progression	Biochimica et Biophysica Acta	2013	826	68.83	14.31
Antioxidant and oncogene rescue of metabolic defects caused by loss of matrix attachment	Nature	2009	825	51.56	11.42
Apoptosis, autophagy, necroptosis, and cancer metastasis	Molecular Cancer	2015	773	77.30	14.35
Clinical significance and molecular characteristics of circulating tumor cells and circulating tumor microemboli in patients with small-cell lung cancer Suppression of anoikis and induction of metastasis by the neurotrophic receptor TrkB	Journal of Clinical Oncology	2012	689	53.00	9.77
The Roles of Autophagy in Cancer	International Journal of Molecular Sciences	2018	670	95.71	11.99
EMT, cell plasticity, and metastasis	Cancer and Metastasis Reviews	2016	640	71.11	17.23

TC: Total citations

cancer, colorectal cancer, etc. Also, annal dynamic metric terms analysis for accurate trends was depicted in Figure 4B. Expression, metastasis, and apoptosis were relatively frequent keywords due to larger nodes. Until now, there remained crucial terms suggesting the current research hotspots including metabolism, statistics, microenvironment, tumor microenvironment, promote anoikis and discovery, due to the lasting time span of the gray mark.

Furthermore, the thematic evolution map illustrates the dynamic development of research themes in the field of anoikis and cancer over multiple time slices in Figure 4C. From 1999–2007, the research primarily focused on fundamental mechanisms, including "anoikis," "adhesion molecules," "pancreatic cancer," and "metastasis." These themes reflect an early exploration of how detachment-induced cell death (anoikis) plays a role in cancer progression and metastasis. In 2008–2011, research shifted toward understanding the specific molecular pathways associated with anoikis resistance. Keywords like "caveolin," "focal adhesion kinase," and "melanoma" emerged, indicating deeper investigations into cancer cell adhesion, signaling pathways, and tumor microenvironment. The 2012–2013 period marked an expansion into therapeutic strategies, with "chemotherapy," "prognosis," and "epithelial to mesenchymal transition (EMT)" becoming prominent themes. The focus on EMT underscored its critical role in metastasis and anoikis resistance, while "chemosensitivity" reflected efforts to overcome drug resistance in cancer treatment. Between 2014–2016, research continued to diversify, with topics such as "bone metastasis," "cancer stem cells," and "gastric cancer" gaining

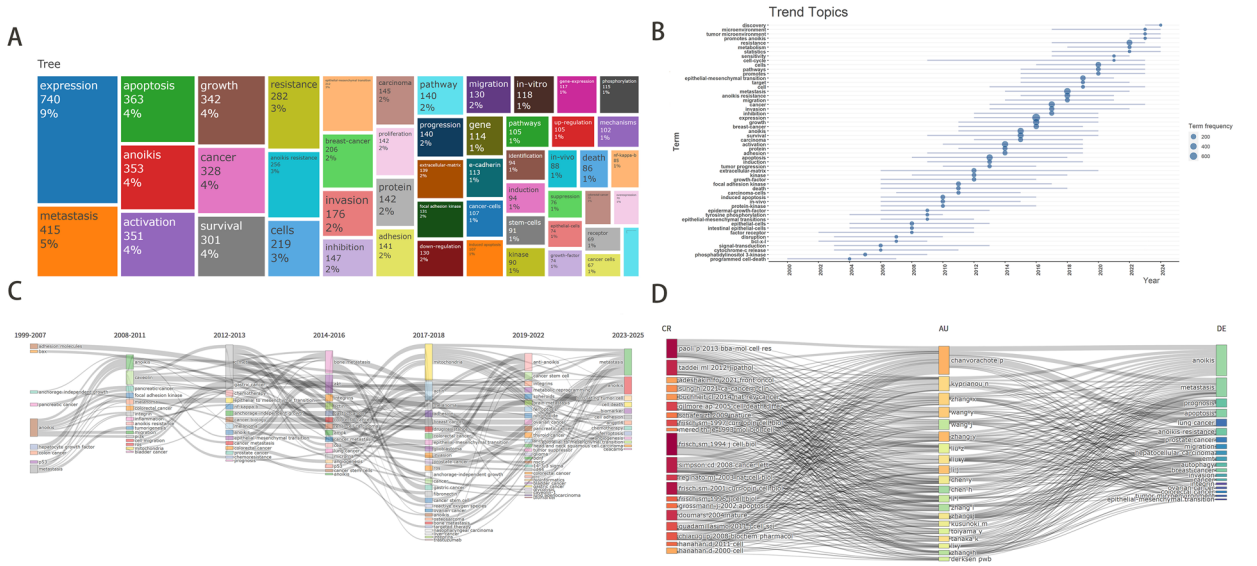

Figure 4. Overview of keywords on related research between anoikis and cancer. **(A)** Research tree map according to keywords (N = 50). **(B)** Trend topic of keywords over time (N = 54). **(C)** Thematic evolution of the research field (1999–2025). **(D)** A three-field plot showing the network between documents (left), author (middle), and keywords (right) of original articles on anoikis and cancer over time.

prominence. Molecular mechanisms, such as "integrins," "AKT," and "ROS" (reactive oxygen species), became central to understanding how cancer cells evade anoikis and acquire invasive properties. From 2017–2018, themes such as "mitochondria," "melanoma," and "drug resistance" dominated. The 2019–2022 period showed a growing focus on "cancer stem cells," "metabolic reprogramming," and "ferroptosis," indicating a shift toward understanding how metabolic pathways influence anoikis resistance. Additionally, themes such as "spheroids" and "circulating tumor cells" signified progress in modeling tumor behavior and studying metastatic processes. Finally, the 2023–2025 period reflects a synthesis of foundational and emerging themes. Topics such as "metastasis," "cell adhesion," and "anoikis resistance" remain central, while novel areas, including "biomarkers," "ferroptosis," and "integrins," suggest potential avenues for future exploration. This phase emphasizes clinical translation, with a strong focus on therapeutic resistance and precision medicine.

Meanwhile, the closed relationships between documents, authors, and keywords in the field of anoikis and cancer research were suggested in Figure 4D. As is shown in Supplementary Figure 5, the top 30 keywords with the strongest citation bursts were analyzed, with epithelial cells ranking first (strength = 25.84). However, it could not be ignored that there were various keywords with long strongest citation bursts timespan, like focal adhesion kinase, extracellular matrix, induced apoptosis, in vivo, etc. Until now, there remained two keywords whose strongest citation burst periods lasted: EMT and pathways, etc.

3.7. Factorial analysis

The multiple correspondence analysis (MCA) created a two-dimensional graph by reducing multi-dimensional data to a low-dimensional form and using a plane distance to measure keyword similarity. Whenever a keyword is near the center, it indicates that it has received more attention, while if it is further from the center, it indicates less interest or a greater detour from the topic [19]. In Supplementary Figure 6, the two dimensions (dimension 1 and dimension 2) together explain 67.35% of the total variation, with dimension 1 accounting for 50.3% and dimension 2 accounting for 17.05%, effectively capturing the main structure of the data. The left cluster (blue) is predominantly associated with foundational and mechanistic studies of anoikis and related processes. Terms like “epithelial-mesenchymal transition (EMT),” “anoikis resistance,” “extracellular matrix,” and “focal adhesion kinase” indicate a focus on molecular pathways regulating cell adhesion, apoptosis, and metastasis. The right cluster (red) encompasses themes related to the clinical and functional implications of anoikis in cancer. Terms like “metastasis,” “cancer cells,” “survival,” and “resistance” dominate this cluster,

emphasizing research on tumor progression, therapy resistance, and cell survival strategies. This analysis highlights the dual focus of current research: understanding the molecular mechanisms of anoikis and applying these insights to address clinical challenges like metastasis and resistance.

3.8. Anoikis-related mechanisms and research trends in typical cancers

According to the research tree diagram, the topic evolution analysis diagram of the research field, and the analysis results of the keywords with the strongest citation outbreaks, it is shown that breast cancer, lung cancer, colorectal cancer, prostate cancer, hepatocellular carcinoma, and ovarian cancer are currently the most researched in the field of anoikis. important cancer types. Through related literature research and combined with the results of this study, we further confirmed that the keywords in many analysis results are indeed the mechanism of anoikis in different tumors, which points out the direction for future research and provides a new way for the development of anoikis in tumors. The clinical translation of apoptosis research provides a theoretical basis, and some of the most interesting and important mechanisms are summarized in Figure 5.

3.8.1. Lung cancer

Lung cancer is a cancer derived from epithelial cells, and its occurrence and development are closely related to anoikis. Therefore, lung cancer occupies a very important place in the research of anoikis in tumors. In the study of the mechanism of anoikis in lung cancer, the epithelial-mesenchymal transition (EMT) effect on TGF-β1/SH2B3-JAK2/STAT3 axis [20,21], changes in the interaction between cells and extracellular matrix (ECM), epidermal growth factor receptor (EGFR) and CamKK2-AMPK signaling pathways are important Most notably, disruption of the normal interaction between lung cancer cells and the extracellular matrix (ECM) affects the susceptibility of cancer cells to anoikis, involving mechanisms such as altered integrin expression [22]. EGFR downregulation sensitizes lung cancer cells to anoikis and inhibits tumor metastasis in vivo [23], CamKK2-AMPK signaling promotes Anoikis resistance in LKB1-deficient lung cancer [24].

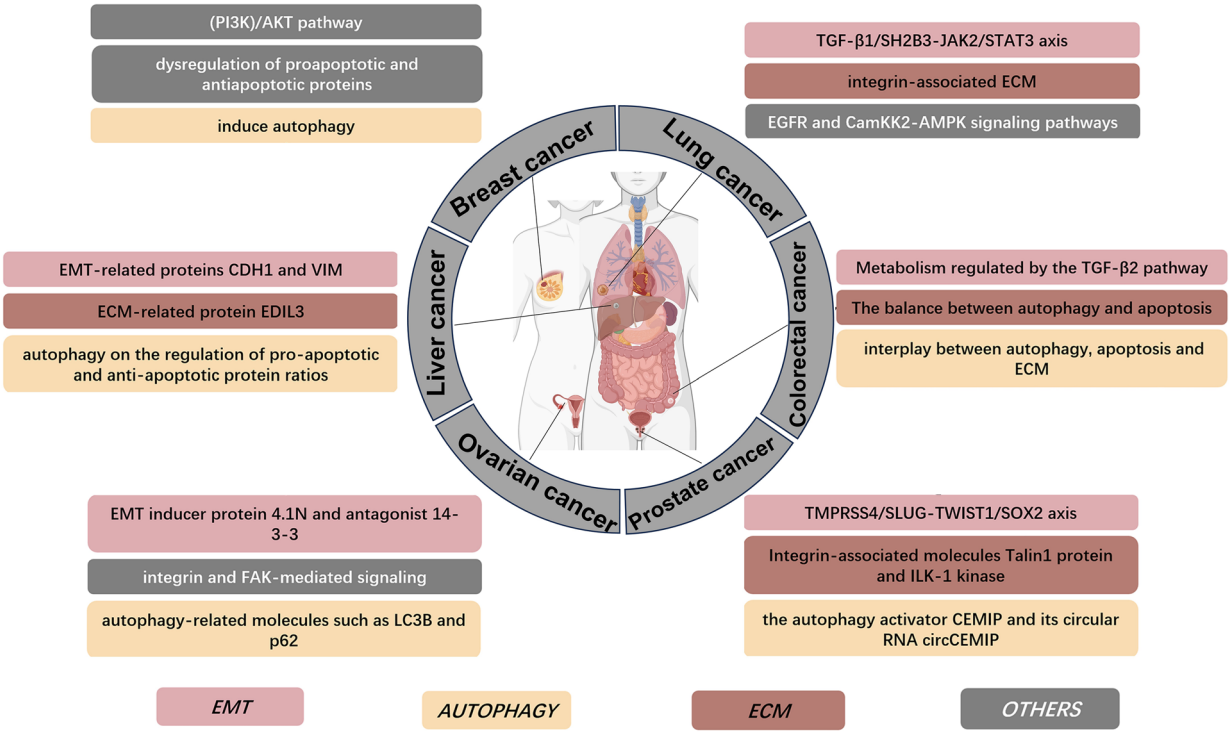

Figure 5. The common points and differences of the six most studied anoikis-related mechanisms are summarized. EMT-related mechanisms are pink entries, ECM-related mechanisms are brown entries, autophagy-related mechanisms are yellow entries, and other mechanisms are gray entries.

3.8.2. Breast cancer

The mechanisms that have garnered significant attention in breast cancer include the activation of the phosphatidylinositol 3-kinase (PI3K)/AKT pathway [25], dysregulation of proapoptotic and antiapoptotic proteins like members of the Bcl-2 family [26], and the induction of autophagy [27]. Autophagy emerges as a prominent term in keyword and citation analyses within this research area.

3.8.3. Ovarian cancer

Extensive attention has been given to the alteration of integrin and FAK-mediated signaling, increased expression of autophagy-related molecules such as LC3B and p62, as well as EMT-inducible proteins in ovarian cancer. Additionally, the development of inhibitors targeting these factors has been extensively studied [28]. LRRC15-β1-integrin-FAK axis has been identified as a potential novel target for ovarian cancer treatment [29]. Additionally, an antibody-drug conjugate (ADC) called ABBV-085, which targets LRRC15, has been reported. Furthermore, antagonists for EMT-inducible protein 4.1 N and 14-3-3, along with inhibitors of endocytosis, show promise as therapeutic approaches for ovarian cancer [30].

3.8.4. Colorectal cancer

The investigation of anoikis in colorectal cancer is centered around various aspects, including the involvement of integrin α6β4 and its downstream pathways [31], the role of EMT mediated by the TGF-β2 pathway [32], and the interplay between autophagy, apoptosis, and the extracellular matrix (ECM) [33]. Specifically, integrin α6β4 can protect colon cancer cells from anoikis by activating the PI3K pathway. EMT is involved in anoikis in colorectal cancer through TGF-β2-stimulated FA metabolic reprogramming and LD formation. ECM regulates anoikis in colorectal cancer by affecting the balance of autophagy and apoptosis, and the expression of autophagy-related proteins, such as ATG3 and ATG7, on the other hand, some oncogenes, such as RAS, can regulate autophagy by downregulating BECN1 Phage mediators to inhibit anoikis.

3.8.5. Prostate cancer

In the realm of prostate cancer research on anoikis, significant attention is given to mediators involved in ECM-cell interaction, particularly integrins and related molecules such as Talin1 protein and ILK-1 kinase [34]. These molecules have been shown to down-regulate epithelial markers like E-cadherin and up-regulate mesenchymal markers, including vimentin, thereby inducing EMT-related pathways such as TMPRSS4/SLUG-TWIST1/SOX2 axis [35]. Another area of focus is the autophagy activator CEMIP and its circular RNA circCEMIP. Mechanistically, CEMIP activates autophagy by up-regulating the expression of TM9SF4 through its interaction with miR-1248. This activation of autophagy inhibits the mTOR signaling pathway, ultimately promoting resistance to anoikis and metastasis of prostate cancer cells [36].

3.8.6. Liver cancer

In the field of hepatic carcinoma research, crucial areas of investigation encompass the study of ECM-related protein EDIL3 [37], the role of EMT-related proteins such as CDH1 and VIM [38], and the impact of autophagy on the regulation of pro-apoptotic and anti-apoptotic protein ratios. EDIL3 activates the FAK-Src-AKT signaling pathway by binding to integrin, thus inhibiting the anoikis of liver cancer cells upon loss of extracellular matrix attachment. The impact of EMT on liver cancer anoikis is two-fold: it regulates the expression of CDH1 and VIM, thereby balancing the sensitivity of liver cancer cells to EDIL3 and ECM attachment signals. Inhibition of autophagy alters the ratio of pro-apoptotic proteins, including Bax and Bid, and anti-apoptotic proteins such as Bcl-2 and Bcl-xL, consequently enhancing the sensitivity of HCC cells to apoptosis induced by ECM detachment [39].

4. Discussion

This bibliometric study presented a comprehensive summary of 2510 publications on anoikis and cancer spanning from the inception of the database to 21 December 2024. It provided an overview of basic information, current research status, developmental trends, anticipated directions, prevailing topics, and offered insights into the global research landscape in this field.

4.1. Basic information

Research reports pertaining to “anoikis and cancer” exhibited a year-on-year increasing trend during the specified retrieval period. China, the United States and Japan emerged as the top three contributing countries. Notably, The University of Texas system from America ranked first among highly productive research institutions, while the University of Texas MD Anderson Cancer Center in the USA secured the second position. Active collaborations between various institutions, especially between China and the US, were observed. For instance, The University of Texas MD Anderson Cancer Center in the US demonstrated closer collaborations with Shanghai Jiao Tong University and Fudan University in China, highlighting the potential for broader collaborative opportunities. Among the top 10 journals in terms of publication volume, the majority (n = 7) were journals from the US and England, underscoring their considerable academic influence. Notably, the journal Oncogene and Cancer Research exhibited the highest publication and citation counts, as well as the highest H-index and Total link strength. It demonstrated strong connections and co-citation with other journals, indicating its position as a pivotal source of literature and significant research accomplishments in the field of “anoikis and cancer” with substantial academic impact and contributions. Among the authors, Chanvorachote P and Zhang Y made significant contributions in terms of publication output, while Chiarugi P ranked first in co-citations, highlighting their significant influence in this field. The VOSviewer visualization map displayed stable and positive collaborations among these active authors and coauthors.

4.2. Result analysis and future research directions

To further investigate the research trend of anoikis in cancer, we analyzed the trend topic of keywords over time and found that “apoptosis”, “metastasis” and “expression” are frequent keywords due to larger nodes. These highlight research hotspots and frontier areas, reflect the importance and influence of research, and provide guidance and priority directions for researchers. Apoptosis is a critical process of programmed cell death, and anoikis is recognized as a distinctive form of apoptosis. Tumor metastasis, a significant aspect of tumor development, is closely associated with anoikis as it involves the loss of adhesion to the stroma and the subsequent ability of tumor cells to escape the primary tumor and invade other tissues. Researchers pay great attention to the important biological processes of cancer development, apoptosis, and metastasis. They hope to study the regulation mechanism of tumor cell apoptosis, the driving factors of metastasis, and the molecules and signaling pathways related to these processes, providing new therapeutic strategies and targets for cancer treatment.

According to the Thematic Evolution Time slices, the dynamic development of research in the field of apoptosis and cancer reveals interesting shifts in research focus during several key periods. Initially, from 1999 to 2007, research revolved around basic mechanisms such as "apoptosis," "adhesion molecules," "pancreatic cancer," and "metastasis." These early studies were aimed at understanding how detachment-induced cell death functions as a tumor suppressor mechanism; In the subsequent period of 2008–2011, research shifted to revealing molecular pathways associated with apoptosis resistance. The emergence of keywords such as "caveolin," "focal adhesion kinase," and "melanoma" marked a more in-depth study of intracellular signaling and the tumor microenvironment. This period was critical for identifying therapeutic targets, as the ability of cancer cells to change their adhesion properties and activate survival signals is associated with poor prognosis and treatment resistance. The research topics thereafter showed a trend of richness and diversity, but the commonality was that they were all related to the mechanisms of tumor occurrence, such as "EMT", "cancer stem cells", "ferroptosis" and "metabolic reprogramming". Finally, the period 2023–2025 reflected a combination of basic and emerging themes, among which "metastasis", "cell adhesion" and "apoptosis resistance" remained central. At the same time, new areas such as "biomarkers" and "ferroptosis" emphasized the shift to clinical translation and precision medicine. This stage emphasizes solving the problem of treatment resistance and optimizing targeted therapies to improve patient treatment outcomes [40].

The Three Field Plot, also known as a three-area map, is utilized to analyze the performance and temporal trends of literature, authors, and keywords in a specific research field. In this context, it highlights the significant contribution of the publication titled "Disruption of epithelial cell-matrix interactions induces apoptosis" authored by Frish SM et al. in J Cell Biol in 1994. This seminal article is recognized as the most cited and influential work, as it introduced and defined the concept of anoikis, established the role of bcl-2

overexpression in cell protection against anoikis, and investigated the mechanistic intervention of certain factors in regulating tumor anoikis sensitivity [41]. Consequently, it set a precedent for further investigations into the field of anoikis. Notably, Professor Pithi Chanvorachote, affiliated with Chulalongkorn University in Thailand, emerges as the most prolific and influential author in this domain.

Epithelial cells were the most cited keyword (intensity = 25.84) due to their prevalence in various tumors, particularly lung and breast cancers, highlighting the significance of the anoikis mechanism in these malignancies. Moreover, apoptosis, focal adhesion kinase, extracellular matrix, and induced apoptosis demonstrated the longest and strongest citation burst time, highlighting their significant relevance to the field of tumor anoikis. Focal adhesion kinase, FAK, an integrin-related protein tyrosine kinase, functions by receiving signals from integrins, growth factors, and mechanical stimulation to activate intracellular PI3K/Akt, Ras/MAPK, and other signaling pathways. Intracellular FAK activity within the tumor microenvironment (TME) may contribute to tumor growth and metastasis via multiple mechanisms, such as promoting angiogenesis, increasing vascular permeability, and inducing matrix fibrosis. Small-molecule FAK inhibitors, including Conteltinib, Defactinib, IN10018, etc., have demonstrated effectiveness in reducing tumor growth and metastasis. These inhibitors have shown promising safety and efficacy profiles in clinical trials, making them potential targets for new anticancer drugs. Combining FAK inhibitors with other chemotherapeutic agents or immune cell activators could provide additional benefits. Small-molecule FAK inhibitors, including Conteltinib, Defactinib, IN10018, etc., have demonstrated effectiveness in reducing tumor growth and metastasis. These inhibitors have shown promising safety and efficacy profiles in clinical trials, making them potential targets for new anticancer drugs. Combining FAK inhibitors with other chemotherapeutic agents or immune cell activators could provide additional benefits [42].

Notably, there is an interrelationship between the keywords with the strongest citation burst strength, focal adhesion kinase, extracellular matrix, and induced apoptosis, which mediate the interaction between cells and the extracellular matrix. ECM can interact with integrins on the cell surface to activate FAK. FAK can initiate the Ras signaling pathway through the adapter protein Grb2, causing cell proliferation [43]. Changes in ECM composition or organization can affect cellular responses to apoptotic signals, and perturbations in ECM-induced apoptosis are associated with tumorigenesis and progression. ECM protein laminin-5 has been shown to promote apoptosis in breast cancer cells [44,45], ECM protein collagen I can promote the induction of apoptosis in cancer cells [46], while fibronectin in ECM can protect cell immunity in apoptosis [47]. In the case of intestinal epithelial cells, the activation of apoptosis is especially important because it controls the replacement and regeneration of the intestinal lining. Effective management of induced apoptosis in intestinal epithelial cells is essential to sustain tissue balance and prevent the buildup of anomalous or impaired cells, which may lead to the development of tumors [48]. Dysregulation of FAK signaling affects the sensitivity of intestinal epithelial cells to apoptotic stimuli, potentially leading to disruption of tissue homeostasis and increased susceptibility to tumor development [8,49]. Understanding these interconnections can provide insight into mechanisms of tumor progression, metastasis, and potential therapeutic strategies targeting tumor anoikis resistance.

We recommend annual or biennial reanalysis of emerging trends to keep the research results current; at the same time, machine learning-based trend prediction models (e.g., time series prediction using LSTM) can be explored to predict future research directions.

4.3. Emerging trends in the study of anoikis in cancer

The keyword analysis showed that "epithelial-mesenchymal transition (EMT)" and "signal pathway" were still in the citation explosion period, indicating that these two directions were currently the hot areas of cancer anoikis research. In recent years, many studies have focused on the molecular mechanism of EMT regulating anoikis resistance and its dynamic plasticity in the metastatic microenvironment. At the same time, targeted intervention strategies for key signaling pathways have become an important breakthrough in translational medicine.

4.3.1. EMT and anoikis in cancer

EMT or epithelial-mesenchymal transition is a process in which epithelial cells lose polarity and adhesion, acquiring mesenchymal properties with enhanced motility and resistance to apoptosis [50]. EMT is an important mechanism for cancer cells to acquire the ability to invade and metastasize. During the EMT process, the

expression of cell adhesion molecules such as E-cadherin decreases, while mesenchymal markers such as N-cadherin and Vimentin increase, thereby reducing cell-to-cell adhesion, enhancing cell motility, and allowing cancer cells to escape immune surveillance and anoikis [51–53]. EMT is closely related to cancer metastasis because it allows cancer cells to escape from the primary tumor, survive in the circulation, and colonize at distant sites. Notably, in the context of anoikis-related mechanisms in cancer, EMT-induced anoikis is mediated by transcription factors such as Snail and Twist, which suppress pro-apoptotic signals and promote mesenchymal phenotypes [54,55]. Multiple signaling pathways regulate EMT-induced anoikis escape: 1. TGF-β signaling pathway: TGF-β upregulates Snail, Twist, and ZEB1/2, inhibits E-cadherin, and thus reduces anoikis sensitivity [56]. 2. PI3K/AKT pathway: UA triggered caspase-dependent apoptosis, FAK/PI3K/AKT signaling pathway, and anoikis associated with epithelial-mesenchymal transition (EMT) in RKO cells [57]. Targeting EMT transcription factors or reversing EMT through therapeutic intervention can restore apoptosis sensitivity and inhibit metastasis, which has important clinical translational value [58].

4.3.2. Pathways associated with anoikis in cancer

Multiple signaling pathways and molecular modulators have been linked to apoptosis resistance, highlighting the complexity of cancer progression.

4.3.2.1. Integrin-mediated survival pathways. Integrins play a role in the connection between cells and the extracellular matrix (ECM) and are important factors in the regulation of anoikis. Dysregulation of integrin signaling, especially through αV/β3 integrin activation of focal adhesion kinase (FAK) and downstream phosphatidylinositol3-kinase (PI3K)/Akt pathway, can promote anoikis resistance [59,60]. For example, botulinum toxin-induced integrin inactivation triggers anikis via the ROCK-MKK4/MKK7-JNK signaling cascade [61]. In contrast, the binding of fibronectin (FN) to integrins can maintain cell survival by inhibiting the activation of this pathway, which was demonstrated in a renal cell carcinoma (RCC) model [59].

4.3.2.2. PI3K/akt and MAPK signaling. The PI3K/Akt axis is a key survival pathway in anoikis resistance. TrkB, a neurotrophin-receptor, promotes metastatic growth in aggregated and suspended cells by activating the PI3K/Akt pathway [62]. In triple-negative breast cancer (TNBC), loss of PTPN14 enhances PI3K/Akt and ERK signaling pathways, enabling anchor independent survival [63]. In addition, the MAPK/JNK pathway is environment dependent: although JNK activation normally induces apoptosis, oncogenic mutations in Ewing's sarcoma up-regulate IL1RAP to inhibit cells from undergoing anoikis through MAPK cross-pathways [64].

4.3.2.3. Metabolic and REDOX adaptations. Metabolic reprogramming is one of the key mechanisms for cancer cells to adapt to changes in the microenvironment, especially playing an important role in anoikis resistance. Studies have shown that cancer cells gain survival advantages after leaving the extracellular matrix (ECM) by enhancing glycolysis, lipid synthesis, and glutamine metabolism [65,66]. For example, metabolic reprogramming affects anoikis by regulating metabolites (such as lactate and ketone bodies) and mitochondrial metabolism in the tumor microenvironment (TME), promoting the invasion and metastasis of cancer cells [65]. IL1RAP maintains REDOX homeostasis by protecting cysteine and glutathione pools, which is essential for survival under detachment stress [64]. Similarly, ANGPTL4 regulates oxidative stress to suppress anoikis in aggressive tumors [67]. In pancreatic cancer, PON2 regulates glucose transport to maintain metastatic growth, a process that is antagonized by AMPK activation [68].

In terms of clinical significance, the keyword "pathway" points to multiple signaling mechanisms associated with anoikis, such as the Wnt/β-catenin, TGF-β, and JAK/STAT pathways [69,70]. These pathways not only contribute to anoikis, but also affect tumor progression, immune evasion, and treatment resistance. For example, targeting the JAK/STAT pathway in lung cancer has been shown to enhance apoptosis sensitivity and improve chemotherapy efficacy [71]. Similarly, combining Wnt/β-catenin signaling inhibitors with conventional therapies can produce synergistic effects by targeting primary tumor growth and metastatic spread [72].

Overall, these findings highlight the intricate interplay between anoikis resistance mechanisms and cancer progression, providing valuable insights for therapeutic intervention. By targeting key molecules such as FAK, regulating tumor ECM, and reversing EMT, it is possible to restore apoptosis sensitivity and develop effective anti-metastatic therapies. Future research should focus on incorporating these insights into clinical practice, using biomarker-driven approaches to identify patients who would most benefit from therapies targeting anoikis resistance pathways [73].

4.5. Discussion on clinical translation of anoikis-related mechanisms

The translation of anoikis resistance mechanisms into clinical applications has shown promising results in cancer diagnosis, treatment, and prognosis. In lung cancer, for example, therapies targeting EGFR mutations have shown significant efficacy. The third-generation EGFR inhibitor osimertinib has become the standard of care for patients with EGFR-mutated lung cancer. Clinical trials have reported that osimertinib prolonged median progression-free survival (PFS) to 18.9 months, compared with 10.2 months for earlier EGFR inhibitors such as gefitinib and erlotinib. Osimertinib has shown potential in sensitizing cancer cells to anoikis by suppressing EGFR-mediated survival pathways [74]. Therapies targeting the PI3K/AKT pathway have been transformative in breast cancer. The SOLAR-1 trial showed that combining the PI3K inhibitor Alpelisib with an endocrine therapy such as fulvestrant prolonged median PFS to 11 months versus 5.7 months with a placebo. Alpelisib effectively disrupts survival signaling cascades, thereby restoring sensitivity to anoikis and reducing metastasis [75]. For ovarian cancer, the LRRC15-β1-integrin-FAK axis has attracted attention as a therapeutic target. data suggest that ABBV-085, which targets LRRC15, effectively reduces anoikis resistance, halts tumor progression, and enhances chemosensitivity. While survival data from clinical studies are pending, this therapy shows promise for tackling anoikis-related mechanisms in ovarian cancer [29]. In colorectal cancer, therapeutic strategies targeting the integrin α6β4 pathway are being explored. Preclinical models suggest that the relocalization of integrin α6β4 to the actin cytoskeleton favors more migratory and anoikis resistant phenotypes. ITGA6 and ITGB4 may serve as useful biomarkers for early CRC detection and prognostic factors, respectively, in noninvasive assays [31]. The extracellular matrix (ECM) -related protein EDIL3 and its downstream signaling pathways in hepatocellular carcinoma (HCC) have been identified as key factors in anti-anoikis. Disruption of EDIL3 linkage to integrin by RGD blockade in selected patients may have potential therapeutic value [37]. We summarize the top six most important cancer types globally (breast cancer, lung cancer, colorectal cancer, prostate cancer, colorectal cancer, colorectal cancer, lung cancer). liver cancer and ovarian cancer), and summarized their commonness and characteristics of the related mechanisms, see Section 3.8 and Figure 5. Relevant treatment strategies and clinical trials are summarized in Table 5. The translation of anoikis mechanisms into targeted therapies has dramatically improved clinical outcomes in some cancer types. However, challenges such as additional drug development, drug resistance, and tumor heterogeneity remain, emphasizing the need for combination therapies and further research to optimize clinical use.

4.6. Similarities and heterogeneity

The results of our study are similar to those of other studies in several respects, but there are also some differences. The fact that breast and colorectal cancers are the most studied cancer types coincides with trends in global cancer incidence and research funding allocation, which are also reflected in other bibliometric studies [76]. In key research directions, such as metabolism, tumor microenvironment, FAK signaling pathway, extracellular matrix, and induction of apoptosis, these topics have indeed received increasing attention in recent studies. This echoes the anoikis resistance mechanism mentioned by Frisch SM in 2013, which includes a discussion of the FAK signaling pathway as well as the EMT mechanism [77]. This study also showed some unique features, such as the discovery of emerging mechanisms such as ferroptosis and metabolic reprogramming. Previous bibliometric analysis of cancer metastasis mainly focused on the classical pathways, such as PI3K/AKT [78].

4.7. Limitations

This paper examines the current hotspots and trends in anoikis research in tumors using bibliometrics and visual analysis. However, there are still some limitations. Firstly, there are few bibliometric software and methods that combine two databases for analysis. Therefore, our data is only collected from the WOS database and only includes English articles and reviews which may miss some research results in other databases. We also considered other databases, such as PubMed and Scopus, but due to differences in indexing strategies and metadata availability, cross-database bibliometric analysis is not mainstream for the time being. In addition, there are many duplicates between PubMed and Scopus and the WOS database, and the

Table 5. Summary table of clinical trials and treatment strategies.

Mechanism of action	Therapeutic agent	Target	Clinical trial phase	Cancer type	Key findings/status	Reference/ ClinicalTrials.gov ID
EMT	Galunisertib	TGF-β receptor inhibitor	Phase I/II	Pancreatic Cancer	Improved overall survival	NCT01373164
EGFR-mediated survival pathways	Osimertinib	EGFR	Phase III	Lung Cancer	Prolonged median progression-free survival (PFS) to 18.9 months	NCT02296125
FAK/ MAPK path	Defactinib and VS-4718+ Avutometinib	FAK inhibitor/Dual RAF/MEK inhibitor	Preclinical study	Ovarian Cancer	Increased median survival of mice	NCT04625270
PI3K/AKT pathway	Alpelisib	PI3K inhibitor	Phase III	Breast Cancer	prolonged median PFS to 11 months	NCT02437318
Integrins	Cilengitide	αvβ3/αvβ5 integrin antagonist	Phase III	Glioblastoma	No significant overall survival benefit in Phase III	NCT00689221
FAK	ABBV-085	LRRC15-β1	---	Ovarian Cancer	Blocked metastatic dissemination in early and late metastatic ovarian cancer cell line xenograft models; no clinical trials are currently available.	[29]
Integrin	---	Integrin α6β4	---	Colorectal Cancer	Relocalization of integrin α6β4 to the actin cytoskeleton favors more migratory and anoikis resistant phenotypes.	[31]
ECM	RGD	EDIL3	---	Hepatocellular Carcinoma	Administration of cilengitide, an RGD-containing integrin antagonist, and silencing of integrin αV, an important RGD-binding integrin, resulted in a blockade of EDIL3-induced anti-apoptotic effects.	[37]

literature included in the WOS database is more extensive and comprehensive than these two databases. Chinese literature databases such as CNKI mainly collect Chinese literature and do not fully meet the international journal indexing standards. Compared with other databases, the calculation methods of its citation network, impact factor and other indicators are different and cannot be included in the joint analysis. Due to copyright restrictions, CNKI does not support the direct export of large-scale citation data, and bibliometric analysis tools have difficulty processing its data. Secondly, some promising high-quality publications may not receive attention due to low citation frequency. These publications may be more valuable than those with high citation frequency. Therefore, future research could be improved in the following two aspects: 1) Integrating data from multiple databases, including PubMed, Scopus, and Chinese databases, to obtain a more comprehensive research sample. 2) Conducting multi-language analyses to reveal research trends in other linguistic domains, thereby providing a more holistic view of global trends in anoikis and cancer research. In addition, although our study conducted a comprehensive analysis of the anoikis-cancer relationship, the search strategy also has some limitations: On the one hand, the search query (TS=(cancer* OR carcinoma* OR neoplasm* OR tumor* OR tumor*)) is designed to capture a wide range of cancer-related terms, but may exclude some niche terms, such as "oncogenesis" or "malignancy". Although these terms are less associated with cancer cell apoptosis in the literature, their omission may slightly affect the completeness of the dataset. On the other hand, there is a precision-recall tradeoff, using the "Topic Search" (TS) field of Web of Science, which scans titles, abstracts, and keywords, giving priority to recall rather than precision. Although this approach ensures comprehensive coverage of relevant studies, it may introduce low-relevant records (e.g., papers that mention "tumor" in irrelevant contexts). On the contrary, limiting the search to the title (TI) or author keywords may improve precision, but the risk is that some key studies may be missed, such as articles where "cancer cell apoptosis" only appears in the abstract. Future research could address these limitations by including additional terms (e.g., "oncogenesis" or "malignancy") and using Boolean operators to improve sensitivity and by applying machine learning-based filters to improve precision without sacrificing recall. Although this study revealed the thematic structure of the anoikis research domain through multiple correspondence analysis (MCA) and Wilcoxon signed rank test analysis, some limitations in the depth and breadth of statistical application should be acknowledged. Future studies could expand the statistics to include effect sizes, confidence intervals, and multivariate regression to enhance the

interpretability of the results. Finally, due to the complexity and uncertainty of future events, there may be deviations or subjective judgments when grasping future research trends. This work reflects current trends in the field of anoikis in tumors while providing a theoretical basis for future research possibilities. We propose an annual or biannual re-analysis of emerging trends to maintain the relevance of our findings; Machine learning-based trend prediction models (such as time-series forecasting with LSTMs) could be explored to anticipate future research directions.

5. Conclusions

According to this bibliometric analysis, the study of anoikis in the field of oncology is rapidly evolving and has great clinical and scientific potential. This study identified major countries, publications, and contributors in the field, with China leading the way in terms of research output and citations. Breast and colorectal cancers are the most studied cancer types, reflecting their relevance in the context of anoikis. Key research directions such as metabolism, tumor microenvironment, focal adhesion kinase, extracellular matrix, and induced apoptosis highlight the growing interest in understanding the molecular mechanisms of anoikis in cancer progression and metastasis.

Importantly, pathways such as EMT and FAK signaling have not only become research hotspots, but also have translational potential for clinical application. For example, FAK inhibitors such as Defactinib are currently under clinical investigation and have shown promise in reducing tumor metastasis and treatment resistance. Similarly, targeting the EMT pathway may provide new therapeutic avenues to overcome apoptotic resistance in aggressive cancers.

Future research should focus on bridging the gap between molecular mechanisms and clinical applications, particularly exploring the role of anoikis in treatment resistance and developing biomarkers for early detection and prognosis. Integration of insights from this study into clinical studies could guide the development of targeted therapies and ultimately improve patient outcomes.

In conclusion, this study provides a comprehensive overview of trends and developments in the field of anoikis research and provides valuable guidance for researchers, clinicians, and policymakers seeking novel therapeutic strategies against cancer.

Authors' contributions

JJ designed and drafted the manuscript, and collected and analyzed the data. SN, WP, DZ, WC, YL, CZ, CD and WZ revised the text of the manuscript. CD and WZ provided revisions and critically reviewed the content of the manuscript. All authors contributed to the article and approved the submitted version.

Consent for publication

All authors have read and approved the content and agree to submit it for consideration for publication in the journal.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

This work was supported by the National Natural Science Foundation of China (No.82372935, No.81974367, No.82003065, No.82172655), the National Natural Science Foundation of Hunan Province (No.2023JJ30873, No.2021JJ70023), and National Multidisciplinary Cooperative Diagnosis and Treatment Capacity Building Project for Major Diseases (Lung Cancer, No. z027002).

Data availability statement

Data included in article/supp. material/referenced in the article.

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