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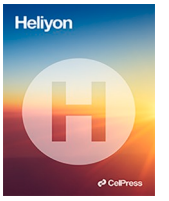

Review article

Global trends of single cell sequence associated in cancer from 2011 to 2024: A bibliometric analysis

Xueliang Wu [a,b,1,**], Jianchun Fan [a,1], Xingmei Zhang [c,***], Tian Li [d,*], Jichao Song [e,****]

[a] Department of General Surgery, The First Affiliated Hospital of Hebei North University, 075000, China
[b] Institute of Cancer, The First Affiliated Hospital of Hebei North University, 075000, China
[c] College of Medical Technology, Chengdu University of Traditional Chinese Medicine, Chengdu, 610000, China
[d] School of Basic Medicine, Fourth Military Medical University, Xi'an, 710032, China
[e] Department of Gynaecology, Xinchang Country People's Hospital/Xinchang County Maternal and Child Health Hospital, 117 Gushan Middle Road, Xinchang, 312500, Zhejiang Province, China

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ABSTRACT

Objective: Exploring the different molecular and clinicopathological features of nodal cancer based on single cell sequencing can reveal the intertumoral heterogeneity in cancer, and provide new ideas for early diagnosis, treatment and prognosis analysis of cancer.
Methods: The hotspots, the features of worldwide scientific output, and the frontiers concerning single cell sequence related to cancer from 2011 to 2024 were determined using our bibliometric analysis. Web of Science Core Collection (WOSCC) database was searched for publications on single cell sequence associated with cancer that were published between 2011 and 2024. According to the journals, keywords, number of records, affiliations, citations, and countries, we conducted a bibliometric analysis. With the use of the data gathered from the WOSCC, geographic distribution was visualized, keyword, affiliation, and author cluster analyses were conducted, and co-cited references were reviewed and a descriptive analysis was also performed.
Results: From the analysis, it was concluded that 6189 articles that were published between 2011 and 2024 in total were identified. Frontiers in immunology is the leading journal with the most publications in field of the research. The five clusters that were identified for hotspots included immunotherapy, single-cell RNA sequencing, hepatocellular carcinoma, proliferation, gene expression appeared the most frequently. Journals, nations, organizations, scholars with most contribution and most referenced publications globally were extracted. Studies have mostly concentrated on the spatial transcriptomics, pan-cancer analysis, hepatocellular carcinoma et al.

* Corresponding author. School of Basic Medicine, Fourth Military Medical University, Xi'an 710032, China.
** Corresponding author. Department of General Surgery, The First Affiliated Hospital of Hebei North University, 12Changqing Rd, Zhangjiakou, 075000, China.
*** Corresponding authors. College of Medical Technology, Chengdu University of Traditional Chinese Medicine, Chengdu 610000, China.
**** Corresponding author. Department of Gynaecology, Xinchang Country People's Hospital/Xinchang County Maternal and Child Health Hospital, 117 Gushan Middle Road, Xinchang 312500, Zhejiang Province, China.
E-mail addresses: wuxl@hebeinu.edu.cn (X. Wu), ZhangXingMei2022@outlook.com (X. Zhang), fmmult@foxmail.com (T. Li), Songjichao1980@sina.com (J. Song).
[1] These authors contributed equally to this work.

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Conclusion: Single-cell sequencing plays a significant role in tumor diagnosis, treatment and prognosis.

1. Introduction

Malignancy is one of the tumours that seriously endanger people life and health. It has become a global public health problem [1–5]. According to the global cancer statistics released by the international cancer research agency of the World Health Organization, in 2020, the number of new cancer patients in the world was about 19.29 million. Among them, breast cancer was 11. 7 % [6]. The growth rate of 7 % exceeded that of lung cancer (11.4 %), becoming "the largest cancer in the world", followed by colorectal cancer (10.0 %) and prostate cancer (7.3 %). In order to control the incidence rate of cancer worldwide, the improvement of the accuracy of cancer detection and diagnosis is critical necessary. The research on biomarkers of diseases such as cancer has always been a hot spot in the field of life science and medicine. The discovery and application of cancer biomarkers have greatly promoted the development of cancer diagnosis, screening and follow-up treatment [7–11].

Single cell sequencing (SCS) is a new sequencing technology, which can analyse the genome, transcriptome and epigenome of a single cell [12]. This technology takes a single cell as the research object, and can deeply study the cell heterogeneity research [13]. Analysis of the different molecular properties of tumour tissues is accomplished by single cell isolation technology and high-throughput sequencing technology, which can be applied to the fields of basic research, clinical diagnosis and drug development [14,15]. In addition, it can also be used to find the cell types of dysplasia in order to find new pathogenesis and biomarkers of cancer [16]. Before the introduction of SCS, the inherent heterogeneity of tumor was still unclear. SCS has revolutionized our understanding of tumor heterogeneity in cancer research. By providing a detailed analysis of the transcriptome of each individual cell in a sample, SCS has enabled researchers to identify new cell subtypes, states, and dynamic cellular transitions during tumor evolution and differentiation [17,18]. This technology has allowed for a deeper exploration of the heterogeneity within the tumor microenvironment, leading to a better understanding of the genetic, metabolic, and other characteristics of thousands of individual cells involved in tumor progression. Integrating clinical information with single-cell sequencing data can help identify novel biomarkers for diagnosis and prognosis, as well as potential treatment targets [19].

Studies must be conducted to measure existing practice, find cell sequence associated with cancer and acquire data or information on the most recent state of the research. Bibliometrics, an established and popular research technique in information science, is a useful instrument for assessing the state of the discipline and accurately reflecting its advancement. It has an important function in revealing the publishing law and predict the future publishing direction of the discipline [20]. Bibliometrics is a convenient and practical method that can assess the developmental trend and direction in a scientific file and elucidate the crucial study hotspots by analysing the features of publications and databases. Besides, it can successfully provide evidence to conduct funding considerations and implementation strategies [21–23]. Results of bibliometric analysis have been discovered in several academic fields, including traditional Chinese medicine, osteomyelitis, knee revision, acute lung injury, oral health providers, anti-vascular endothelial growth factor therapy [24] and prenatal health [25–27], and it can summarize the current research status and hotspots related to diseases. Nevertheless, bibliometric research on SCS associated with cancer is still rare. Thus, our study aimed to systematically analyse studies on SCS associated with cancer and summarize the present situation and hotspots in this area of science.

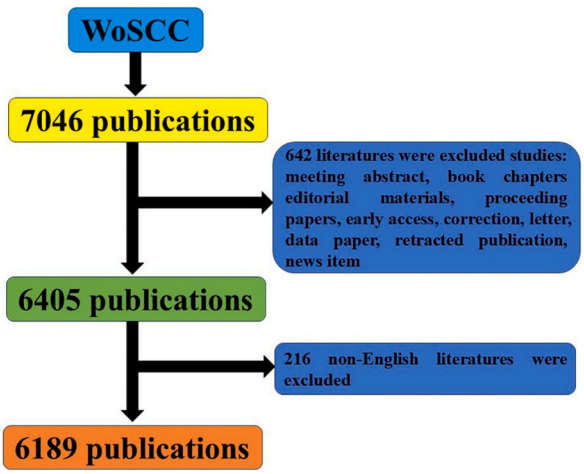

Fig. 1. Flowchart of the screening process.

2. Materials and methods

2.1. Data sources and search strategies

Due to its ability to deliver a thorough and standardized collection of data, WOSCC has been utilized extensively. The literature dataset for this study was conducted on the basis of WOSCC. Since the database is updated quickly, literature was acquired on the same day (April 14, 2024) to eliminate any potential discrepancies. The period of literature retrieval was established from 2011 to 2024 to investigate the trends in worldwide science in SCS associated with cancer study. The following search strategy was performed: (TS = (Neoplasms) OR TS = (Neoplasia) OR TS = (Neoplasia) OR TS = (Neoplasm) OR TS = (Tumours) OR TS = (Tumour) OR TS = (Cancer) OR TS = (Cancers) OR TS = (Malignancy) OR TS = (Malignancies) OR TS = (Malignant Neoplasms) OR TS = (Malignant Neoplasm) OR TS = (Neoplasm, Malignant) OR TS = (Neoplasms, Malignant) OR TS = (Benign Neoplasms) OR TS = (Neoplasms, Benign) OR TS = (Benign Neoplasm) OR TS = (Neoplasm, Benign))AND (TS = (Single-cell sequencing)). Original articles and reviews were included in the analysis among different publication types. Fig. 1 depicts the retrieval procedure used in our investigation.

2.2. Data extraction and processing

First, the WOSCC database was used to retrieve the original data. The data includes the number of publications and citations, publication year, affiliations, H-index, references, nations/regions, authors, journals, and keywords. The majority of the raw data in our analysis were regarded as credible, even if inexact analysis could not entirely be avoided due to varied forms of cited journals, the same abbreviated name of different authors, and various versions of cited references. VOS viewer v.1.6.10.0 (Centre for Science and Technology Studies, Leiden University, Leiden, the Netherlands) and Cite Space (6.2.R6) were used to analyse the data [28,29].

2.3. Bibliometric analysis

Important bibliometric indicators that are frequently used to identify bibliographic materials include the quantity of publications and citations. Since there are two major ways to evaluate the quality of research, in our study the number of publications (Np) and the number of citations (Nc) were used to assess production and impact, respectively. When a third item cites both items, it is referred to as co-citation. Keywords co-occurrence measured the keywords with the highest frequency in the same literature [30], and the evaluation of co-cited sources and co-occurring keywords might clarify study hotspots associated with macrophages in SCS associated with cancer. The H-index is utilized to evaluate academic contributions made by scholars and predict future technological discoveries [31,32]. H-indices link productivity and impact by identifying thresholds that connect Np and Nc. A researcher would have an H-index if they published H publications, each of which received at least H citations [33]. Especially, H index was used to assess academic accomplishments of specific individuals and to evaluate the publications of a magazine, an institution, a nation, or an area [34]. The impact factor (IF) obtained from the latest edition of Journal Citation Reports (JCR) has been widely regarded as one of the primary metrics to assess the quality and impact of medical journals [35]. Bibliometric analysis single cell sequence associated with cancer were performed using VOS viewer and Cite Space to produce more systematic result based on co-occurrence and co-citation [36].

3. Results

3.1. A summary of records on SCS associated with cancer

The search strategy identified 6189 reviews and articles published between 2011 and 2024. The total NC among them was 167187.

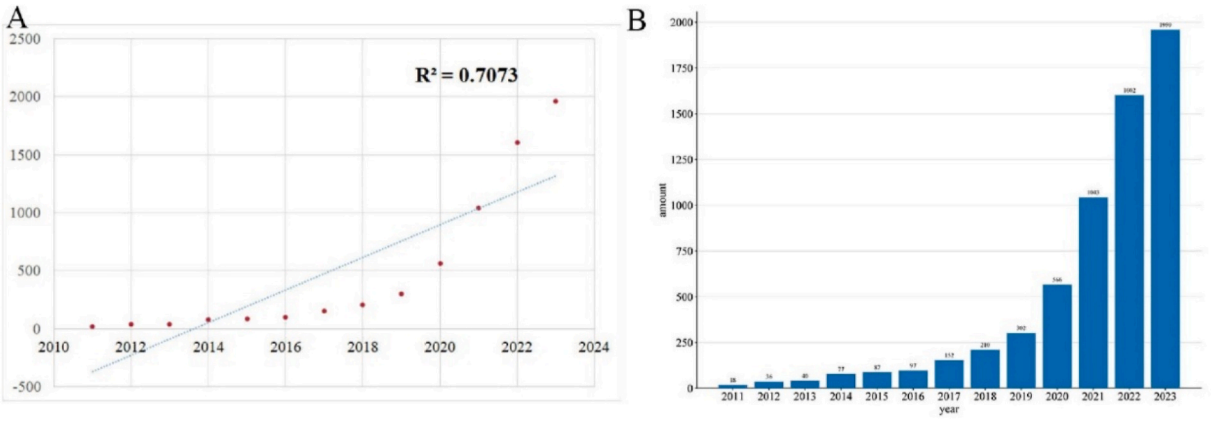

Fig. 2. The trend of annual publication number. (A) Curve fitting of the of the total annual growth trend of publications ($R^2 = 0.7073$). (B) The number of publications from 2011 to 2024.

The average Nc per article was 31.51, and the H-index for all publications was 192.

3.2. The trend of annual publication number

The correlation coefficient (R^2) between the yearly NP and the year of publication was 0.7073 (Fig. 2A). The annual Np associated with SINGLE CELL SEQUENCE ASSOCIATED WITH CANCER is shown in Fig. 2B. In general, the annual number of papers released rose from 18 in 2011 to 1959 in 2024, and Np reached its peak value in that same year.

3.3. Contribution of country/region to global publications

The top 10 high producing nations/areas (in terms of the Np) were shown (Table 1). China came in top place with the most articles published (2898). The US (2296) ranked second, and third-placed was Germany (472). With 110694 citations, the US-published papers accounted for 66.21 % of all citations, followed by China (43018) and Germany (18718). Additionally, the H-index for the US was the highest (161). The geographic distribution map of the number of documents issued by different countries/regions was shown in Fig. 3A, and the annual number of publications in the top ten countries was shown in Fig. 3B. The cooperation and relationships between countries/regions were shown in Fig. 3C and D.

3.4. Analysis of authors and affiliations

Table 2 showed that Aviv Regev and the other top 9 scholars produced a total of 234 articles. Aviv Regev from the HARVARD UNIVERSITY was the top researcher in the area of SCS associated with cancer investigation, followed by Zhang Zemin in Peking University, Tong li in BROAD INSTITUTE, Orit Rozenblatt-Rosen in BROAD INSTITUTE. Regev, Aviv had an obviously high Nc. The collaborative relationship between authors was shown in Fig. 4A. The top 20 most influential authors were shown in Fig. 4B, with Cheng Quan, Wang Zeyu, Dai Ziyu, and Zhang Qi having a high level of influence at present. The most influential author was Regev and Aviv. The clustering time span of research directions among different authors was shown in Fig. 4C.

3.5. Analysis of affiliations

Table 3 showed the top ten affiliations with the greatest number of articles on SCS associated with cancer. In terms of Np, HARVARD UNIVERSITY came in first, followed by CALIFORNIA SYSTEM UNIVERSITY and TEXAS SYSTEM UNIVERSITY. HARVARD had the most Nc (39303), greatest H-index (86). Although Np of the HARVARD MEDICAL SCHOOL in the US was relatively low, its Nc and H-index were greater than those in UNIVERSITY OF CALIFORNIA SYSTEM, CHINESE ACADEMY OF SCIENCES, SHANGHAI JIAO TONG UNIVERSITY, UNIVERSITY OF TEXAS SYSTEM. All affiliations were from the US and China. The collaborative relationship between affiliations was shown in Fig. 4D. The top 20 most influential affiliations were shown in Fig. 4E. The most influential affiliation was Howard Hughes Medical Institute. The clustering time span of research directions among different affiliations was shown in Fig. 4F.

3.6. Evaluations of journals

In Table 4, Frontiers in immunology (325 publications, IF: 7.3) published the most papers related to SCS associated with cancer., followed by Nature Communications (238 publications, IF: 16.6) and Frontiers in oncology (181 publications, IF: 4.7). All the top 10 journal had high H-index, citations and IF.

3.7. Assessment of paper global citations score (GCS)

Fig. 5 illustrated the quantity of GCS per year for the top ten publications. The first-place paper, written by Patel, AP, and published in Science in 2014, had a GCS of 2789. Anoop P. Patel et al. found inherent variability in the expression of multiple transcriptional

Table 1
Publications in the 10 most productive countries/regions.

Country/Area	NP	NC	H-index
China	2898	43018	96
the US	2296	110694	161
Germany	472	18718	66
the UK	336	14050	59
Japan	246	5134	35
Canada	227	10673	46
Italy	197	5985	35
Netherlands	197	10158	47
Australia	178	8905	38
France	174	7185	42

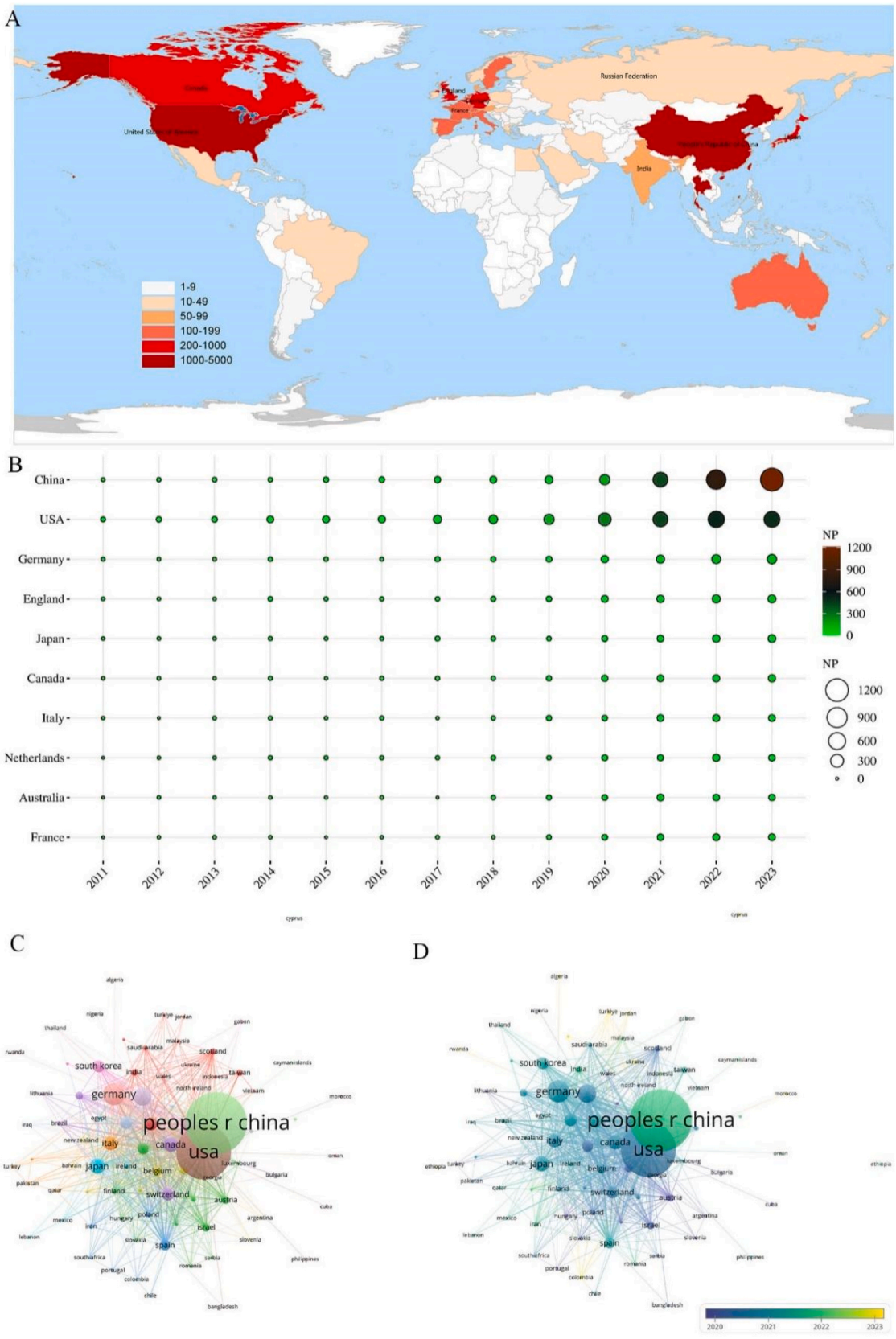

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Fig. 3. Country analysis of single cell sequence associated with cancer related research. (A) Geographical distribution of research articles during 2011–2024. (B) The annual publication quantity of the top ten countries. (C)Network diagram of national cooperative relations. (D) Network diagram of national cooperative relations by AYP.

Table 2
The top 10 authors with the most publications.

Author	Affiliation	NP	NC	H-index
Aviv Regev	Harvard University	30	12269	27
Zhang Zemin	Peking University	26	8025	19
Tong li	Broda Institute	26	11815	23
Orit Rozenblatt-Rosen	Broda Institute	24	11815	23
Cheng QUAN	Central South University	22	269	9
Tang Fuchou	Peking University	22	1441	16
Nicholas E. Navin	University of Texas System	22	3501	19
Wu Catherine J.	Dana-Farber Cancer Institute	22	936	13
Tirosh Itay	Harvard Medical School	21	11272	19
Aparicio Samuel	University of British Columbia	19	2631	15

processes associated with oncogenic signalling, proliferation, complement/immune reaction, and hypoxia by analysing 430 cells from 5 major glioblastomas using single-cell RNA SEQ in this study. Additionally, they noticed various of expression status associated with dryness, which prompted them to target potential in vivo regulators of dryness. What is more, they also demonstrated the potential prognostic significance of this intra-tumour heterogeneity by discovering that the known glioblastoma subtype classifier was variable in expression in single cell inside the tumour. As a result, they exposed previously unappreciated heterogeneity in different regulatory processes in glioblastoma prognosis, biology, and treatment [37]. Tirosh, I. et al. used single-cell RNA-seq to examine 4645 isolated single cells from 19 patients in order to examine endothelial, immunological, stromal, and malignant cells. In particular, "MITF high" tumours also contain "AXL High" tumour cells since all tumours comprise malignant cells with two alternative transcription states. Cell-to-cell interactions were among the features of the tumour micro environment that were discovered by single-cell analysis. Depletion programs and their connection to T cell activation and clonal growth, as well as their variation across patients, were discovered by analysis of tumour-filtered T cells. In general, they are beginning to illuminate the cellular environment of malignancies and how single-cell genomics might illuminate targeted and immunotherapy [38]. Simone Picelli et al. introduced smart-seq from a single cell for transcription analysis, and they then improved the approach to increase sensitivities, precision, and full-length transcription coverage. Furthermore, they offered a thorough plan for Smart-SEQ that would enable the production of full-length cDNA and sequencing libraries using common supplies. From cell selection to final library preparation for sequencing, the complete technique takes two days. Depending on the policy and sequencer, sequencing will take a further one to three days. Chain specificity and the inability to identify non-polyadenylate are current drawbacks (POLYa-ribonucleic acid) [39]. Tang, ZF et al. presented that GEPIA2 is an updated and enhanced version that offers higher resolution insights and more functionalities. It features 198,619 isoforms and 84 cancer subtypes, extending gene expression quantification from the gene level to the transcript level. Users can analyse specific cancer subtypes and compare between subtypes. GEPIA2 also includes new analysis techniques for gene signature quantification inspired by single-cell sequencing studies. Additionally, users can upload their own RNA-seq data for customized analysis and comparison with TCGA and GTEx samples [40]. Newman, AM et al. introduced CIBERSORTx, which is a machine learning method that extends the framework for inferring cell type specific gene expression profiles without the need for physical cell separation. CIBERSORTx minimizes platform specific variations and enables single-cell RNA sequencing data to be used for large-scale tissue dissection. They evaluated the efficacy of CIBERSORTx in various tumor types. Single cell reference atlas is used to dissect a large number of clinical specimens, revealing cell type specific phenotypic states associated with different driver mutations and responses to immune checkpoint blockade [41]. Dagogo-Jack et al. discussed the driving forces for tumor heterogeneity and the methods used for combatting its consequences and this heterogeneity. They also investigate the role that clinical evaluation of tumour heterogeneity can play in the advancement of more effective customized treatments [42]. Using a mouse model of tagged mammary tumours, Aceto, N. et al. show that CTC clusters are not the result of endovascular aggregation but rather develop from low-clonal tumour cell populations. CTC clusters are less frequent in cycles than individual CTCS, but their transfer potential increases by 23–50 times. In breast cancer individuals, single cells resolved RNA sequencing of clusters of CTC and single CTC was matched in individual blood samples, identifying highly differentially expressed cell linker element plaklyon (Lycaon pictus). In mouse models, down-regulation of plakcape hunting (lycaon pictus) eliminates CTC clusters formation and inhibits lung metastasis. CTC cluster abundance and high tumour plakcape (Lycaon pictus) levels were linked to poor outcomes in breast cancer patients. CTC clusters, which were uncommon but have a significant impact on the metastasis and development of cancer, were therefore produced from multicellular colonies of original tumour cells that are joined together by the intercellular adhesion that plaklyon depends on [43]. Sidharth V. Puram et al. refined HNSCC subclasses by malignant and mesenchymal components, and *p*-EMT was identified as an independent predictor of lymph node metastasis, grade, and unfavourable clinical aspects by merging single-cell transcriptome and mass expression patterns from hundreds of tumours. The findings shed light on the HNSCC ecosystem, defining matrix relationships and P-EMT programs linked with transfer [44]. 5063 single T cells were extracted from peripheral blood, tumours, and nearby normal tissues of 6 patients with hepatocellular carcinoma (HCC) for the deep single-cell RNA sequencing study that Chunhong Zheng et al. suggested. They were able to identify 11

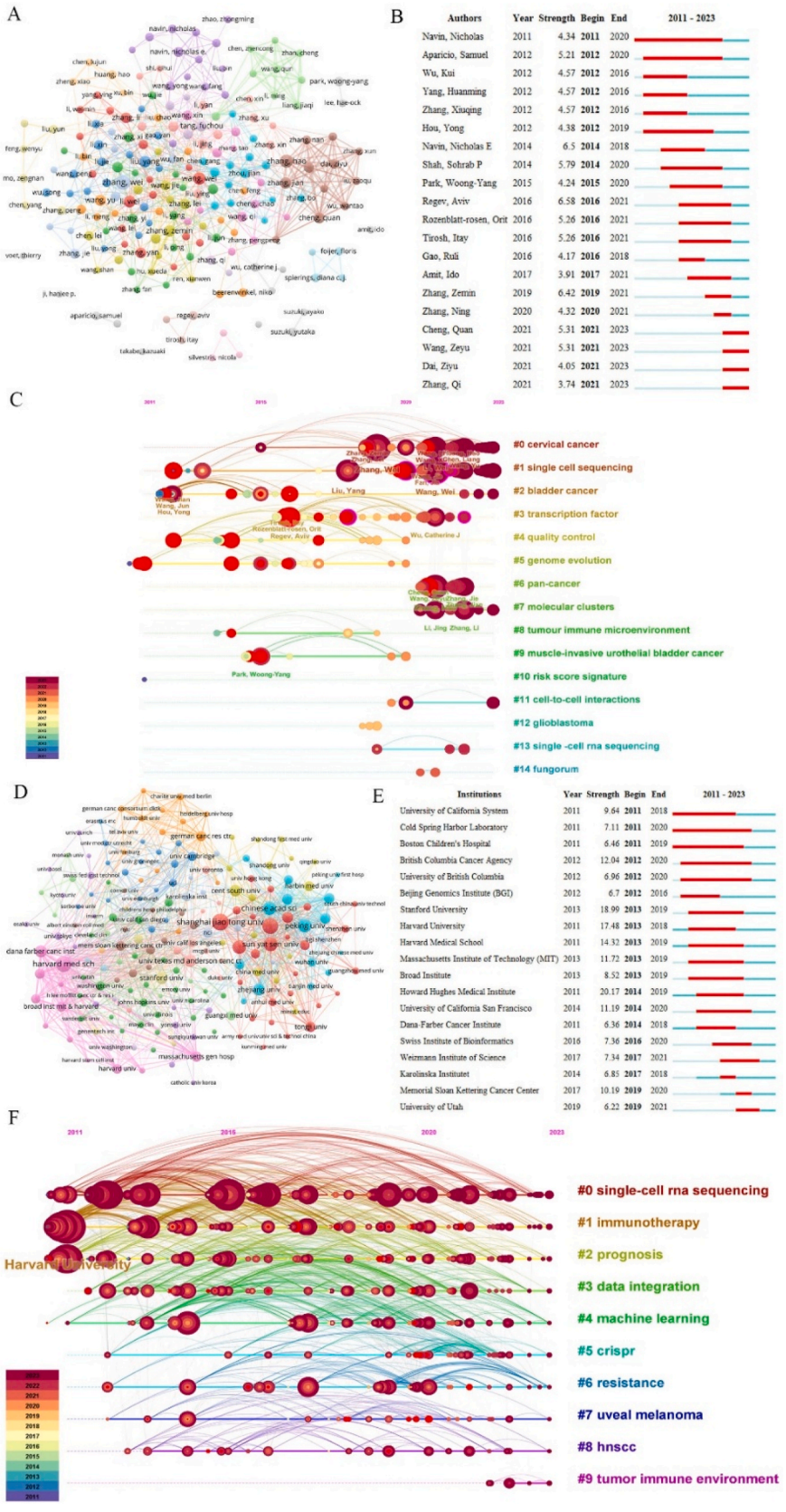

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Fig. 4. Diagram on authors and affiliations of studies related to single cell sequence associated with cancer. (A) Network of authors. Of the 40088 authors, 201 authors had at least 9 documents. (B) The top 20 authors with the highest burstness. (C) Time span clustering diagram for authors. (D) Network of affiliations, 198 affiliations had at least 19 documents. (E) The top 20 affiliations with the highest burstness. (F) Time span clustering diagram for affiliation.

Table 3
The top 10 productive affiliations.

Affiliation	Country	NC	NP	H-index
Harvard University	the US	369	39303	86
University of California System	the US	287	15679	67
Chinese Academy of Sciences	China	271	6087	38
Shanghai Jiao Tong University	China	271	4971	34
University of Texas System	the US	268	15559	59
Harvard Medical School	the US	257	27475	68
Fudan University	China	240	3532	32
Sun Yat Sen University	China	191	3813	28
Chinese Academy OF Medical Sciences Peking Union Medical College	China	184	4263	29
Massachusetts Institute of Technology Mit	the US	184	23325	62

Table 4
The top 10 most active journals.

Journal	NP	NC	IF(2022)	H-index
Frontiers in Immunology	325	3143	7.3	24
Nature Communications	238	11165	16.6	60
Frontiers in oncology	181	1328	4.7	20
Cancers	141	1277	5.2	17
Frontiers in Genetics	114	728	3.7	13
Scientific Reports	111	1156	4.6	18
Journal for Immunotherapy of Cancer	95	1404	10.9	21
International Journal of Molecular Sciences	94	788	5.6	13
Cell Reports	81	3913	8.8	29
Frontiers in Cell and Developmental Biology	81	1072	5.5	16

T-cell subpopulations and trace their developmental paths using the transcriptional patterns of these individual cells in combination with assembled T-cell receptor (TCR) sequences. In HCC, specific subpopulations such as Tregs and characteristic CD8+T cells are preferentially enriched and may be clonal amplified, and they identified the exclusive genes for every subpopulation. One of the genes, Layilin, increased the number of Tregs and activated CD8+T cells while suppressing CD8+T cell function in vitro. This transcriptome data summary offers insightful information and a wealth of resources for comprehending immunological state in cancer [45]. Helmink, BA et al. assessed the potential functional contributions of B cells via bulk and single-cell RNA sequencing, which demonstrate clonal expansion and unique functional states of B cells in responders. Mass cytometry showed that switched memory B cells were enriched in the tumours of responders. Together, these data provide insights into the potential role of B cells and tertiary lymphoid structures in the response to ICB treatment, with implications for the development of biomarkers and therapeutic targets [46]. Citation frequency of different publications in different years was shown in Fig. 5.

3.8. Analysis of Co-cited reference

Due to the large number of referenced references, the minimum number of citations for a reference is 83. The retrieved papers cited a total of 202846 references, of which 197 were chosen for co-citation analysis (Fig. 5A). The line connecting two nodes signified that both nodes had been quoted in a publication, and the shorter line suggested a closer association between the two publications. The node's size indicated the entire connection strength and number of common references in the document. Additionally, different colour nodes were used to divide the paper into different clusters. The research between distinct clusters has a link, but it is not a close one. Cluster 1 (in red) had 68 references that mostly demonstrated on the tools and procedures necessary for data analysis and processing in single cell sequencing technology, as well as its application in various malignancies. Cluster 2 (in green) had 54 references, the majority of which focused on single cell sequencing for genome identification. Cluster 3 (in blue) had 39 references centred on single-cell sequencing detects genetic or chromosomal mutations at the cellular level. Cluster 4 included 36 references paid attention to single cell sequencing in glioblastoma. For further studies on the co-citation of single-cell sequencing detects genetic or chromosomal mutations at the cellular level. The top 20 most influential cited articles are shown in Fig. 6B. Tirosh, I published an article titled "Dissecting the Multiple Ecosystem of Metastatic Melanoma by Single Cell RNA seq" in 2016 with the highest impact of 95.09. The time span clustering of co-cited reference was shown in Fig. 6C. Spatial transcriptomics, pan-cancer analysis, and hepatocellular carcinoma were current research hotspots.

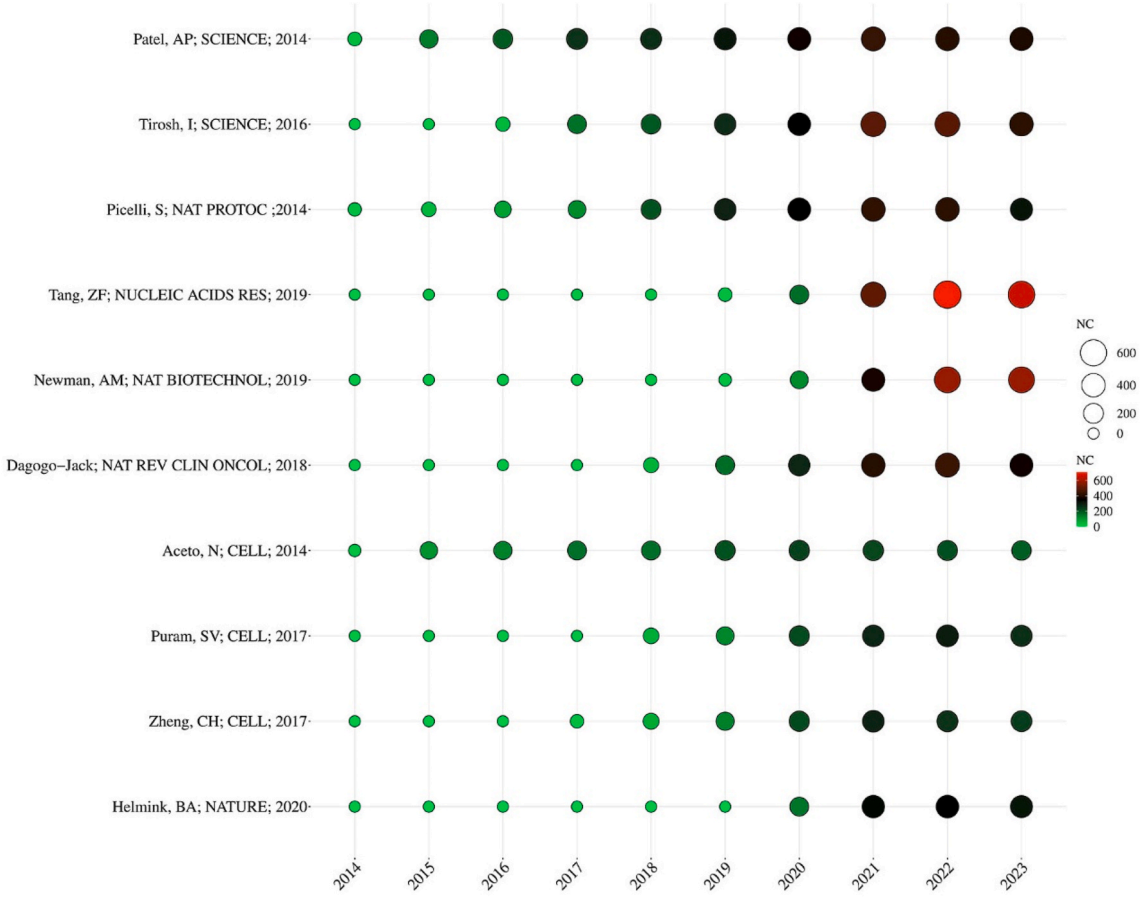

Fig. 5. The annual number for global citations of papers with high GCS.

3.9. Analysis of Co-cited journals

Due to the large number of referenced journals, the minimal number of journal citations is 266 (Fig. 7A). The retrieved journals cited a total of 10845 journals, and 266 journals were chosen for co-citation analysis. The top ten journals cited frequently were Nature (17660), Cell (16575), Nat Commun (11487), Science (10754), P Natl Acad Sci USA (8465), Nat Methods (7430), Nat Biotechnol (6631), Cancer Res (6462), Nucleic Acids Res (6106), Nat Med (5851). The top 20 most influential journals were shown in Fig. 7B, and Genome Res had the highest burstness (121.05). The time span clustering of co-cited journals was shown in Fig. 7C.

3.10. Analysis of Co-cited authors

The minimum number of citations of scholars is 124 because of masses of quoted scholars (Fig. 7D). The retrieved authors were a total of 121712, and 200 authors were chosen for co-citation analysis. The top ten authors cited frequently were Stuart, T (936 times), Butler, A (820 times), Tirosh, I (805 times), Subramanian, A (677 times), Zhang, L (654 times), Wang, Y (625 times), Li, H (625 times), Trapnell, C (597 times), Aran, D (565 times), Newman, AM (556 times). The top 20 most influential co-cited author were shown in Fig. 7E, and Navin N had the highest burstness (91.39). The time span clustering of co-cited authors was shown in Fig. 7F.

3.11. Analysis of research hotspots

In addition to the search terms, VOS viewer and Cite Space were used to analyse the keywords retrieved from the titles and abstracts of 6189 publications (Fig. 8). Cluster 1 in Fig. 8A was primarily concerned with the use of SCS in cancer diagnosis which mostly concerned with fundamental research. Cluster 2 was primarily concerned with the application of SCS in breast cancer, which involves the investigation of treatment resistance and cancer immune response. Cluster 3 paid attention to the basic research of SCS in cancer mainly focuses on animal and cell level research. Cluster 4 investigated the SCS studies done at the DNA and chromatin levels. Clusters 5 was mainly about discovery and clinical study of tumour markers by SCS.

The most often occurring keywords were ‘expression’, ‘cancer’, ‘heterogeneity’, ‘gene’ and ‘evolution’, indicating that studies

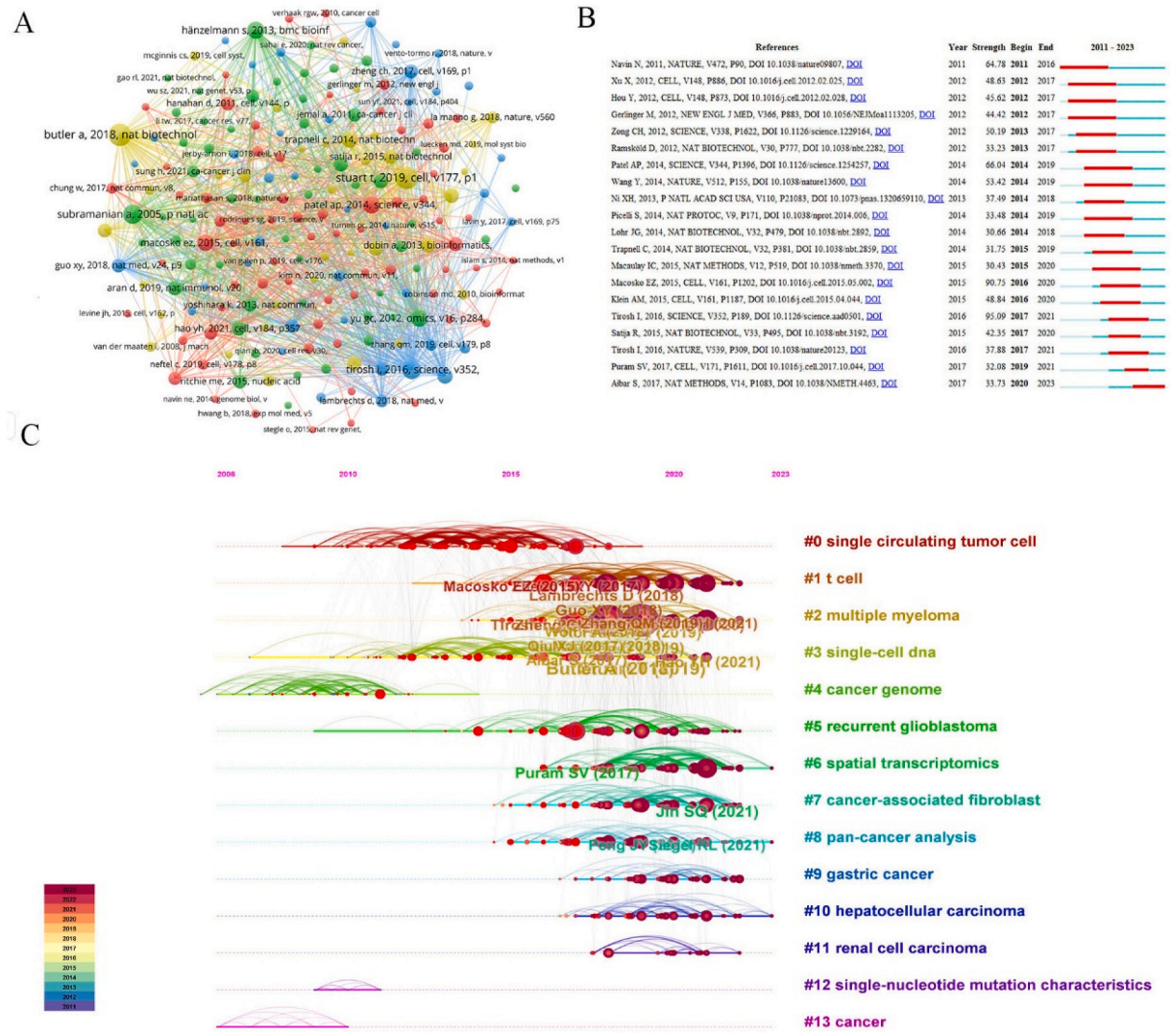

Fig. 6. Co-cited reference map of single cell sequence associated with cancer related research. (A) Network of co-cited references. Of the 202846 references, 133 references were cited at least 83 times. (B) The top 20 co-cited references with the highest burstness. (C) Time span clustering diagram for co-cited references.

related to SCS associated with cancer mainly concentrated at the genetic level. In Fig. 8B, the colours of all keywords were separated using VOS viewer according to the average publication year (APY). In recent years, the following terms appeared frequently: 'tumor microenvironment' (cluster 3, APY: 2022,21), 'immunotherapy' (cluster 2, APY: 2022.10) and 'single cell sequencing' (cluster 5, APY: 2022,00). Besides, 'cancer' (cluster 4, APY: 2021.20), 'heterogeneity' (cluster 1, APY: 2020.73) and 'expression' (cluster 1, APY: 2021.42) were the main topics in this field, which shown that SCS technology can evaluate the transcriptome expression level of cells with high throughput at the single cell level, clearly display the heterogeneity of cells, and offer a novel method for the study of multicellular biological heterogeneity [47]. The top 20 keywords with the most burstiness were shown in Fig. 8C. The time span clustering of keywords is shown in Fig. 8D.

3.12. Bibliographic coupling analysis

When two articles cite the same citation and establish a coupling relationship, this is referred to as bibliographic coupling (Fig. 9). Author literature coupling promotes the analysis of coupling to the author level, not just at the paper level, with the author of the paper as the main object [48]. When extended to the author level, the document coupling becomes a dynamic relationship. With the change of the paper, the author document coupling is also changing dynamically. Therefore, the bibliographic coupling analysis becomes more analytical significance [49]. Fig. 9A displayed the country analysis of bibliographic coupling. The top ten countries were the US (117393 times), China (48958 times), Germany18968 (times), England (14263 times), Sweden (10938 times), Canada (10818 times),

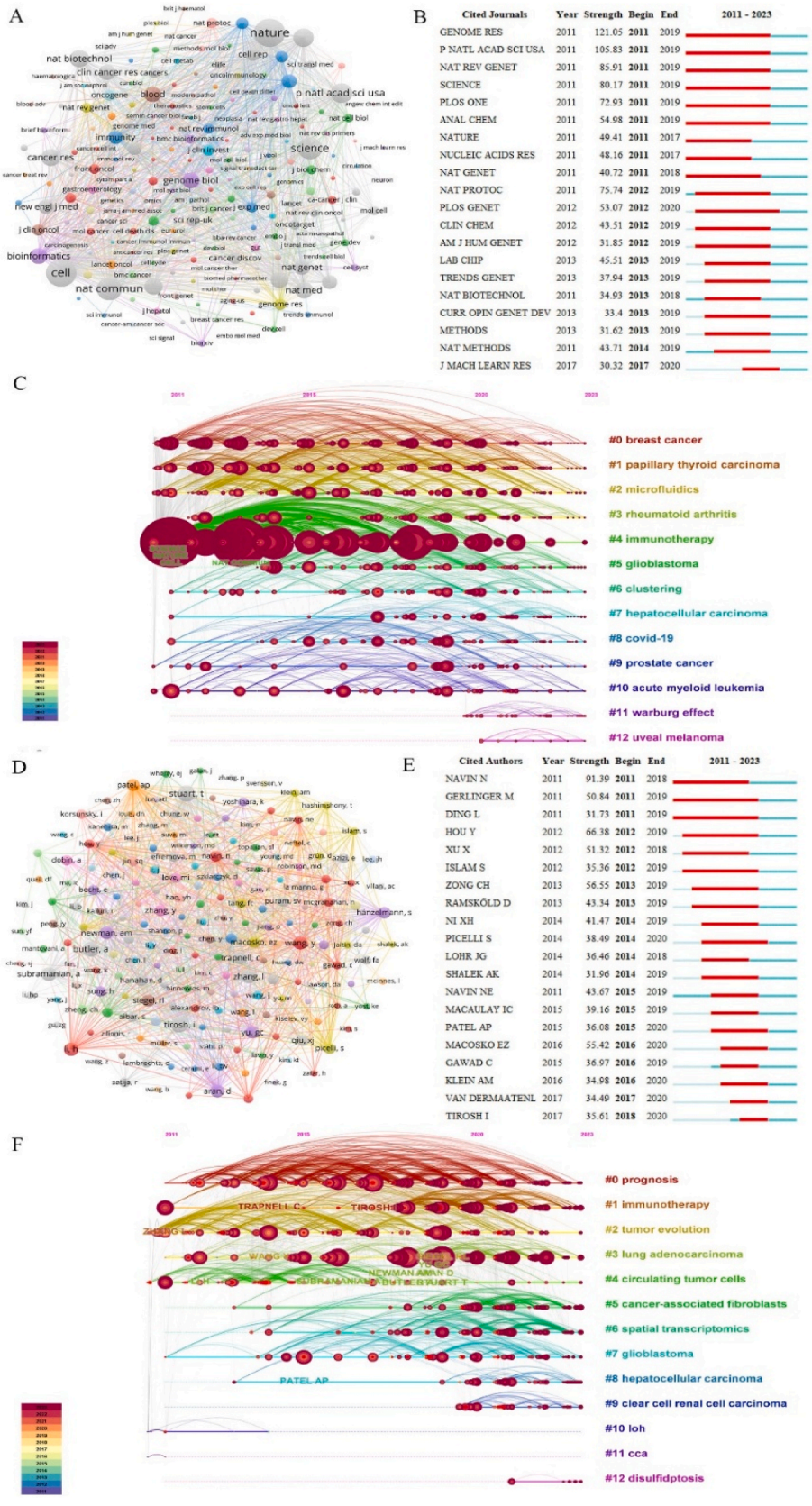

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Fig. 7. Co-cited author map of single cell sequence associated with cancer related research. (A) Network of co-cited journals. Of the 10845 journals, 200 were cited at least 266 times. (B) The top 20 co-cited reference with the highest burstness. (C) Time span clustering diagram for co-cited references. (D) Network of co-cited authors. Of the 121712 authors, 200 were cited at least 124 times. (E) The top 20 co-cited authors with the highest burstness. (F) Time span clustering diagram for co-cited authors.

Netherlands (10257 times), Switzerland (9952 times), Australia (8992 times), Israel (7922 times). The top ten affiliations were Massachusetts Gen Hosp (20940 times), Harvard Med Sch (17152 times), Mit (16599 times), Harvard Univ (15928 times), Stanford Univ (15340 times), Dana Farber Canc Inst (14673 times), Peking Univ (13283 times), Univ Texas Md Anderson Canc Ctr (11575 times), Howard Hughes Med Inst (10948 times), Broad Inst Mit & Harvard (9569 times). The top ten publications were Patel (2014, 2877 times), Tirosh (2016a, 2499 times), Picelli (2014, 2325 times), Tang (2019, 2177 times), Navin (2011, 1853 times), Newman (2019, 1821 times), Dagogo-jack (2018,1793 times), Aceto (2014, 1652 times), Puram (2017, 1335 times), Zheng (2017, 1269 times). The top ten journals were Cell(16554times), Nature (15631times), Nature Communications (11261 times), Science (9658 times), Nature Biotechnology (6046 times), Nature Medicine (5897 times), Nucleic Acids Research (5357 times), Nature Methods (4425 times), Cell Reports (3917 times), Genome Biology (3871 times). The top ten authors were Zhang, Zemin (7479 times), Regev, Aviv 5305 (times), Tirosh, Itay 4918 times), Navin, Nicholas E. (3436 times), Navin, Nicholas (2985 times), Hicks, James (2653 times), Wang, Yong (2048 times), Gao, Ruli1984 (times), Sei, Emi 1779 (times), Zhang, Lei(1608 times).

4. Discussion

In this paper, we used VOS viewer and Cite Space to conduct a bibliometric analysis on the WOSCC database to investigate the hotspots and developing patterns of research on SCS associated with cancer. 6189 papers were published between 2011 and 2024 in total were identified. The largest number of publications was released in 2024, according to the polynomial fitting curve, which demonstrated that the intensity and breadth of academic research on SCS associated with cancer were rising with each passing year. The number of publications was increasing every year.

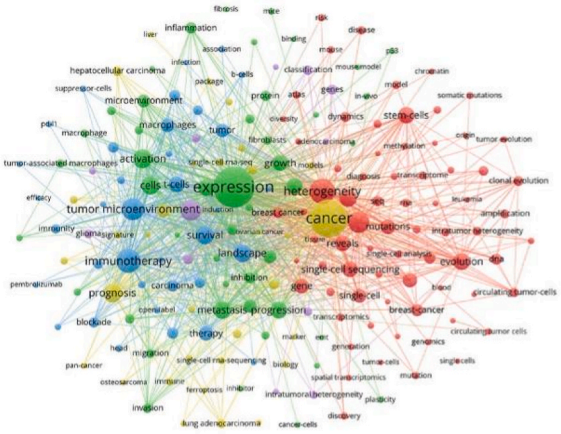
The rapid growth of annual NP is mainly due to groundbreaking publications with high GCS. China was a high-yielding nation in this filed as it was placed first among the top countries/regions in Np. In this research field, the top institutions and researchers in the world were found in the US, which also has relatively high Nc, Np, and H index. As a result, during the past 13 years, the US has experienced remarkable growth in this area. Furthermore, the high IF of the top 10 prolific journals showed that it is not difficult to publish research on SCS associated with cancer in high-quality journals. Amongst the top ten papers with high GCS, 2 papers were included in Science, 1 were included in Nature, and 3 were included in Cell. This result revealed that potential research breakthroughs on SCS associated with cancer have been published in Nature, Cell, and Science. Additionally, it prompted any authors who could be interested in this topic to think about publishing in these publications. Most studies in this field involved both fundamental and clinical research, according to an assessment of co-cited references and keywords, proving that SCS associated with cancer has been comprehensively and systematically studied.

The analysis of research hotspots shows that heterogeneity, immunotherapy, single-cell RNA sequencing, hepatocellular carcinoma, proliferation, gene expression were the research hotspots of the application of single cells in the field of tumour. One of the features of malignant tumours is tumour heterogeneity [50]. It indicates that throughout the course of a tumour's growth, its daughter cells exhibit changes in molecular biology or genes after repeated divisions and proliferation, leading to variations in the tumour's pace of growth, capacity for invasion, susceptibility to medications, prognosis, and other factors. Traditional batch transcriptome sequencing is difficult to obtain the heterogeneity of tumour cell population, and liquid ultra-high throughput is a quantum technological leap in high-throughput sequencing of mRNA at the cell level which has developed into a potent tool for researching cell heterogeneity when the tissue sample size is small. It can capture rare cell types at the same time, The most accurate description of the complex structure of tumour microenvironment. Single cell sequencing technology not only has higher accuracy in detecting gene expression level, but also can detect trace gene expression and rare non coding RNA, provide new strategies and molecular targets for tumour prevention and treatment [51], and draw high-resolution cell map in normal tissue.

Carcinogenesis is generally considered to be a multi-step and multi factor driven process of progressive development, modifications to cancer cell colony growth, invasion, transmission, and survival. The network of intracellular and intercellular signal transduction cascades controls these cell colonies, and the process is more intricate [52]. Macrophages are differentiated from monocytes in blood after penetrating blood vessels. Large foreign bodies, old waste excreted by cells, red blood cells at the end of their life, and foreign things at the site of inflammation can all be swallowed and dealt with by them. They are white blood cells that offer a variety of defences mechanism. For a long time, tumour associated macrophages have been classified as a kind of immune cells with anti-tumour effect. With more and more in-depth studies, it also plays a vital role in tumour progression [53]. Lymphocytes with heterogeneity participate in anti-tumour immune response, mainly including NK cells, B lymphocytes, T lymphocytes, macrophages and derived suppressor cells [54].

Integration SCS data with clinical information can aid in the discovery of new diagnostic and prognostic biomarkers, as well as potential treatment-related cell types or states. SCS has played a crucial role in redefining disease classifications by uncovering novel molecular insights. The advancement of SCS technology has addressed various clinical challenges, allowing for the study of tumor heterogeneity at the individual cell level, analysis of the tumor microenvironment, tracing of tumor cell origins, and elucidation of mechanisms underlying metastasis and recurrence. This technology provides valuable support for the prevention, treatment, and prognosis of tumor in clinical settings. Moving forward, researchers can more accurately and rapidly identify tumor-related genetic

A



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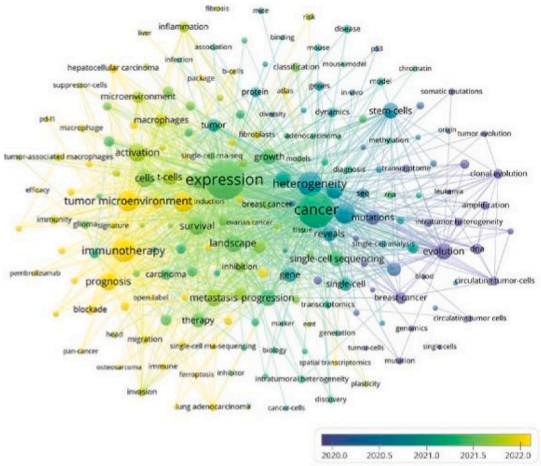

C

Keywords	Year	Strength	Begin	End	2011 - 2023
evolution	2011	32.44	2011	2019	
amplification	2011	25.91	2011	2019	
breast cancer	2011	14.67	2011	2018	
single cells	2011	13.98	2011	2020	
dna	2012	36.02	2012	2019	
genome	2012	20.07	2012	2019	
mutations	2012	19.94	2012	2019	
lung cancer	2012	13.73	2012	2019	
circulating tumor cells	2013	34.51	2013	2019	
clonal evolution	2013	21.72	2013	2018	
intratumor heterogeneity	2013	18.3	2013	2019	
nucleotide	2013	18.13	2013	2020	
single cell	2011	16.76	2013	2018	
messenger rna seq	2013	11.49	2013	2019	
copy number variation	2014	19.01	2014	2019	
whole genome amplification	2014	15.97	2014	2020	
rna seq	2014	21.2	2015	2020	
heterogeneity	2013	19.76	2015	2019	
stem cells	2012	16.06	2016	2020	
somatic mutations	2012	12.25	2016	2019	

D

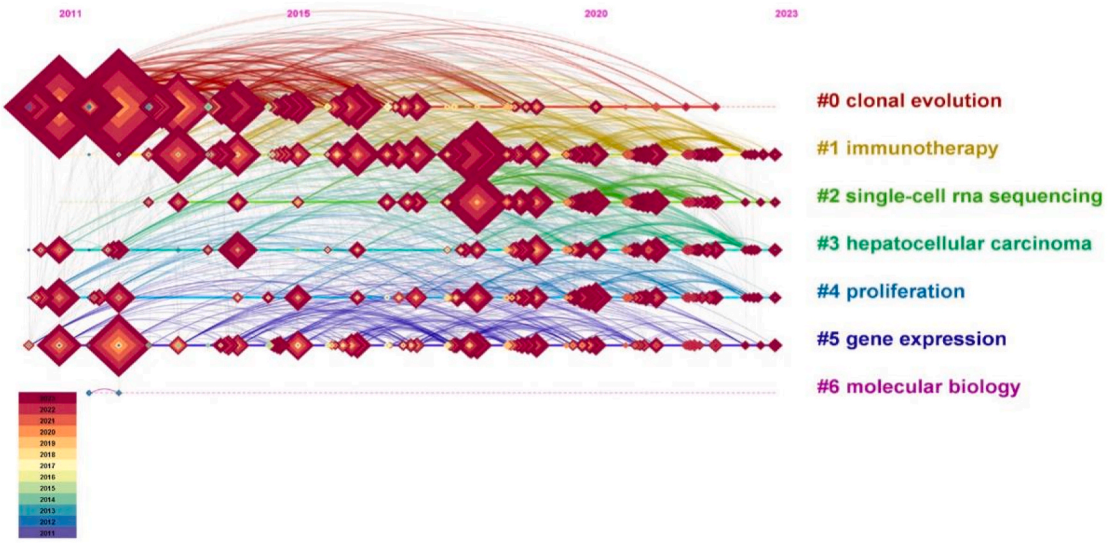

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Fig. 8. Single cell sequence associated with cancer keyword network. (A) Network diagram of keywords. (B) Network diagram of keywords by AYP. (C) The top 20 keywords with the highest burstness (D) Time span clustering diagram for keywords.

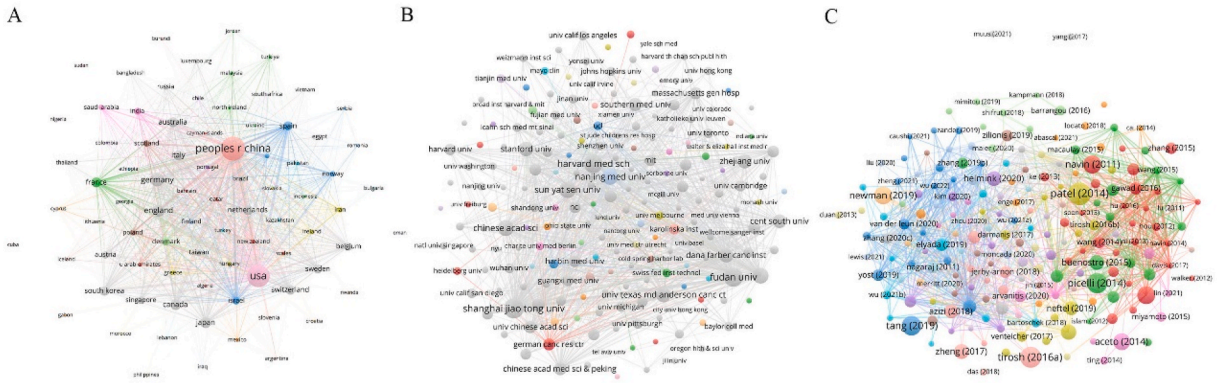

Fig. 9. Bibliographic coupling country analysis map of single cell sequence associated with cancer related research. (A) Network map of bibliographic coupling countries. (B) Network map of bibliographic coupling affiliations. (C) Network map of bibliographic coupling documents. (D) Network map of bibliographic coupling journals. (E) Network map of bibliographic coupling authors.

mutations and clonal configurations, unravel pathogenic mechanisms and clone evolution, and offer guidance for tumor diagnosis and treatment.

Visualization and analysis with bibliometric method of development trends and hotspots in the research field of SCS associated with cancer can provide valuable insights. Nevertheless, there were some limitations in our research, including the inclusion of only English reviews and articles from WOSCC, potential missed information by not analysing the full text of publications using VOS viewer and Cite Space, and a lag in coverage due to the exclusion of some new publications.

5. Conclusion

In our study, quantitative and qualitative analysis was conducted on the most relevant authors and countries, the highly cited papers, leading journals in the publications of SCS associated with cancer from 2011 to 2024. The analysis intended to visualize the findings on SCS associated with cancer research. Over the past 13 years, the number of publications on SCS associated with cancer had a continuous and stable growth. The US and China had a significant impact in this field. Hotspots in SCS associated with cancer research included immunotherapy, single-cell RNA sequencing, hepatocellular carcinoma, proliferation, and gene expression. Our study can effectively aid researchers identify hotspots, and frontiers in research related to SCS associated with cancer.

Data availability statement

The original contributions presented in the study are available on https://www.jianguoyun.com/p/DR_9kVwQuaiFChje_rEFIAA.

Ethics approval and consent to participate

Not applicable.

Consent to publish

Not applicable.

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CRediT authorship contribution statement

Xueliang Wu: Writing – original draft. **Jianchun Fan:** Writing – review & editing. **Xingmei Zhang:** Writing – review & editing, Formal analysis, Data curation. **Tian Li:** Data curation, Conceptualization. **Jichao Song:** Writing – review & editing, Validation, Software, Resources.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Xueliang Wu reports financial support was provided by The First Affiliated Hospital of Hebei North University. All authors declare that there is no competing of interest. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Abbreviations

Web of Science Core Collection WOSCC
Single cell sequencing SCS
number of publications Np
number of citations Nc
impact factor IF
Journal Citation Reports JCR
hepatocellular carcinoma HCC
T-cell receptor TCR

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