Investigation and Characterization of the Current Status, Development Trends and Future Prospects on Chondrosarcoma: A Bibliometric Analysis

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Research Article

Keywords: Chondrosarcoma, Bibliometric analysis, Research topics, Hotspots, Development trends

Posted Date: May 6th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1593614/v1

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Abstract

Background The Chondrosarcoma (CS) is the second most frequent common malignant bone tumor, with variety in terms of histopathology, clinical behavior and prognostic outcome. Although the exploration of this topics is extensive, the management for advanced CS is still exceptional challenging. A comprehensive understanding of the profile of the research status and determination of novel directions is of urgent need.

Methods The Web of Science Core Collection (WOSCC) dataset was queried to collect all relevant publications related to CS on March 1, 2022. Bibliometric analyses of the acquired data were conducted with CiteSpace and VOSviewer software on these publications, to evaluate the collaborations among different countries, institutions and authors, as well as to explore the current hotspots and future directions in this field.

Results Ultimately, we identified and analyzed a total of 4181 records in English. There was a noticeable increasing annual trend in publications since 1970s. The United States contributed to almost half of the records included, with a leading position in this field. The universities and institutes from United States, European and Asian countries such as Leiden University, Harvard University, China Medical University, Mayo Clinic and Memory Sloan Kettering Cancer Center were the biggest nodes in every cluster of the collaboration network. Active collaborations among the countries were observed. As for the productive authors, Tang, Chih-Hsin featured the highest number of publications among all authors (91 documents), while Hascall, Vc had the highest average citations (79.35 times). Keywords co-occurrence analysis divided the CS studies into 9 clusters: human CS cell, skull base, p53 expression, long bone, cartilage matrix, chondroid chordoma, endoplasmic tissue stress, pelvic sarcoma and connective tissue growth factor. Together with the citation burst of references, the cluster analysis of keywords co-occurrence suggested that the basic studies on human CS cells to investigate the mutant genes, related signaling pathways and novel alternative modalities to treat refractory CS is an upsurge of research with great significance.

Conclusions The present bibliometric study summarizes the clinical research of CS on study type, most prolific countries, institutions, authors, keywords co-occurrence and references with citation burst. These findings may assist the new scholars to better understand the current status and research trends to guide future practice and directions.

Introduction

As a heterogeneous group of cartilaginous malignancies, chondrosarcomas (CS) are of diversity in histopathology, which consist of six main subtypes (conventional, myxoid, mesenchymal, dedifferentiated, juxtacortical and clear cell) with more than 90% of cases representing the primary conventional type[1–3]. In addition to arising de novo due to sporadic mutations (isocitrate dehydrogenase-1/2, IDH-1/2), secondary CS can originate from malignant transformation of pre-existing
benign cartilaginous lesions, such as osteochondromas or enchondromas[4–7]. CS compromise approximately one-third of all malignant bone tumors, with therapeutic outcomes varying greatly depending on the clinical, histological and pathological grade[8, 9]. Complete surgical resection with clear margins with or without local adjuvant treatment remains the mainstay of treatment modality for patients with localized disease whenever possible. Low grade tumors confined to the bone can be managed by extensive intralesional curettage in selected cases, for the purpose of minimizing functional disability without increasing recurrence rate[10, 11]. The patients presenting with unresectable disease at the time of diagnosis or recurr ing with metastasis disease following previous surgery are more amenable to systemic therapy[12, 13], while the conventional chemotherapy and radiotherapy have shown modest efficacy in CS and lead to relatively low survival rates and considerable morbidities in some cases because of the extracellular matrix, low percentage of dividing cells and indigent vascularity[14–17]. In conclusion, the etiology of CS involves quite complex mechanisms, which are not fully understood, and the novel management alternatives to improve prognosis remain to be settled. Therefore, to help researchers gain insight into this field, discovering the current developmental status and hotspots of CS in both orthopedic and oncological specialties is highly required.

With the rapid development of medical science and technology in treatment of CS over the past couple of decades, an increasing number of research papers have been recorded online on this topic, with a variety of publication types. Based on this, it is important for us to better understand and learn more from the developmental trends and novel advancements of CS. However, rapidly learning about the current landscape of specific medical research is still a challenge. Fortunately, the emergence of bibliometric analysis provides a method to statistically and quantitatively visualize the evidence in a certain field according to the information in published records. Bibliometric analysis has become the most favorable tool for describing the status and exploring the research direction, by objectively presenting the research contributions of different countries, institutions and authors from a large number of published studies and predicting the research hotspots and trends[18, 19]. Up to date, however, no bibliometric analysis concentrating on the CS has been conducted and even less attention has been focused on prediction of research hotspots. This study aims to conduct a comprehensive investigation of the current academic status and clinical issues, and to predict the potential progress on the field of CS over the next couple of decades, which may be taking us closer to effective therapies for CS.

**Methods**

**Data sources and collection**

We performed a comprehensive collection of all of the original articles and reviews from the Web of Science Core Collection (WOSCC) without restriction of the publication date on March 1, 2022, to reduce bias incurred by database updating. The retrieval strategy employed for search was as follows: (TS=Chondrosarcoma*) (the symbol "*") is a retrieval symbol of WOS advanced retrieval, which means to search for words prefixed with the word before "*". Medical Subject Headings (MeSH) terms are a type of standard vocabulary that can be adopted to perform continuous co-word cluster analysis and reflect the
main topic of the literatures. We conducted an online search in PubMed based on the screening criteria of (“Chondrosarcoma” [MeSH]) and no other synonyms were obtained, which was developed by the National Center for Biotechnology Information (NCBI) of the National Library of Medicine (NLM), so the keywords to make retrieval on WOSCC was determined as the one above-mentioned. In this study, language restrictions were applied for literature search and downloading processes, after which only publications in forms of English were included in the final analysis.

**Inclusion and exclusion criteria**

Inclusion criteria were published records, mainly including articles and reviews on CS. We excluded the studies which were not in relationship with CS, duplicates, conferences abstracts, letters, news items, editorial materials and retraction or withdrawn publications, for consistent and accurate information collection from multi-analysis results based on published studies. All data were independently collected by two authors (SJT and ZZQ) with screening the titles and abstracts to selected the articles after standard training, Full-text retrieved in selected publications when necessary. Disagreements were discussed and solved between the 2 reviewers and further discrepant opinion was settled by the senior author (YTQ).

**Social network map software**

CiteSpace software (version 6.0.R1, Drexel University, Philadelphia, PA, USA) was used for network analysis of developmental dynamics, future trends, hotspots and key points in scientific literature of a certain topic. Burst detection, to identify references that appear with an abrupt change in frequency at a specific period, were considered to be hot references at that point in time. Clustering (or co-citation, i.e., both A and B are cited by C) analysis of references was also conducted. We used VOSviewer software (version 1.6.18, Leiden University, Netherlands) to visualize the collaborations between authors of a list of publications as well as those between countries, institutions, and high frequency keywords. One classification method uses a metric based on the number of co-authored articles, which allowed authors, institutions, countries or keywords to be clustered, where those belonging to the same group cooperated more with each outer. In the network maps, unequal-size nodes with different colors represent differences in the number or frequency of published records in clusters among the same research topics. Lines between nodes indicate the strength of collaborations (the stronger the collaboration is, the thicker the line displays). We also used overlay visualization, in which the color of the nodes represents the average year in which each author, institution, country or keywords was used. The data obtained from WOSCC were converted to TXT format with Full Record and Cited References and imported into CiteSpace and VOSviewer. Both above software analysis was conducted by another author specializing in the bibliometric analysis (LC).

**Statistical analysis**
Stata software for Windows (version 15, Stata Corp, College Station, TX) was used for data analysis and figure production. Continuous variables were presented as mean and standard deviation or median and interquartile range depending on the obedience of normal distribution. Categorical variables were expressed using frequencies and percentages.

Results

A total of 8773 publications were identified from WOSCC. The publications with non-English language (n=489) were excluded. After screening titles and abstracts of remaining studies, duplicates, unrelated topics and meeting abstracts were also excluded. Finally, 4181 studies were included for bibliometric analysis (Figure 1).

Global publishing trends

As shown in Table 1, we only included studies in form of articles and reviews. As a result, a total of 4181 publications (3835 articles and 347 reviews) met our inclusion criteria. The Figure 2 shows the publication trends of the field of CS. The early stage (before 1970s) saw fluctuations in the number of publications around 1 to 5 documents per year. While since then, the publications continue to increase from 1990s and 2010s, respectively, with a noticeable upward trend reaching a peak publication number of 250 in 2021. However, there was a plateau period during the 2000s. The result indicates the lack of notion of this disease in the early period while since then the specific direction of CS was quite clear during the two burst stages and the field of CS had become a research hotspot capturing global research attention.

Contributions of countries and institutions

A large number of different countries participated in publishing studies on CS over the past decades. We included the top 25 prolific countries to visualization analysis and made a network map of these productive countries (Figure 3A and 3B). As shown in this figure, the United States was the largest contributor (2042 publications), followed by Japan (584 publications), China (427 publications), Germany (346 publications) and Italy (328 publications), and the other prolific counties were displayed in Table 2. The network map for countries formed 4 clusters, and there were active collaborations among the countries and clusters. The Figure 3A revealed that the cooperation between the United States and Canada was closet, followed by the cooperation between China, Italy, Japan and England. Furthermore, the results of Figure 3B also showed that among the top 10 countries, the United States contributed to the research on this topic earlier than other countries in published time, which may indicate that the exploration of CS in the early stage was mainly took place in the USA. Although Japan and China had the 2nd and 3rd number of publications worldwide, the relatively recent publication date lead to less average citation times and total link strength.
As shown in Figure 4, a network map was created for institutions involved in the research of CS and formed 9 clusters (#0-8), which represents the main subtopics of research on CS (Figure 4A). The most representative institution of each cluster was also displayed in Figure 4B, with the size of nodes larger than others. The Leiden University (cluster 0, Orthopedics), Memory Sloan Kettering Cancer Center (cluster 1, Oncology), University of Texas MD Anderson Cancer Center (cluster 2, Biochemistry & Molecular Biology), Okayama University (cluster 3, Rheumatology), Harvard University (cluster 4, 5 and 6, Clinical Neurology, Radiology, Nuclear Medicine & Medical Imaging and Cell Biology), China Medical University (cluster 7, Surgery), Mayo Clinic (cluster 8, Pathology) were the biggest nodes in each cluster, respectively. The results indicates that the Harvard University made the most contribution on this region due to its leading position in 3 clusters. The number of cluster label was negatively correlated with the density of the network. Therefore, this figure also suggests that the academic exchanges were abundant in the orthopedics while weak in the pathology.

**Author co-citation analysis**

A co-citation relationship among authors is established when two or more authors are cited in one or more subsequent papers at the same time. We can obtain a clear picture of core authors and their contributions to a certain field by analyzing the authors’ co-citation networks. Therefore, we performed cited-authors analysis to find the top 10 most cited authors, the details of which are listed in the Table 3. The scholar, Chih-Hsin Tang from the China Medical University, Taiwan, was the most prolific author and had the highest number of publications (91 publications). However, the team of Hascall, Vc was outstanding among the authors for having the highest average citation times of 79.35 even if the documents of this researcher were all published before the year of 2000. The network map and overlay visualization of the top 50 productive authors was also created using VOSviewer (Figure 5). The node size was positively associated with the cited counts of authors, and the thickness of the lines between every two nodes represented the frequency of being co-cited between those two authors. From the co-cited network map of authors, we could find that whereas the research on this field is extensive, there is less active cooperation among these authors given that there was almost no formed cluster and the lines connecting the nodes were sparse.

**Research trend analysis through detection of references burst**

References burst detection was applied to acquire a quick glimpse of future search trends, which defined as those studies that are cited frequently over a period of time. The top 25 references with the strongest citation burst were shown in Figure 6, where the blue line represents the time interval, and the time period in which the reference was found to have a burst is labeled with a red line, indicating the first year and last year of the duration of the burst. As shown in this figure, the references with citation burst first appeared in 1979, which illustrated the structure of the complex between hyaluronic acid, the hyaluronic acid-binding region, and the link protein of proteoglycan aggregates from the warm rat CS cells. This article was published on the Journal of Biological Chemistry by Faltz, L et al. [20]. The most recent citation burst was an article to investigate the influence of surgical margin on local recurrence-free
survival and disease-free survival by Stevenson J et al. publishing on the European Journal of Surgical Oncology[21]. The article with the strongest citation burst was published in Oncologist in 2008 by Gelderblom H et al., which was a review providing an overview of the histopathology, classification, diagnostic procedures and the therapy of CS[22]. Only three references with citation burst appeared in the period from 1980 to 1990 and six references appeared from 2000 to 2010. Most of the references had citation bursts between 2010 and 2019, which indicates that the direction of the studies on CS has been much clear and attracted much attention during this period. The top 25 references with citation burst were almost published by different authors, except one author, Bovee, J, who came from the Leiden University and published two articles in 2005 and 2010, respectively, both with citation burst duration of 4 years. The first paper was a review published on Lancet Oncology illustrating the emerging pathways in the development of CS and related targeted treatment[23], and the second one was another review depicting the molecular pathology of cartilage tumors and possible therapeutic targets, which was published on Nature Review Cancer. Both of the studies summarized the novel signaling pathways and encouraged the investigation into the therapeutic efficacy of molecularly-target agents.

Analysis of references co-citation

Next, we performed clustered network analysis of references co-citation to conduct a more in-depth study. Studies usually cite published documents correlated to the subject to bolster the conceptions of the authors. If two studies have many common references, they are inclined to be homogenous. Based on this logic, we could divide the articles included into several clusters to present the main topics in the field of CS. Consequently, clustering analysis with a network map for co-cited articles was created in Figure 7, for being another method to describe the research trends. After calculation, a network map for keywords was generated and a total of 9 clusters were formed (#0-8). The labels were salient noun phrases extracted from the keywords in each cluster, which included #0 human chondrosarcoma cell, #1 skull base, #2 p53 expression, #3 long bone, #4 cartilage matrix, #5 chondroid chordoma, #6 endoplasmic reticulum stress, #7 pelvic sarcoma and #8 connective tissue growth factor. The cluster tags are reversely correlated with the number of articles for each cluster, namely, the cluster #0 contains the largest number of articles while the cluster #8 contains the least.

A timeline view of the distinct co-citations of articles was shown in Figure 8 to present all the related topics of cited literatures in chronological order more clearly. The bold timeline indicated that the clustering topics was a hotspot during this period. Citation tree-crosses with different sizes on the timeline represented some keywords with a high frequency. The bigger the cross was, the more frequently the keyword appeared. We found that the cluster #0 had been a hotspot since 1990s and reached its peak moment at the same time, and the investigation on this topic is still going on. The cluster #5 lasted for the shortest time with a sharp drop before 2000s, indicating the differential diagnosis of CS from other chondroid tumors at that time was no longer a hard issue. The cluster #1, #3 and #7 are the clusters exploring the management alternatives in different anatomical locations. The studies on these 3 clusters also first appeared in 1990s, while the researches on skull base had an early stagnation compared to those on long bone and pelvis. The cluster #2, #4 and #8 explored the pathogenesis, tumor
microenvironment and novel alternatives with treatment potential of CS before 2010s, while the cluster #6 was an emerging research field and getting increasing attention since then.

**Discussion**

In the current study, a comprehensive literature search was conducted in the WOSCC database on the topics of the CS. A total of 4181 publications in English were retrieved, which could erase the potential of ungrasping the authors’ intention due to language misinterpretation. Our statistical and quantitative analysis found a significant improvement in research on the field of CS and an increasing number of orthopedic and oncology experts focused their insights on this region. Although those studies have been highly extensive, they are relatively chaotic and lack hotspots analysis. Bibliometric analysis is an interdisciplinary science emerging in recent years, which could use mathematical and statistical methods to make analysis on a specific field, and thus offer the possibility of visualizing the present state from multiple dimensions and making reasonable prediction of future directions base on the published record. Therefore, we summarized in this study the contributions and research collaborations of the countries, institutions and authors in the field of CS, as well as the research hotspots and new trends of investigations. Researchers new to this field can easily gain useful and relevant information from our bibliometric analysis, and avoid repeated research.

From Figure 2, we could see that the annual growth trend of publication outputs related to CS is generally on the rise. It can be divided into four stages, including a stagnation period (before 1970), a slow growth period (1970 to 2000), a plateau period (2000 to 2010) and a rapid growth period (after 2010). The studies on CS were sparse before 1970s with publications less than 5 per year. Since then, there was an increment in the number of publications till 2000s. After a short plateau period from 2000 to 2010, the researches made a robust rise. We found that the studies during the first peak of publication were mainly morphology, histology, pathology, immunochemistry, and molecular analysis of CS, which reveals the primary focus of researchers in the early stage was to identify the histological and pathological features of CS, as well as mutations that may be associated with CS in the molecular level. Although the number of studies published from 2000 to 2010 was still relatively large, we can speculate from the plateau stage that it may be a symbol demonstrating the oversaturation of previous studies and the determination of new research directions being made afterwards. Since then, the number of publications began to show a consistent upward trend again.

The United States had the highest absolute productivity ranking, which contributed more than half of the publications, followed by Japan, China, Germany and Italy. We could learn from the Figure 4 that the institutions or universities outstanding in each cluster were mainly from the United States, especially the Harvard University, which was a prominent contributor of 3 clusters. Among the top 5 countries, only China is a developing country, showing that the research capacity of developing countries in this filed is weak, which could also be reflected by the low average citations (11.27 times). This situation might be influenced by the amount of financial support available for conduction of basic experiments on CS. Therefore, developing countries should come up with strategies to promote research in this field and
actively learn from developed countries. The developed countries should make more collaborations with
developing countries to promote the medical progression. Although the United States published the most
records worldwide, Netherlands (which ranks in the 8th) had the highest average citations (36.48 times).
Citations differed from the number of documents, as did the cooperation of countries and regions: United
States, Italy, England, Netherlands, Germany, France and Canada showed the strongest cooperation, with
a high total link strength among the countries. This was mainly because the studies on CS were
published earlier in these countries, which was indicated by the dynamics and trends of countries over the
years in the Figure 3B.

Similarly, the analysis of institutions and authors almost matched the distribution by countries and
districts. The institutes from United States (Harvard University, Mayo Clinic, Memory Sloan Kettering
Cancer Center and University of Texas MD Anderson Cancer Center), European Universities (Leiden
University, University of Bologna and Heidelberg University), Japan Universities (Okayama University and
Niigata University) and Chinese Universities (China Medical University), have taken leading places in CS
papers, with steady collaborations in global groups. Moreover, among the authors who contributed to
publications, the top 50 authors were situated in the collaboration networks that account for large
proportions of research, mainly from the above-mentioned countries and institutes. However, the network
map analysis for authors could generate almost no clusters and lines representing link strength, which
indicates that less active collaborations had been implemented during the past few decades among the
prolific authors. We call for strengthening the exchanges and cooperation between researchers to better
promote the development of his field.

The dynamics of a field can be characterized, in part, by articles with citation burst. References with
citation burst refer to the sudden increase of citations of certain documents in a certain period, which can
help us find emerging topics and research topics that have attracted much attention in a certain field. We
selected the top 25 references with intense citation bursts. The first 3 references with citation burst were
studies concentrating on the histological and biological features of CS. Two of them investigated the
biosynthesis of proteoglycan aggregates from CS cells and both published on *Journal of Biological
Chemistry*[20, 24]. And then, the four references with citation burst from 1990 to 2000 shifted the research
emphasis to myxoid CS, a rare subtype of CS[17, 25-27]. During the 2000 to 2010, the researchers started
to put their insight to the genetic level and related pathways in CS. While in the second decade of 21
century, the references burst were most clinical studies which investigated novel therapeutic approaches
and prognosis of patients with CS. The Leiden University ranked the first for contributing 6 papers among
the top 25 references with citation burst, followed by Harvard University, which were also illustrated in the
Figure 4 that these universities were at leading position in this field. The *Cancer, Annals of Oncology,
Journal of Biological Chemistry* and *Journal of Joint and Bone Surgery* were the journals published the
most references with citation burst (3, 2, 2 and 2 records, respectively). New researchers could read
articles from these journals preferentially to get the hotspots on this field, and give priority to these
journals above others for new manuscript submission.
Keywords co-occurrence, together with the reference citation burst, could both indicate the research trends and hotspots. A lot of keywords were used in the studies published on research in the field of CS, while the majority of the keywords appeared once and only a little of them had a frequency of greater than five, revealing that only few keywords are frequently used. In the current bibliometric study, cluster analysis of co-occurrence keywords showed that there were 9 clusters in this file. Of the 9 clusters in visualization maps to explore key topics and future directions, cluster 0 represented the studies on human CS cell and the timeline view demonstrated that this cluster last the longest period of time with the investigation on this topic still continuing. The keywords in the cluster #0 mainly consist antigen, monoclonal antibody, inhibitor, pathway and isocitrate dehydrogenase, which describe the new hotspots of CS in addition to surgical resection. As a chemo- and radioresistant tumor, conventional adjuvant therapies show little benefit and the surgical resection is the mainstay of treatment. While the patients with unresectable or recurrent disease still have a poor prognosis. Much research interest should be focused on the other novel therapies, such as molecularly-target agents, inhibiting abnormal MicroRNAs expression[28-31], inactivation of glucose metabolism[32, 33], downregulating the tumor cell activity[34-36], suppressing the matrix metalloproteinase (MMP)[37-39], targeting IDH mutations[40-43] and Indian hedgehog (IHH) signaling pathway[44-47] and immunotherapy[48-50], all of which apparently requires substantial basic experiments on CS cells to make some breakthrough of these aspects. Cluster #1, #3 and #7 were the studies investigating the treatments of CS on different anatomical locations. We could learn from the 3 clusters labels that CS is commonly originate from these regions[51-55]. The common keywords in these 3 clusters were chemotherapy, radiotherapy, surgery, resection and follow-up, meaning that these studies were concentrating on the clinical efficacy and safety of preexisting treatments, and the prognosis of patients with CS. While the reconstruction in the long bone and pelvis is an intractable issue after resection, which is not often encountered in the skull base CS. Modified methods for reconstruction based on current techniques and a better design of prosthesis are the hot topics of these investigations[56-60], and that explains why the cluster #3 and #7 are much enduring. The gene p53 (cluster #2) could suppress tumor cell, playing the role of monitoring aberrant cell division and inducing cell apoptosis if repair process could not be initiated. Although the tumor suppressor p53 gene has been extensively studied in the field of cancer, the mutations of p53 are thought to be relatively low in CS compared to other alterations in the genetic level. And a higher incidence of p53 mutation is found in the late stage of CS or other atypical CS, which only accounts a small fraction of CS. It suggested that the p53 may be correlated with the progression instead of initiation of CS[55, 61-63]. It is why the cluster #2 had an early stagnation of investigation before 2007. While combined with other treatment regimen currently used for certain altered pathways, appropriate p53 target agents can be potential therapeutic alternatives[3, 64]. There is a same situation for the cluster #4, which elucidated the substances of extracellular cartilage matrix (ECM) of CS cells to explore the tumor microenvironment (TME). The studies on this topic were used to attract much attention before 2000, while since then, researchers shifted their sights into other regions. Enhancing endoplasmic reticulum (ER) stress (cluster #6) has shown great effect as a tumor suppressor of CS. In both vivo and vitro studies, treatment with enhancing ER stress could induce apoptosis of CS cells via mitochondrial dysfunction, which could be a promising approach in CS treatment[65-67]. However, no updating researches have been forthcoming in recent years, which could
suggest the clinical efficacy of this modality needs to be further ascertained. Previous studies have revealed that connective tissue growth factor (CTGF) could be induced by hypoxia and therefore promotes tumor angiogenesis in human CS cells[68, 69]. However, the studies to date failed to demonstrate meaningful clinical activity of target the gene of CTGF on the prevention of CS.

Limitations and strengths

Nevertheless, we were aware of several potential limitations of this current study. First, we only searched records from the WOSCC and only included papers in English and in form of article and review, which might result in selection bias. Second, the number of related papers on CS may increase rapidly, that the constant updating of the database may lead to a difference between bibliographic analysis data and the actual research progress. Third, the error of the database itself may also lead to a deviation of the results, such as mislabeling document types and less inclusive of the documents. Fourth, although the data had been manually standardized, bias might exist due to the authors with the same name or the keywords of various expressions. Finally, by using the software, we might have overlooked some information, which may result in errors in data analysis, even if there are some reasonable and unavoidable differences on the same outcomes between CiteSpace and VOSviewer. Acknowledging the limitations above-mentioned, however, to be the best of our knowledge, this is the first study to perform bibliometric analysis on research in the topic of CS. The current study aimed to identify collaboration networks among authors, countries, and institutions and illustrate the development trends, current hotspots and future directions in this field.

Conclusions

The number of publications related to CS has increased dramatically since 1970s. The United States led absolute productivity ranks by contributing more than half of the total publications, followed by Japan, China, Germany and Italy. Collaboration networks consisted mainly of institutes and authors from the above-mentioned countries. In terms of the top productive authors, the collaboration seems to be less active, and thus multicenter cooperation among the specialists should be advocated. The new ideas on investigations of the mechanism involving the mutant gene and related signaling pathway and exploring novel alternative tactics to replace conventional therapy is of top priority. Overall, we believe that this article is of guiding significance for CS and that the above research directions might contribute to a breakthrough in the future.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication
All authors have consented for publication of this article.

**Availability of data and materials**

The datasets supporting the conclusions of this article are available from the corresponding authors upon reasonable request.

**Competing interests**

The authors declare that there are no conflicts of interest.

**Funding**

Not applicable.

**Author contributions**

Conception and study design: TQY; Collection and analysis of data: JTS and ZQZ; Provision and interpretation of data: TQY, RLY, WG and XDT; Figures preparation: JTS, CL and KWJ; Manuscript writing and reviewing: All authors; Final approval of manuscript: All authors.

**Acknowledgements**

Not applicable.

**References**


**Figures**
Figure 1

Flowchart of inclusion and exclusion process.
Figure 2

Growth trends of publications on CS.

Figure 3
VOSviewer network map of the countries/regions involved in CS research. (A) The network map of countries/regions. (B) Dynamics and trends of countries/regions over years.

Figure 4

CiteSpace network map of the institutions involved in CS research and related investigation field. (A) The network map of the institutions. (B) The subtopics and outstanding institutions of each cluster.
Figure 5

VOSviewer network map of the authors in the field of CS.
## Top 25 References with the Strongest Citation Bursts

<table>
<thead>
<tr>
<th>References</th>
<th>Year</th>
<th>Strength Beginning</th>
<th>Strength End</th>
</tr>
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### Figure 6

References with the strongest citation burst on CS from 1927 to 2022.
Figure 7

CiteSpace clustered networks of the co-cited references on CS.
Figure 8

Timeline view of the 9 clusters of the co-cited articles in the field of CS.