Clinical Case Reports and Studies
2023 Volume 3, Issue 4
DOI: 10.59657/2837-2565.brs.23.077

BioRes Scientia
Value your Research

Research Article

Open Access

Fundamental Cognizance and Scholarly Exploration of Immune-Related Notions in Head and Neck Squamous Cell Carcinoma (SCC) From 2012 To 2022: A Bibliometric Analysis

Rui Miao[1,2], Wenyang Ma[3], Shujie Liu[3*]

[1]*Department of Otolaryngology Head and Neck Surgery, Xiangya Hospital, Central South University, Changsha, Hunan, China.*

[2]*Otolaryngology Major Disease Research Key Laboratory of Hunan Province, Changsha, Hunan, China.*

[3]*Harbin Medical University Cancer Hospital, Operating Room, Harbin, China.*

[*]*Corresponding author: Shujie Liu.*

Abstract

Background and Objective: Immunization holds profound research significance and promising application potential in the realm of head and neck squamous cell carcinoma (HNSCC). Regrettably, only a paucity of bibliometric data has been dedicated to a systematic examination of this domain. The present study endeavors to holistically assess the research landscape encompassing immunization and allied concepts in HNSCC. It shall encompass an exhaustive review of countries, institutions, authors, and journals involved in this sphere, while also evaluating the knowledge framework through keyword co-occurrence analysis.

Methods: The method employed for subject retrieval involved accessing the Web of Science core collection to obtain works and reviews concerning HNSCC immunity. Subsequently, bibliometric analysis was conducted utilizing the Cite Space and VOS viewer software.

Results: Between 1 January 2012 and 31 October 2022, a total of 1,744 English works and reviews were considered in the analysis. The research contributions emanated from 402 institutions, primarily from 57 countries and regions. In terms of journals, CANCERS published the highest number of works, other journals in the fields of molecular biology, biological immunology, and clinical medicine also made substantial contributions. Over the course of time, the landscape of research hotspots gracefully evolved. Certain illustrious terms such as “open label”, “t cell”, “immunotherapy”, and “tumor microenvironment” elegantly emerged, gracing the scholarly stage with their profound frequency.

Conclusion: This study presents a thorough and all-encompassing assessment of HNSCC research within the context of immunity, achieved through the utilization of bibliometric and visualization methodologies. By offering insights into the dynamic evolution of immune-related concepts in HNSCC, this paper will undoubtedly aid researchers in gaining a deeper understanding of this complex domain.

Keywords: immunity; head and neck squamous cell carcinoma; bibliometric analysis; citespace; VOSviewer

Introduction

Head and neck tumors rank as the seventh most prevalent cancer globally [1]. Head and neck squamous cell carcinoma constitute approximately 90% of all head and neck tumor cases, predominantly arising from anatomical regions like the upper respiratory and upper digestive tracts. In the year 2018, there were 890,000 reported new cases and 450,000 deaths worldwide. Alarmingly, the incidence of this cancer type continues to surge, with an estimated 30% increase projected by the year 2030, resulting in around 1.08 million new cases annually [2, 3].

Currently, the treatment approach for head and neck tumors involves multimodal strategies, primarily encompassing surgery, radiotherapy, cytotoxic chemotherapy, and immunotherapy. Immunotherapy has exhibited the ability to identify and control tumor growth; however, tumor cells can still elude recognition and elimination by the immune system [4]. Recent studies have made significant strides in devising novel methodologies to counteract tumor immune evasion [5], resulting in immunotherapies that are less toxic and minimally invasive [6]. Initially employed in patients with recurrent or metastatic head and neck squamous cell carcinoma [7],

immunotherapy has proven transformative in altering the disease trajectory, leading to improved efficacy and enhanced safety [8-11].

Researchers have been continually refining the integration of immunotherapy and chemotherapy, while also conducting numerous clinical trials to explore the use of immunotherapy in early-stage head and neck tumors, including neoadjuvant, concurrent, and adjuvant therapy[6]. Consequently, the optimization of immunotherapy regimens in conjunction with existing treatment modalities, and further exploration of its potential application in head and neck SCC, remains a focal point for current and future studies in the realm of immunization for HNSCC. The study employed bibliometric analysis, specifically collaborative network analysis and literature co-citation analysis [12], to assess the quality of research. By scrutinizing the research profiles of various national institutions and researchers across time, the study generated a knowledge map to depict the evolution of scientific knowledge within the research field [13, 14].

Thus, the primary objective of this study was to examine the literature pertaining to immunization-related research in HNSCC from 1 January 2012 to 31 October 2022. Through the analysis of main characteristics, the study aimed to offer insights into the current status and prevailing trends in these studies.

Materials and methods

Data collection

The Web of Science (WoS) database has gained widespread acceptance among researchers as a highly reliable digital literature resource [15]. It is regarded as the most suitable database for conducting bibliometric analysis. For this study, data collection and analysis were conducted using the Scientific Citation Index Extension (SCI-Expanded) of the Web of Science Core Collection (WoSCC). The utilization of literature from this database ensures the accuracy and credibility of the study's conclusions.

To prevent errors and omissions resulting from continuous updates of the database, the literature search and data download were completed within a single day (10 January 2023) and covered the time span from 1 January 2012 to 31 October 2022. The retrieval formula was set as TS = ("Head and Neck Squamous Cell Carcinoma" OR "Squamous Cell Carcinoma of Head and Neck" OR "HNSCC" OR "SCCHN") AND TS = ("Immune" OR "Immunity" OR "Immunization" OR "Immuno"). Only works and reviews were included, with the exception of non-English literature. The search results were exported in text form, containing the "full-text record and cited literature," and formatted as "clear document." After the detailed literature selection process, 1,744 documents were ultimately analyzed, as depicted in **Figure 1**.

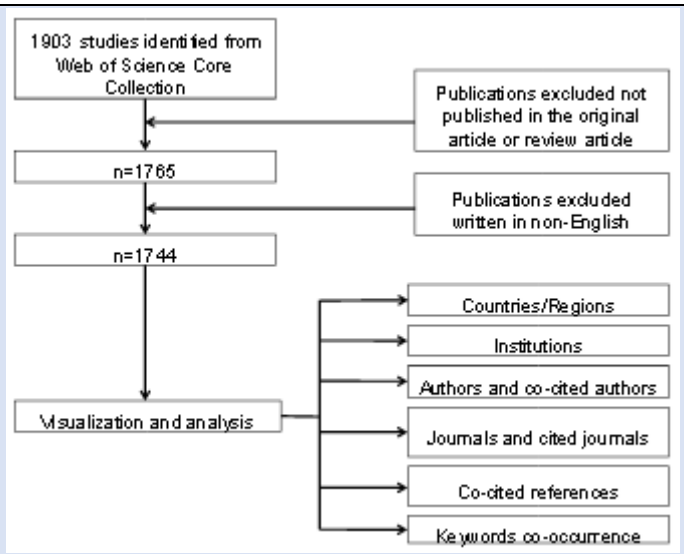

Figure 1: Flow chart of literature screening.

Data analysis and visualization

We conducted a comprehensive analysis of the data obtained from the WoSCC database, which included citation reports and search results. The data encompassed various aspects such as the annual number of publications, annual citations, publications from different countries and institutions, and categories. The information was imported into Microsoft Excel 2019, Tableau Public,

VOSviewer, CiteSpace, and the online bibliometric platform (https://bibliometric.com/) for further examination [16-18].

To process the raw data, Tableau Public, a computer science software developed by Stanford University, was employed to create a world map depicting the distribution of publications. Furthermore, the researchers established a network of national and regional collaborations using an online website (https://bibliometric.com/). These comprehensive analyses allowed for a thorough exploration and visualization of the research data related to the study.

VOS viewer is a software tool designed for the construction and visualization of bibliometric networks [19]. In this study, the researchers utilized VOS viewer to create country/regional, institutional, and author collaboration density maps. For all elements of the VOS viewer analysis, the researchers employed the total counting method, assigning equal weight to all analysis methods. In the country/regional cooperation network map, countries were included only if they had at least 10 articles. Similarly, for the institutional cooperation density map, institutions were considered if they had a minimum of 5 documents. In the author cooperative density map, authors were included if they had at least 5 documents. To optimize the visualization, the researchers set the Layout parameters to Attraction 10, Repulsion 1, and maintained the default values for other parameters. This approach allowed for a clear representation of the collaborative networks and relationships between different countries, institutions, and authors in the field of study.

Cite Space, developed by Professor Chen Chaomei, serves as a valuable tool for visual analysis of academic literature within a specific research field or discipline[20]. In the present study, Cite Space was utilized for several analyses, including national/regional, institutional, and author cooperative network analysis, co-citation analysis (and cluster analysis), journal bi-graph superposition analysis, and keyword co-occurrence analysis, in order to gain a comprehensive understanding of the knowledge structure and research directions within the field[21].The minimum outbreak duration was set at 1 year, covering each year from January 2012 to October 2022. The selection criterion used was the g-index, where k=25. The pruning method employed was Pruning Slice Network, with all other parameters left at their default values. To identify significant focal points within the domain, the researchers manually calculated node centrality by clicking on "calculate node centrality" in the menu. Nodes with centrality values of 0.1 or higher were considered to play a hub role in the network.

In the keyword co-occurrence analysis, the researchers excluded keywords present in the search formula and those that were not closely related to immunity. Synonyms were combined, and keywords that appeared more than 53 times were represented as nodes in the visual analysis.

Result

Publication and citations

After conducting literature screening (**Figure 1**), a total of 1,903 articles were retrieved from the Web of Science Core Collection (WoSCC), out of which 1,744 articles were in English literature. As of 31st October 2022, all the references in these articles were cited a total of 40,995 times, with an average of 23.48 citations per article. The data originated from 57 countries/regions, involved 402 institutions, were published in 408 journals, and credited to 520 authors.

As illustrated in **Figure 2**, there has been a significant surge in both the number of publications and the frequency of citations since 2012. This trend has been particularly prominent after the year 2020, indicating an intensified interest and activity in the field of study during this period.

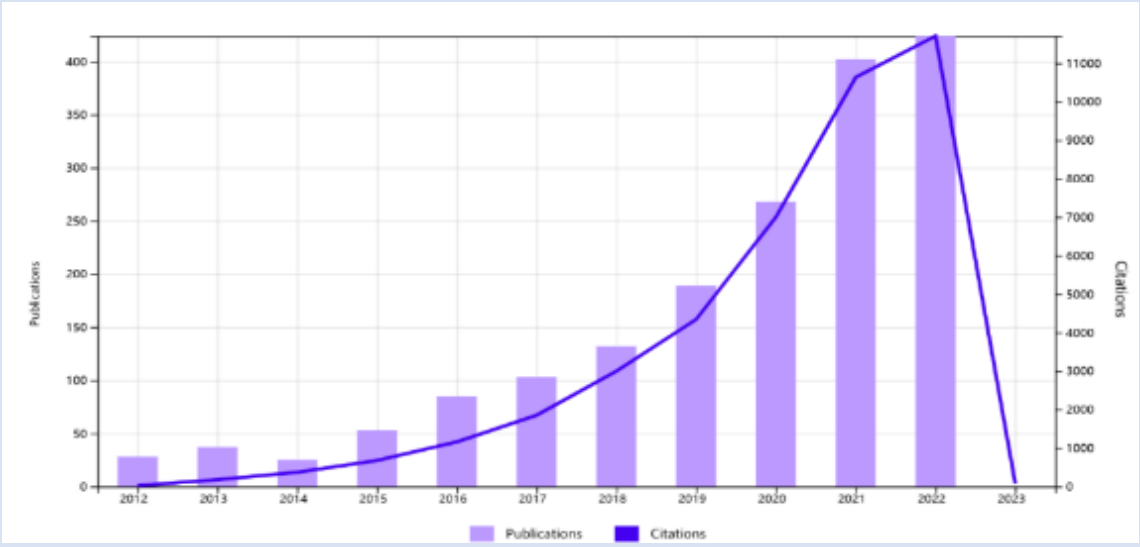

Figure 2: Time distribution map of publication amount and citation frequency.

Country / regional distribution

The studied literature is distributed across 57 countries and regions. **Table 1** presents the top 10 highly productive countries and regions in the field. The United States, China, and Germany stand as the top three countries with the highest contribution.

Table 1: The top 10 high-output countries/regions and institutions.

Rank	Countries/Regions	Number of publications	Centrality	Institution	Number of publications	Centrality
1	USA	623	0.45	Univ Pittsburgh	89	0.17
2	CHINA	608	0.04	Sun Yat Sen Univ	58	0.08
3	GERMANY	196	0.05	Wuhan Univ	49	0.01
4	JAPAN	117	0.1	Univ Michigan	48	0.15
5	ITALY	96	0.15	Shanghai Jiao Tong Univ	38	0.16
6	FRANCE	68	0.09	Harvard Med Sch	34	0.14
7	ENGLAND	66	0.22	Johns Hopkins Univ	33	0.11
8	NETHERLANDS	42	0.04	Cent South Univ	31	0.03
9	CANADA	41	0.05	Dana Farber Canc Inst	30	0.07
10	SOUTH KOREA	39	0	Ohio State Univ	29	0.06

Using Citespace, a visual analysis was performed for each country and region to understand their posting situation and centrality (**Figure 3A**). The node size in the visualization represents the number of publications, while the color of the circle indicates the publication year, with colder colors indicating earlier publications and warmer colors representing more recent publications. The purple outer ring indicates a high centrality, and connections between nodes represent cooperation between countries. The results demonstrated that the United States, Italy, Great Britain, Spain, and Japan hold more central positions in the field.

Furthermore, Cite Space and VOS viewer were employed to analyze and visualize the cooperation between countries (**Figure 3B** and **Figure 3C**). In these visualizations, red indicates high levels of cooperation between countries, and it is evident that the United States, China, and Germany engage in significant collaboration.

Additionally, a time-dependent cooperation network diagram was created using VOS viewer (**Figure 3D**). In this visualization, node size indicates the number of publications, and the color of connections between nodes represents the average time of collaboration. Blue indicates earlier collaborations, while yellow signifies more recent collaborations. Notably, Chinese researchers have demonstrated a heightened involvement in the field, particularly in recent times.

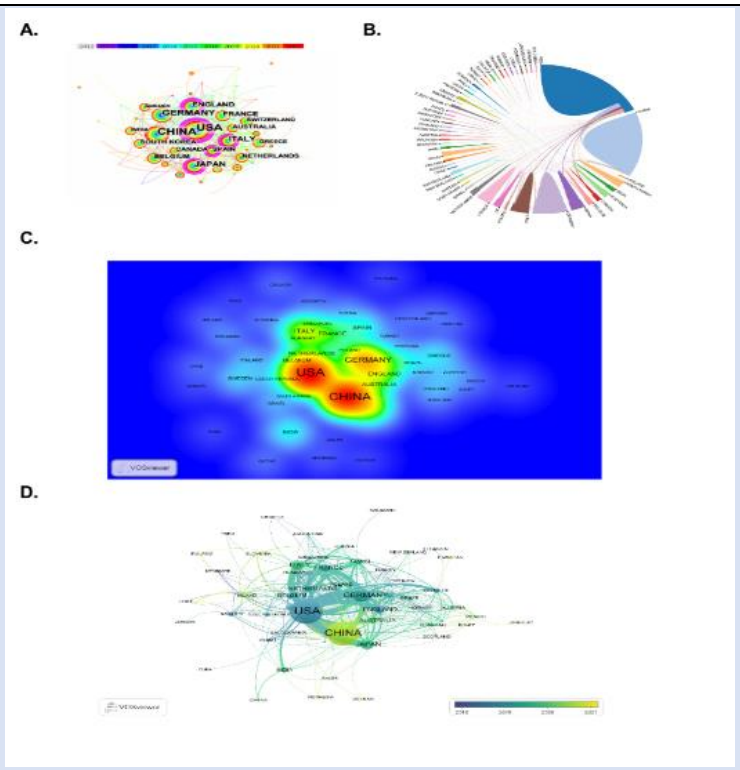

Figure 3: Number of publications and cooperation in each country / region.

(A) The magnitude of the node signifies the volume of publication, while the hue of each node's circular form represents the temporal span of literature published from 2010 to 2022. The cooler tones symbolize the earlier periods, whereas the warmer shades indicate the more recent times. The outermost ring, colored in purple, denotes the realm of scholarly thought, and the interconnection between nodes signifies the collaborative relationships between nations.

(B) Intercontinental collaboration.

(C) International cooperation, with red denoting the intensity of collaboration.

(D) The dimensions of the nodes reflect the quantity of articles published, and the links between nodes signify the partnerships formed. Distinct colors indicate various average years of literature publication. The darker the shade, the greater the volume of published data, whereas the brighter hues indicate a closer proximity of the publication time to the present.

Institutional analysis

A visual analysis of research institutions in the field was conducted, and **Table 1** presents the top 10 research institutions based on the number of publications. The University of Texas MD Anderson Cancer Center holds the highest number of articles (89), followed by Sun Yat-sen University in China (58) and Wuhan University in China (49).

Using Citespace, a visualization of each research institution's centrality was performed (**Figure 4A**). In this visualization, the node size indicates the number of publications, while the color of each circle represents the publication year, with colder colors denoting earlier publications and warmer colors signifying more recent publications. A purple outer ring around a node indicates a high centrality of the institution. This analysis provides valuable insights into the contributions and centrality of various research institutions within the field, showcasing the significance of specific institutions and their involvement over time. The results of the analysis reveal that certain institutions possess higher centrality scores. Univ Pittsburgh has a centrality score of 0.17, followed by Shanghai Jiao Tong Univ with a score of 0.16, Univ Michigan with a score of 0.15, Harvard Med Sch with a score of 0.14, Univ Texas MD Anderson Canc Ctr with a score of 0.12, Johns Hopkins Univ with a score of 0.11, and Univ Chicago with a score of 0.1. These institutions are identified as having high centrality within the field.

Using VOS viewer, the cooperation between institutions was visualized (**Figure 4B**), with red indicating high cooperation intensity. The visualization demonstrates that Univ Pittsburgh, Univ Chicago, Stanford Univ, Dana Farber Canc Inst, Univ Michigan, and several other institutions exhibit a high level of cooperation intensity. Notably, despite

Sun Yat Sen Univ having a large number of published articles, its cooperation intensity is relatively lower.

To depict the time characteristics of the cooperative network, a time-dependent cooperation network diagram was created using VOS viewer (**Figure 4C**). In this visualization, the node size represents the number of publications, and the color of connections between nodes indicates the average time of collaboration. Blue connections represent earlier collaborations, while yellow connections signify collaborations closer to the present time. This analysis provides a deeper understanding of the temporal aspect of collaborative efforts among institutions within the field. Indeed, it is evident that in the recent period of time, Chinese research institutions such as Huazhong University of Science & Technology, Fudan University, Central South University, and Shanghai Jiao Tong University have exhibited a remarkably high level of participation in the field of study. This increased involvement indicates their significant contributions and active engagement in research related to immunity in head and neck tumors. Such high participation from these Chinese institutions plays a crucial role in advancing research progress and fostering international collaborations, leading to a more comprehensive understanding of the field and its advancements.

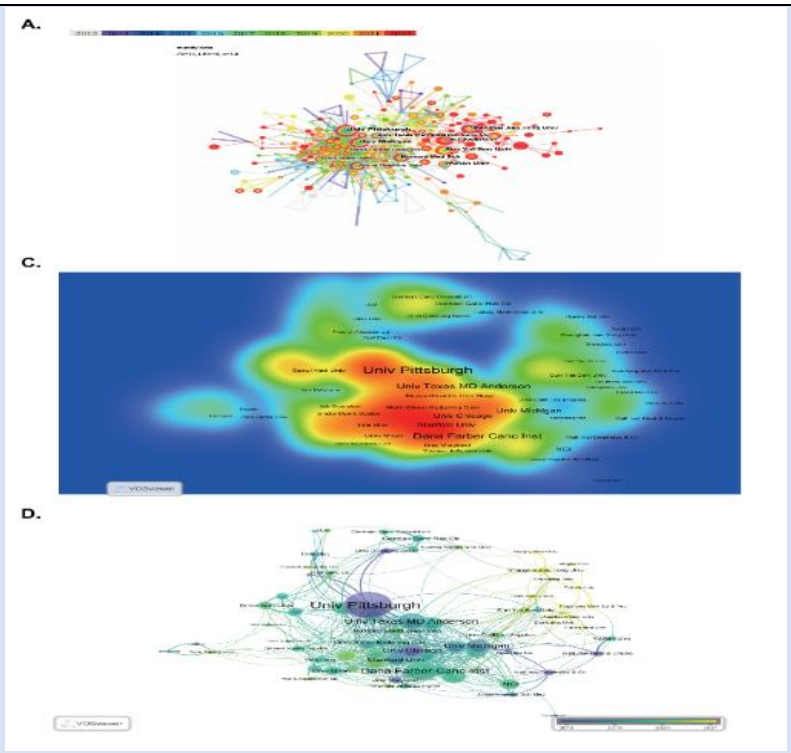

Figure 4: The quantity of published articles and collaborative endeavors among diverse institutions.

(A) The magnitude of the node denotes the volume of publications, while the hue of each node's circular form represents the temporal span of literature published from 2010 to 2022. The cooler tones symbolize the earlier periods, whereas the warmer shades indicate the more recent times. The outermost ring, colored in purple, symbolizes the realm of profound intellect, and the connection between nodes indicates the harmonious relationship between institutions.

(B) Interagency collaboration, with red denoting the intensity of cooperation.

(C) The dimensions of nodes signify the number of articles published, and the links between nodes indicate the partnerships formed. Distinct colors represent various average years of literature publication. The darker the shade, the higher the data, while the brighter hues indicate a closer proximity of the time to the present.

The author analysis

The number of publications by an author can serve as an indicator of their research level and contribution to a specific field. The author cooperative network enables a comparison of the number of collaborations between authors and provides insights into the strength of collaborations [22]. Co-cited authors are those who are jointly cited by two or more papers, forming a co-citation relationship. Analyzing co-cited authors can help identify influential authors in a

specific field and reveal frequently co-cited papers[23].As displayed in **Table 2**, Ferris, Robert L has the highest number of publications in this field (n=53), followed by Sun, Zhi-Jun (n=23), Zhang, Wen-Feng (n=19), Deng, Wei-Wei (n=18), and Uppaluri, Ravindra (n=18).

Table2: The top 10 high-output authors and co-cited authors.

Rank	Author	Number of publications	Centrality	Co-cited Author	Number of co-citations	Centrality
1	Ferris, RobertL	53	0.24	FERRIS RL	730	0.1
2	Sun, Zhi-Jun	23	0	SEIWERT TY	404	0.04
3	Zhang, Wen-Feng	19	0	COHEN EEW	338	0.02
4	Deng, Wei-Wei	18	0	BURTNESS B	332	0.03
5	Uppaluri, Ravindra	18	0.07	VERMORKEN JB	288	0.03
6	Laban, Simon	16	0.07	BRAY F	285	0.02
7	Bu, Lin-Lin	14	0	LAWRENCE MS	258	0.06
8	Licitra, Lisa	14	0.02	LEEMANS CR	256	0.04
9	Mao, Liang	13	0	ANG KK	255	0.04
10	Saba, Nabil F	12	0.03	GILLISON ML	228	0.03

Using Citespace, the post and centrality of each author were visualized (**Figure 5A**). In this visualization, the node size represents the number of publications, while the color of the circle indicates the publication year, with colder colors signifying earlier publications and warmer colors indicating more recent ones. The purple outer ring around a node indicates high centrality, and connections between nodes represent cooperation between scholars. It is evident that Ferris and Robert L have the most publications and the highest centrality in this field.

Furthermore, VOS viewer was employed to visualize the cooperation between scholars (**Figure 5B**). Red color indicates a high cooperation intensity between scholars. The visualization highlights that Ferris, Robert L, Luginbuhl, AM, Sun, Zhi-Jun, Fietkau, Rainer, and other scholars have a high cooperation intensity. To demonstrate the time characteristics of the scholars' cooperation network, a time-dependent cooperation network diagram was created using VOS viewer (**Figure 5C**). In this visualization, node size indicates the number of publications, and the color of connections between nodes represents the time of publication or collaboration. Blue connections indicate earlier collaborations, while yellow connections signify collaborations closer to the present time. It can be observed that Uppaluri, Ravindra, Fietkau, Rainer, Zhu, Gangcai, Wang, Juncheng, Gadwa, Jacob, and other researchers have been more actively engaged in this field recently.

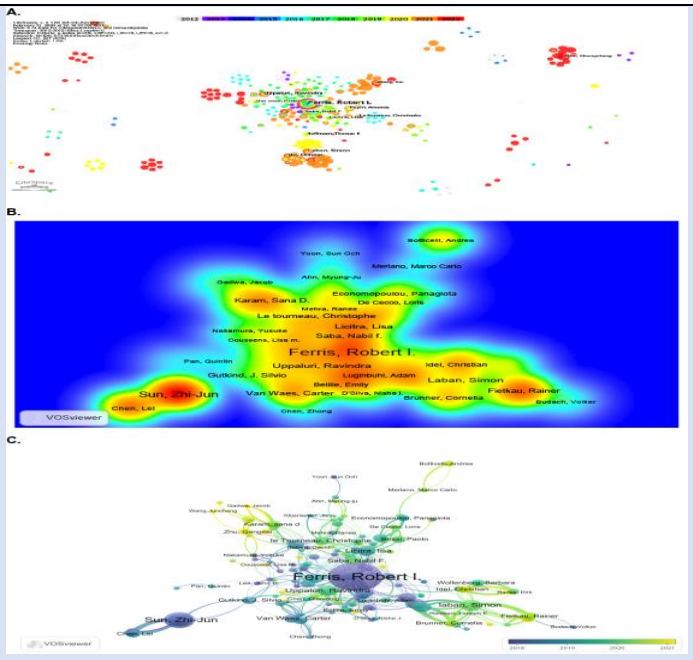

Figure 5: The abundance of scholarly publications and collaboration among erudite minds.

(A) The magnitude of the node symbolizes the volume of publications, and the hue of each node's circular form represents the temporal span of literature published from 2010 to 2022. The cooler tones symbolize the earlier periods, while the warmer shades represent the closer, current time. The purple outer ring embodies the realm of profound intellectualism, and the interconnection between nodes signifies the harmonious relationship between academic institutions.
(B) The scholarly camaraderie, with red denoting the intensity of cooperation.
(C) The dimensions of nodes indicate the number of articles published, and the links between nodes signify the existence of collaboration. Distinct colors reflect various average years of literature publication. The darker the color, the greater the publication data, while the brighter hues suggest a closer proximity of the publication time to the present.

Analysis of journals and cited journals

In our analysis of 1,744 articles, a visual analysis using VOS viewer was conducted to identify the most productive, contributing, and influential journals in the field. The results revealed that these articles were published across 408 academic journals and cited by 855 academic journals. As shown in **Table 3**, the journal "CANCERS" published the most articles in this field (110 articles), with an impact factor of 6.575. It was followed by "FRONTIERS IN ONCOLOGY" (82 articles, Impact factor: 5.732) and "ORAL ONCOLOGY" (77 articles, Impact factor: 5.972).

Table 3: The top 10 high-output journals and cited journals

Rank	Journals	Number of publications	IF	Cited Journals	Number of co-citations	IF/JCR
1	cancers	110	6.575/Q1	CLIN CANCER RES	1193	13.801/Q1
2	frontiers in oncology	82	5.738/Q2	CANCER RES	1176	13.312/Q1
3	oral oncology	77	5.972/Q1	NEW ENGL J MED	1053	176.079/Q1
4	frontiers in immunology	65	8.786/Q1	J CLIN ONCOL	1038	50.717/Q1
5	clinical cancer research	50	13.801/Q1	NATURE	898	69.504/Q1
6	frontiers in genetics	44	4.772/Q1	ORAL ONCOL	893	5.972/Q1
7	oncoimmunology	41	7.723/Q1	INT J CANCER	770	7.316/Q1
8	head and neck-journal for the sciences and specialties of the head and	40	3.821/Q1	NAT REV CANCER	732	69.800/Q1
9	international journal of molecular sciences	38	6.208/Q1	PLOS ONE	725	3.752/Q2
10	journal for immunotherapy of cancer	37	12.469/Q1	LANCET ONCOL	712	54.433/Q1

Regarding citation frequency, "CLINICAL CANCER RESEARCH" received the highest number of citations (cited frequency: 1193 times) and had an impact factor of 13.801. It was followed by "CANCER RESEARCH" (cited frequency: 1,176 times, Impact factor: 13.312), "NEW ENGLAND JOURNAL OF MEDICINE" (citation frequency: 1053 times, Impact factor: 176.079), and "JOURNAL OF CLINICAL ONCOLOGY" (citation frequency: 1038 times, Impact factor: 50.717). These findings highlight the most prominent and influential journals in the field of study, based on the number of publications and citation frequency of the articles analyzed. Among the top 10 journals in terms of the number of publications, 9 of them are in the Q1 division of the Journal Citation Report (JCR 2022). Two of these journals have an impact factor (IF) greater than 10. Specifically, "Clinical Cancer Research" has the highest IF among them with a value of 13.801. Among the 855 cited academic journals, 4 journals have been cited more than 1000 times, and all of them are also located in the JCR 1 area, indicating their high impact and significance in the field.
The dual plot superposition of journal analysis is a visual analysis method used to analyze, compare, and examine the thematic connections between cited and citing journals. This approach introduces a two-plot topic superposition design on a global science map, which allows for the visualization of the distribution of journals across topics, citation links, and central topics for domain-specific research. This method provides valuable insights into the relationships and

thematic connections between journals and helps researchers understand the knowledge structure and impact of journals in a specific research domain [16, 24]. **Figure 6** represents a superposition of the publications of HNSCC papers related to immunity from 2012 to 2022. The left side of the figure shows the reference map, while the right side shows the citation map. Each colored curve is drawn from a theme in the reference graph, pointing to a topic in the citation graph. These curves have the same starting point and the same foothold point, resulting in intersections. The color of the curve represents different categories, and the thickness of the curve indicates the strength of the reference relationship between the two subjects.

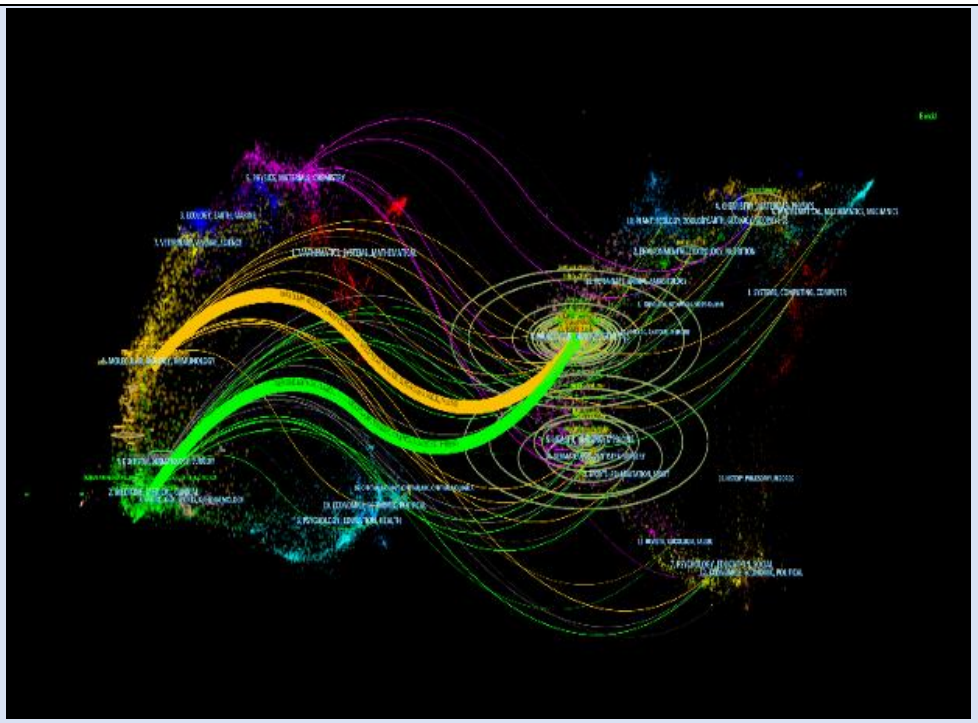

Figure 6: An analysis of the journal through dual-plot superposition. On the left and right sides are the referenced journals, and the colored paths represent the intricate web of citation relationships.

The analysis in **Figure 6** reveals that papers published in journals related to molecular/biology/genetics are classified as being related to molecular/biology/immunology and medicine/medical/clinical. This suggests that there is a thematic link between papers focusing on molecular biology, genetics, and those dealing with immunology and clinical medicine within the context of HNSCC and immunity research. The superposition visualization helps identify the connections and relationships between different themes and categories, providing a more comprehensive understanding of the knowledge structure and thematic links within the domain of HNSCC papers on immunity.

Co-cited authors and co-cited literature were analyzed

In our analysis of the references of 1,744 articles and the authors, we found that 873 scholars met the conditions for total citation, and 943 documents met the conditions for total citation. **Table 2** presents the number of co-citations and centrality of the top 10 co-cited authors. Ferris, Robert L is the most co-cited author with 730 co-citations, followed by SEIWERT TY with 404 co-citations, and COHEN EEW with 338 co-citations. Ferris, Robert L is also the only co-cited author with a centrality of 0.1, indicating their significant influence in the co-citation network.

To visualize the co-citation relationships among the co-cited authors, Citespace was used (**Figure 7A**). In this visualization, the node size represents the total co-citation frequency of the co-cited authors, and the colors in each circle of the nodes indicate the publication period of the literature from 2010 to 2022. Colder colors represent earlier times, while warmer colors represent more recent times. Lines between nodes represent the presence of co-citation relationships between co-cited authors. Cold color lines indicate co-citation mainly occurring in the early period, while warm color lines indicate co-citation occurring in the near future. **Figure 7B** emphasizes

the co-citation case of Ferris, Robert L, providing a detailed view of their co-citation relationships. **Table 4** lists the top 10 co-cited references, shedding light on the most influential and frequently co-cited papers within the field of study.

Table 4: The top 10 co-cited papers

Rank	DOI	Number of co-citations	IF/JCR
1	10.1056/NEJMoa1602252	437	176.079/Q1
2	10.1016/S0140-6736(19)32591-7	287	202.731/Q1
3	10.3322/caac.21492	282	286.130/Q1
4	10.1016/S1470-2045(16)30066-3	258	54.433/Q1
5	10.1016/S0140-6736(18)31999-8	221	202.731/Q1
6	10.1172/jci.insight.89829	153	1.095/Q4
7	10.1016/j.oraloncology.2018.04.008	153	5.972/Q1
8	10.1038/nature14129	152	69.504/Q1
9	10.1200/JCO.2016.70.1524	132	50.717/Q1
10	10.1038/s41572-020-00224-3	128	65.038/Q1

The most cited articles in the field of HNSCC and immunization studies are "Nivolumab for Recurrent Squamous-Cell Carcinoma of the Head and Neck" with the first author being Ferris RL, which has received a total of 437 citations. The second most cited article is "Pembrolizumab alone or with chemotherapy versus cetuximab with chemotherapy for recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-048): a randomised, open-label, phase 3 study" with the first author being Burtness B, which has received a total of 287 citations.

Out of the top 10 articles, nine are listed in the Journal Citation Report (JCR) and belong to the Q1 category, indicating that the co-cited literature in HNSCC and immunization studies is of high quality and holds significant influence in the academic community. Notably, Ferris RL has contributed 2 out of the top 10 cited articles. One of the articles was published in the prestigious New England Journal of Medicine (Q1, IF: 176.079), while the other article was published in ORAL ONCOLOGY (Q1, IF: 5.972). In **Figure 7C**, we visualized the results of the co-citation analysis using Citespace software. The node size indicates the co-citation frequency, and the colors in each circle of the nodes represent the time period from 2010 to 2022. Cooler colors represent earlier times, while warmer colors represent more recent times. The lines between nodes represent two documents being co-cited, and the thickness of the connection indicates the co-citation intensity. The color of the connecting lines represents the average time of the co-cited relationship between the two articles. Cold colors indicate earlier co-citation relationships, while warm colors indicate more recent co-citation relationships.

We utilized Cite Space to perform the keyword clustering analysis of the co-cited literature (**Figure 7D**). Keyword topic classification results include "ctla-4"(cluster #0),"cuproptosis"(cluster #1),"prognosis"(cluster #2)," metastatic"(cluster #3),"tumor-infiltrating lymphocytes"(cluster #4),"radiotherapy"(cluster #5),"premalignant oral lesions"(cluster #6),"premalignant"(cluster #7),"exosomes"(cluster #8),"nivolumab"(cluster #9) and "warburg effect"(cluster #10);Subject classification results include "oncology"(cluster #0),"dentistry,oral surgery & medicine"(cluster #1),"genetics&heredity"(cluster #2),"otorhinolaryngology"(cluster #3),"pharmacology&pharmacy"(cluster #4),"medicine,general&internal"(cluster #5),"multidisciplinary sciences"(cluster #6),"immunology"(cluster #7),"transplantation"(cluster #8),"biochemistry&molecular biology"(cluster #9) and "pathology"(cluster #10).Lastly, we utilized Cite Space to display the keywords of co-cited literature categorized by topic classification, aiming to explore further research trends (**Figure 7F**). The analysis revealed that the research hotspots have gradually shifted from topics such as "premalignant," "warburg effect," and "ctla-4" to newer areas of interest, including "cupropotosis," "prognosis," "metastatic," "exosomes," "radiotherapy," and "tumor-infiltrating lymphocytes."

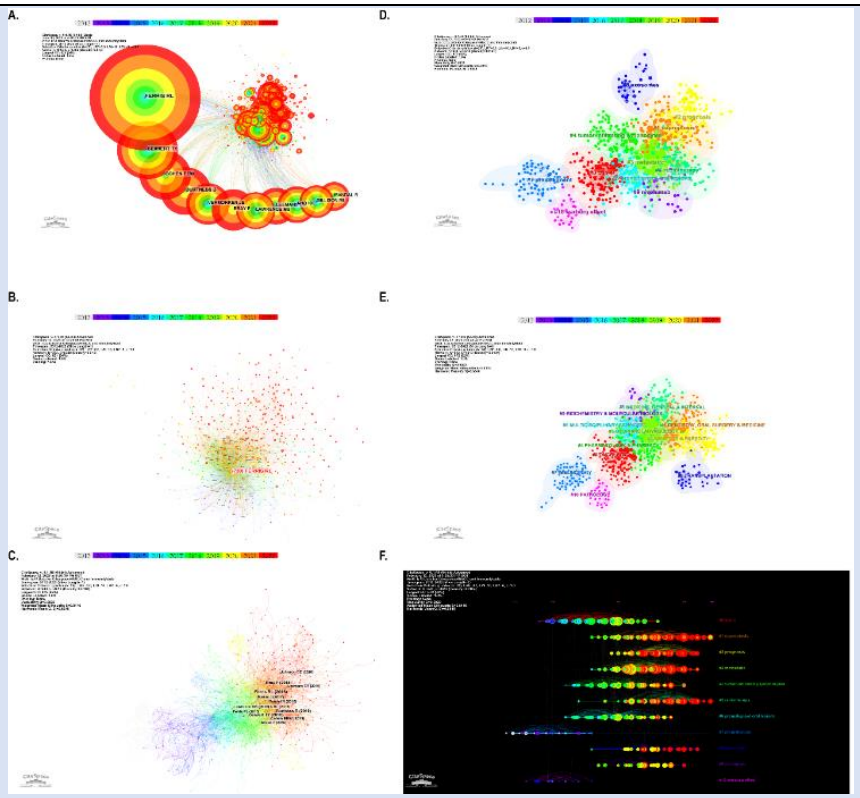

Figure 7: Analysis of the interwoven co-citation relationships among esteemed authors and their shared literary works.

(A) The size of each node signifies the total frequency of citations for a particular author, while the color of the circular nodes represents the temporal span of literature published from 2010 to 2022. The cooler tones denote earlier times, whereas the warmer hues indicate a closer proximity to the present. The lines connecting the nodes symbolize the existence of citation relationships between the authors. Cold lines predominantly occurred in the early days, whereas warm lines emerged from more recent citations between the authors.

(B) The co-citation scenario involving the distinguished Ferris, Robert L.

(C) The size of each node corresponds to its cited frequency, and the color of the circles represents the temporal span of literature published from 2010 to 2022. The cooler shades signify earlier publications, while the warmer tones indicate more recent works. The connections between nodes signify the citation relationships between two literary works, with the thickness of the connection representing the intensity of citations. The color of the connection indicates the average time of the cited relationship, with colder shades suggesting an earlier relationship and warmer shades denoting a more recent citation association.

(D) Subject categorization based on the keywords of the co-cited literature.

(E) Subject classification based on the thematic content of the co-cited literature.

(F) A chronological display of the keywords of the co-cited literature, organized according to their themes.

Keyword co-occurrence analysis

Keywords serve as eloquent vessels of standardized terms, elegantly expressing the essence of literature, while facilitating its preservation and dissemination[25]. Within the realm of scholarly exploration, these luminous keywords unlock the secrets of research frontiers and hotspots. Our celestial endeavor involved employing the Citespace software to illuminate the collective keywords, including the ethereal author-provided expressions, extracted from the ethereal tapestry of 1744 articles. After delicate curation and classification, we unveiled 327 clusters of celestial keywords, among which 10 were conjoined more than 90 times. As evidenced by **Table 5**, illustrious terms like "open label" (n=208), "t cell" (n=200), "immunotherapy" (n=185), and "tumor microenvironment" (n=160) shone brightly with their frequent appearances. Subsequently, we embarked on a wondrous journey of keyword co-occurrence analysis, gazing upon the structure visualization **(Figure 8)** where each node bore the radiant mark of co-occurrence frequency, adorned with hues that spanned the celestial timeline from 2010 to 2022. The cooler shades representing earlier epochs, and the warm, captivating tones denoting closer proximity to the present moment. The ethereal connections

between nodes symbolized the harmonious co-occurrence relationships between these celestial keywords. It became evident that "t-cells," "regulatory t cell," and other ethereal expressions had graced the scholarly cosmos with their early co-occurrence, while "tumor environment," "open label," "immunetherapy," "immune checkpoint inhibitor," "pembrolizumab," "nivolumab," and their celestial peers shimmered in recent years. Though "immune infiltration" (n=26), "prognostic signature" (n=18), "prognostic factor" (n=14), and "durvalumab" (n=11) appeared with modest frequency, they, too, unveiled their brilliance in the celestial dance of co-occurrence after the majestic year of 2021.

Table 5: The top 20 co-occurred keywords

Rank	Keywords	Number of occurrences	Rank	Keywords	Number of occurrences
1	open label	208	11	dendritic cell	70
2	t cell	200	12	Immune response	63
3	immunotherapy	185	13	blockade	62
4	tumor microenvironment	160	14	inhibition	55
5	nivolumab	141	15	multicenter	54
6	regulatory t cell	130	16	immune checkpoint	54
7	pembrolizumab	127	17	metastatic head	53
8	Immune checkpoint inhibitor	101	18	identification	53
9	cetuximab	95	19	growth factor receptor	53
10	tumor infiltrating lymphocyte	93	20	lymphocyte	53

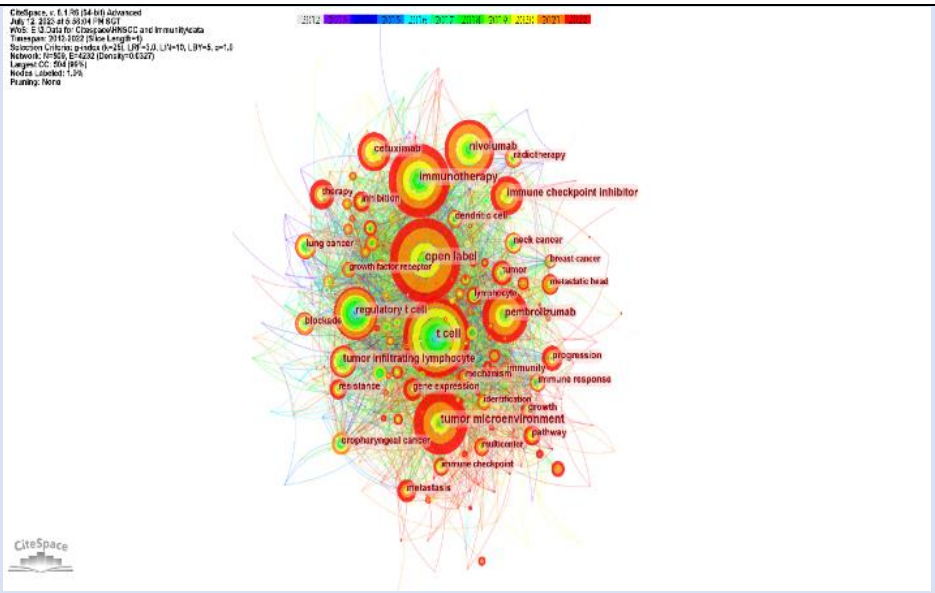

Figure 8: Keyword co-occurrence exploration. The magnitude of nodes signifies the degree and recurrence of co-occurrence. The hue of each circle represents the extant keywords spanning from 2010 to 2022, with cooler tones denoting earlier occurrences and warmer shades indicating a closer proximity to the present. The interconnection between nodes embodies the co-occurrence relationship between the respective keywords.

Discussion

In head and neck squamous carcinoma (HNSCC), the primary mechanism underlying tumor recurrence or metastasis lies in the interplay between PD-L1 on the surface of CD8 T lymphocytes and PD-1. This interaction weakens the cytolytic activity of CD8 T cells against tumor cells, subsequently suppressing the immune system's ability to eliminate cancer cells, leading to immune escape. Notably, immunotherapeutic approaches for HNSCC, such as nivolumab and pembrolizumab, both immune checkpoint inhibitors, are humanized IgG4 antibodies targeting programmed cell death 1 (PD-1). These agents are particularly effective for patients expressing PD-L1, as they modulate the immune

response to cancer. In 2016, they were approved for the treatment of platinum-refractory recurrent and metastatic HNSCC [7, 10, 26].Recent years have witnessed significant advances in verifying the immunogenicity of HNSCC and the development of related immunosuppressive agents. These novel agents boast low toxicity and invasiveness while demonstrating superior efficacy[6, 8-11]. Consequently, it is essential to comprehend the present state of HNSCC research within the realm of immunity over the past decade and delve into further in-depth analysis.

Based on the current research landscape of HNSCC and its immune aspects over the last decade, we embarked on a bibliometric analysis to explore the knowledge base and structural dynamics within this domain. Employing the cutting-edge tools of Citespace and VOSviewer, we artfully evaluated the collaborative network map encompassing countries, institutions, and authors. In addition, through the analysis of the journal co-citation graph, we discerned the trajectory of knowledge transfer within the subject area. Lastly, the literature co-citation and keyword co-occurrence analyses allowed us to unravel the knowledge base, structural elements, and research hotspots pertaining to the role of immunity in HNSCC.

Over the past 11 years, HNSCC and immune-related research have gained ever-increasing academic attention, manifesting a remarkable surge in the past four years. In his seminal work, American sociologist Freeman L. (Freeman, 1979) proposed the concept of "number centrality" (betweenness centrality) as a metric to gauge the centrality of a node relative to others in a graph. This measure primarily assesses the bridge function of a node within the entire network structure, thus evaluating its influential position among the set of nodes [27, 28].

Henceforth, the United States, China, and Germany have ascended as the top three prolific nations. From our data analysis, it emerges that the United States holds the highest centrality. Following the United States, the United Kingdom, Italy, Japan, and Spain shine on the stage of significance. However, China, despite securing the second position in the number of publications, lacks centrality, possibly due to the plethora of standalone publications in the country.

Delving deeper into the scientific contributions and collaborative network map, we find that among the top ten institutions in terms of publications, six hail from the United States and four from China. The University of Pittsburgh in the United States embarked on research early on, boasting the highest number of publications (n=89), and exhibiting profound collaborations with diverse institutions, thus radiating its strong centrality (c=0.17). Similarly, Shanghai Jiao Tong University, despite ranking fifth in the number of articles (38), exhibits commendable centrality (c=0.16). In contrast, Sun Yat-sen University from China possesses the second-highest number of publications (58), but its research centrality remains relatively low (c=0.08). To enhance its collaborative ties with other institutions worldwide, fostering cooperation would be judicious.

Shifting our gaze to the scientific contributions and cooperative network map, we discern that Ferris and Robert L occupy the forefront with the largest number of posts (n=53), followed by Sun, Zhi-Jun (n=23), Zhang, Wen-Feng (n=19), Deng, Wei-Wei (n=18), and Uppaluri, Ravindra (n=18). However, among these five esteemed authors, only Ferris, Robert L commands a centrality value greater than 0.1 (c=0.24), emblematic of their research's bridging effect and significant influence across the field. The high quality of their work and their emphasis on cooperation with others contribute to this distinction. On the contrary, the remaining four authors exhibit low centrality, indicative of their relatively independent stance, possibly lacking in communication and cooperation.

An interesting observation is the notable centrality (c=0.1) of Thomas K. Hoffmann, despite not being within the top five in terms of publications. Such high centrality reflects the constructive impact and influence of his research on related investigations across the entire research landscape. Our investigation has illuminated that the top 10 most active journals account for approximately one-third (31.32%) of the total publications in this domain, indicating a notable concentration of research endeavors within this cluster. Notably, the journal "CANCERS" takes the lead with the highest number of publications (110), while "CLIN CANCER RES" emerges as the most cited, as corroborated by the double graph superposition analysis. This recurrent citation pattern pertains to papers published in journals classified under the purview of molecular/biology/genetics and molecular/biology/immunology/medicine/medical/clinical, accentuating the prevailing research focus on the molecular biology and clinical medicine aspects of immunity in HNSCC.

Of noteworthy significance, the majority of journals within the top 10 rankings for both publications (80%) and citations (90%) boast an impressive impact factor (IF> 5). Such a trend underscores the substantial academic contributions and research achievements associated with these journals. Moreover, it serves as a testament to the elevated research quality in the realm of HNSCC immune-related investigations. The analysis of co-cited authors unveils influential figures within specific fields and brings to light their frequently co-cited papers[23]. Among all the co-cited authors, two luminaries have garnered over 400 citations each: FERRIS RL (n=730) and SEIWERT TY (n=404). However, upon closer examination, it becomes apparent that only FERRIS RL enjoys a high centrality (c=0.1). FERRIS RL and his team are actively engaged in unraveling the roles of immunosuppressive molecules, such as immune checkpoint receptors like PD-1[29-32], CTLA-4[33], and TIM-3[34-37], as well as investigating the intricacies of the immune microenvironment in personalized cancer immunotherapy[38-40]. In parallel, they keenly focus on the clinical application of immunization in HNSCC[8, 26, 41, 42]. Notably, alongside conducting relevant clinical trials, FERRIS RL provides consensus suggestions for emerging immunotherapy[43], thereby not only enlightening clinicians on the potential of immunotherapy in HNSCC but also contributing to the standardization of immunotherapeutic approaches in this domain. Our co-cited literature analysis reveals the remarkable frequency of citations for FERRIS RL papers within this research domain, a fact further substantiated by the co-cited author analysis. Through literature co-citation analysis, we have successfully identified the most influential works in immune-related studies of HNSCC[44]. Among the top 10 cited articles, two notable ones, authored by Ferris and Robert L, stand as randomized clinical studies investigating the effects of navuzumab in the treatment of HNSCC[8, 26].Simultaneously, the chronicle presentation of the topic classification within the co-cited literature aids us in gaining a deeper understanding of the research trends (**Figure 7F**). Evidently, the research focal points have undergone a gradual shift, evolving from "premalignant" and "warburg effect" to encompass "cupropotosis", "prognosis", "metastatic", "radiotherapy", "exosomes", "tumor-infiltrating lymphocytes", and other intriguing facets. Our quest for knowledge continues as we delve into the research hotspots and frontiers of HNSCC immunity through keyword co-occurrence analysis. This analysis represents a profound extension and expansion of the aforementioned hotspots. Unlike co-citation analysis, keyword co-occurrence analysis unveils novel terminologies that may emerge as hotspots in future research endeavors.

The keywords "open label" (n=208), "t cell" (n=200), "t cell" (n = 200), "immunotherapy" (n=185), and "tumor microenvironment" (n=160) have emerged as prominent focal points in the realm of research. The co-occurrence of terms such as "t-cells" and "regulatory t cell" signifies their early prominence, indicating that they were the subjects of intense investigation in the initial stages. On the other hand, keywords like "tumor microenvironment", "open label", "immunotherapy", "immune checkpoint inhibitor", "pembrolizumab", and "nivolumab" have prominently emerged in recent years, suggesting their significance as potential future research areas. Furthermore, while the keywords "immune infiltration" (n=26), "prognostic signature" (n=18), "prognostic factor" (n=14), and "durvalumab" (n=11) exhibit a lower frequency of co-occurrence, they have gained considerable traction after the year 2021.

The fundamental constituents comprising the Tumor Microenvironment (TME) in Head and Neck Squamous Cell Carcinoma (HNSCC) encompass an array of intricate cellular elements, including immune cells, fibroblasts, mesenchymal cells, hematopoietic and bone marrow-derived cells, vascular endothelial cells, and nerves[45, 46]. Notably, among these cellular components, T cells occupy a position of paramount significance within the TME. They primarily consist of CD4 and CD8 T lymphocytes, each with unique roles, wherein CD4 T cells exhibit the potential for further differentiation into regulatory T (Treg) and helper T (Th) cells. Of particular importance, cytotoxic CD8 T lymphocytes, endowed with the remarkable ability to recognize and dismantle tumor cells, play a pivotal role in exerting profound antitumor activities [47].

Th cells, through their orchestration of intricate molecular interactions, serve as potent promoters of the anti-tumor prowess exhibited by CD8 T cells, bestowing upon them a harmonious synergy in their mission against malignancy [48]. On the other hand, Treg cells, though wielding their own significance, present a contrasting role as they manifest an inhibitory influence on the immune response within the Tumor Microenvironment (TME).In the intricately woven fabric of the TME, immune

checkpoint receptors emerge as pivotal players, holding the delicate balance between controlling the immune system, curbing autoimmunity, and finely regulating the inflammatory responses. Remarkably, the activation of immune checkpoint receptors on CD8 T cells exerts a multifaceted impact, tempering their potent tumor-inhibitory capabilities [49-51].

At present, LAG-3, CTLA-4, TIM-3, and PD-1 stand as eminent immune checkpoint receptors, gracefully gracing the surface of CD8 T cells. The enchanting interplay of PD1/PDL1 has been the focus of in-depth investigations in the realm of HNSCC. Admirably, navulumumab and pabolizumab, enchanting as the most studied immune checkpoint inhibitors, embark on a profound journey, targeting the exquisite PD/PD-L1 pathway. Alas, as they navigate this path, they unravel the delicate balance within CD8 T cells, evoking both admiration and concern, as they bestow upon them the gift of hyperactivation, which at once infuses them with profound potential and yet, at the same time, gently attenuates their anti-tumor ardor [52].In the realm of immune cells, LAG-3 takes its place with dignity and grace, adorning the noble NK cells, the esteemed CD4 and CD8 T lymphocytes, the virtuous B lymphocytes, and the wise DC. The expression of LAG-3 on Treg is a symphony of elegance, elevating their function to greater heights, while the gentle act of blocking its expression, like a soft breeze, gently diminishes Treg numbers, allowing the radiant CD8 T cells to ascend in their splendor and embrace the stage of enhanced antitumor effects [53].In the realm of immune cells, TIM-3 graces the NK cells and T lymphocytes with its presence. In the captivating AML mouse model, the union of CD M-3 with PD-1 [54] accentuated the presence of CD8 T cells, bearing the hallmarks of PD-1 and TIM-3, in HNSCC patients undergoing cetuximab monotherapy. Alas, this union seemed to cast a shadow upon the efficacy of cetuximab treatment, perhaps stemming from the subtle induction of immune tolerance [55].In the days to come, the limelight shall continue to grace the PD-1 / PD-L1 pathway, along with its companion immune checkpoint inhibitors [56]. The union of immune checkpoint inhibitors with chemotherapy, radiotherapy, and surgical interventions in clinical research shall gain ever-increasing popularity [57]. Moreover, the quest for hitherto undiscovered immune checkpoints and their translation from fundamental research to clinical practice shall emerge as a scintillating hotspot within this domain. Nonetheless, as chemotherapy and immunotherapy exert their influence on the tumor microenvironment, a more profound investigation of the TME shall be required to elucidate the intricate biological landscape of HNSCC. In this vein, I anticipate that exploring the TME shall serve as one of the frontiers and hotspots in the future of HNSCC immunization research [58].

Conclusion

This study presents a comprehensive exposition of HNSCC research in the realm of immunity through the artful utilization of bibliometric and visualization methods. By harnessing the power of CiteSpace and VOSviewer, we delve deeper into the current panorama, evolutionary trajectories, cutting-edge hotspots, and forthcoming trends in HNSCC as of October 31, 2022. Immunization, without a doubt, assumes a pivotal role in the treatment of HNSCC. At the forefront of this research domain, we find eminent countries such as the United States and China, both steering the course of knowledge. Notably, FERRIS RL stands as an illustrious academic pioneer in this field, and the research terrain resonates predominantly with the realms of molecular biology and clinical medicine. As we peer into the future, the research directions unfurl toward "tumor microenvironment," "immune checkpoint inhibitors," "pembrolizumab," and "nivolumab," hinting at their imminent prominence in the tapestry of forthcoming investigations. This profound inquiry imparts invaluable insights to investigators, enlightening them on the structural fabric and developmental odyssey of HNSCC research in the realm of immunity, while offering dynamic cues tethered to the passage of time.

Declarations

All authors disclosed no relevant relationships. Our article does not contain any studies involving human or animal participants.

Ethics approval and consent to participate

We had obtained ethical approval from the ethics committee.

Consent for publication

Not applicable.

Availability of data and materials

All data that support the findings of this study are available from the corresponding authors **upon** reasonable request.

Conflict of Interest

The authors declare that they have no conflict of interest.

Funding

Not applicable.

Authors' contributions

RM, JL conceptualized the project, all data analysis. WM contributed to guide the data analysis, and manuscript writing.

Acknowledgements

We would like show sincere appreciation to the editors and reviewers for critical comments on this article.

References

1. Mehanna H, Paleri V, West CM, Nutting C. (2010). Head and neck cancer--Part 1: Epidemiology, presentation, and prevention. *BMJ*, 341:c4684.
2. Ferlay J, Colombet M, Soerjomataram I, Mathers C, Parkin DM, Pineros M, et al. (2019). Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. *Int J Cancer,* 144(8):1941-1953.
3. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. (2018). Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin., 68(6):394-424.
4. Drake CG, Jaffee E, Pardoll DM. (2006). Mechanisms of immune evasion by tumors. *Adv Immunol*, 90:51-81.
5. Yang Y. Cancer immunotherapy: harnessing the immune system to battle cancer. J Clin Invest. (2015). 125(9):3335-3337.
6. Chow LQM. (2020). Head and Neck Cancer. *N Engl J Med.*, 382(1):60-72.
7. Jia L, Zhang Q, Zhang R. (2018). PD-1/PD-L1 pathway blockade works as an effective and practical therapy for cancer immunotherapy. *Cancer Biol Med.,* 15(2):116-123.
8. Ferris RL, Blumenschein G, Jr., Fayette J, Guigay J, Colevas AD, et al. (2018). Nivolumab vs investigator's choice in recurrent or metastatic squamous cell carcinoma of the head and neck: 2-year long-term survival update of CheckMate 141 with analyses by tumor PD-L1 expression. *Oral Oncol.,* 81:45-51.
9. Cohen EEW, Soulieres D, Le Tourneau C, Dinis J, Licitra L. et al. (2019). Pembrolizumab versus methotrexate, docetaxel, or cetuximab for recurrent or metastatic head-and-neck squamous cell carcinoma (KEYNOTE-040): a randomised, open-label, phase 3 study. *Lancet,* 393(10167):156-167.
10. Seiwert TY, Burtness B, Mehra R, Weiss J, Berger R. et al. (2016). Safety and clinical activity of pembrolizumab for treatment of recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-012): an open-label, multicentre, phase 1b trial. *Lancet Oncol.*, 17(7):956-965.
11. Burtness B, Harrington KJ, Greil R, Soulieres D, Tahara M. et al. (2019). Pembrolizumab alone or with chemotherapy versus cetuximab with chemotherapy for recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-048): a randomised, open-label, phase 3 study. *Lancet,* 394(10212):1915-1928.
12. Zhang R, Qi S, Dai W, Chen S, Zhang Y, Tian W, et al. (2021). Publication trends and hotspots in enhanced recovery after surgery: 20-year bibliometric analysis. *Br J Surg,* 108(2):e62-e64.
13. Teles RHG, Moralles HF, Cominetti MR. (2018). Global trends in nanomedicine research on triple negative breast cancer: a bibliometric analysis. *Int J Nanomedicine*, 13:2321-2336.
14. Paniagua Cruz A, Zhu KY, Ellimoottil C, Dauw CA, Sarma A, Skolarus TA. (2020). Characterizing the Benign Prostatic Hyperplasia Literature: A Bibliometric Analysis. *Urology,* 136:202-211.
15. Daugherty A, Hegele RA, Lu HS, Mackman N, Rader DJ, Weber C. (2022). Web of Science's Citation Median Metrics Overcome the Major Constraints of the Journal Impact Factor. *Arterioscler Thromb Vasc Biol.* 42(4):367-371.
16. Qin YF, Ren SH, Shao B, Qin H, Wang HD, Li GM, et al. (2022). The intellectual base and research fronts of IL-37: A bibliometric review of the literature from WoSCC. *Front Immunol,* 13:931783.
17. Xie X, Lei P, Liu L, Hu J, Liang P. (2022). Research trends and hotspots of COVID-19 impact on sexual function: A bibliometric analysis based on Web of Science. *Front Public Health*, 10:976582.
18. Chen L, Liu Y, Cai J, Ji Z, Zou J, Chen Y, et al. (2022). Global Trends in Research of Androgen Receptor Associated with Breast Cancer From 2011 to 2020: A Scientometric Analysis. *Front*

Endocrinol (Lausanne), 13:887612.
19. van Eck NJ, Waltman L. (2010). Software survey: VOSviewer, a computer program for bibliometric mapping. Scientometrics, 84(2):523-538.
20. Chen C. (2004). Searching for intellectual turning points: progressive knowledge domain visualization. Proc Natl Acad Sci U S A., 101(1):5303-5310.
21. Baminiwatta A, Solangaarachchi I. (2021). Trends and Developments in Mindfulness Research over 55 Years: A Bibliometric Analysis of Publications Indexed in Web of Science. *Mindfulness (N Y),* 12(9):2099-20116.
22. Yang Q, Yang D, Li P, Liang S, Zhang Z. (2021). A Bibliometric and Visual Analysis of Global Community Resilience Research. *Int J Environ Res Public Health*, 18(20).
23. Cheng P, Tang H, Dong Y, Liu K, Jiang P, Liu Y. (2021). Knowledge Mapping of Research on Land Use Change and Food Security: A Visual Analysis Using CiteSpace and VOSviewer. *Int J Environ Res Public Health*, 18(24).
24. Du Z, Wang T. (2023). Knowledge domain and dynamic patterns in multimodal molecular imaging from 2012 to 2021: A visual bibliometric analysis. *Medicine (Baltimore),* 102(4):e32780.
25. Demir N, Ekin N, Torgutalp M, Wahlin S, Efe C. (2020). Two decades of research on autoimmune liver disease in Turkey. *Turk J Gastroenterol*, 31(12):877-882.
26. Ferris RL, Blumenschein G, Jr., Fayette J, Guigay J, Colevas AD. et al. (2016). Nivolumab for Recurrent Squamous-Cell Carcinoma of the Head and Neck. *N Engl J Med.* 375(19):1856-1867.
27. Fronzetti Colladon A, Naldi M. (2020). Distinctiveness centrality in social networks. *PLoS One,* 15(5):e0233276.
28. Ryan D, Emond M, Lamontagne ME. (2014). Social network analysis as a metric for the development of an interdisciplinary, inter-organizational research team. *J Interprof Care*, 28(1):28-33.
29. Li J, Jie HB, Lei Y, Gildener-Leapman N, Trivedi S, Green T, et al. (2015). PD-1/SHP-2 inhibits Tc1/Th1 phenotypic responses and the activation of T cells in the tumor microenvironment. *Cancer Res,* 75(3):508-518.
30. Overacre-Delgoffe AE, Chikina M, Dadey RE, Yano H, Brunazzi EA, Shayan G, et al. Interferon-gamma Drives T(reg) Fragility to Promote Anti-tumor Immunity. Cell. (2017). 169(6):1130-41 e11.
31. Zandberg DP, Menk AV, Velez M, Normolle D, DePeaux K, Liu A, et al. (2021). Tumor hypoxia is associated with resistance to PD-1 blockade in squamous cell carcinoma of the head and neck. *J Immunother Cancer,* 9(5).
32. Kikuchi M, Clump DA, Srivastava RM, Sun L, Zeng D. et al. (2017). Preclinical immunoPET/CT imaging using Zr-89-labeled anti-PD-L1 monoclonal antibody for assessing radiation-induced PD-L1 upregulation in head and neck cancer and melanoma. *Oncoimmunology*, 6(7):e1329071.
33. Jie HB, Schuler PJ, Lee SC, Srivastava RM, Argiris A. et al. (2015). CTLA-4(+) Regulatory T Cells Increased in Cetuximab-Treated Head and Neck Cancer Patients Suppress NK Cell Cytotoxicity and Correlate with Poor Prognosis. *Cancer Res*, 75(11):2200-2210.
34. Ferris RL, Lu B, Kane LP. (2014). Too much of a good thing? Tim-3 and TCR signaling in T cell exhaustion. *J Immunol*, 193(4):1525-1530.
35. Shayan G, Srivastava R, Li J, Schmitt N, Kane LP, Ferris RL. (2017). Adaptive resistance to anti-PD1 therapy by Tim-3 upregulation is mediated by the PI3K-Akt pathway in head and neck cancer. *Oncoimmunology*, 6(1):e1261779.
36. Li J, Shayan G, Avery L, Jie HB, Gildener-Leapman N. et al. (2016). Tumor-infiltrating Tim-3(+) T cells proliferate avidly except when PD-1 is co-expressed: Evidence for intracellular cross talk. *Oncoimmunology*, 5(10):e1200778.
37. Liu Z, McMichael EL, Shayan G, Li J, Chen K. et al. (2018). Novel Effector Phenotype of Tim-3(+) Regulatory T Cells Leads to Enhanced Suppressive Function in Head and Neck Cancer Patients. *Clin Cancer Res*, 24(18):4529-4538.
38. Kurten CHL, Kulkarni A, Cillo AR, Santos PM, Roble AK, Onkar S, et al. (2021). Investigating immune and non-immune cell interactions in head and neck tumors by single-cell RNA sequencing. Nat Commun. 12(1):7338.
39. Ruffin AT, Li H, Vujanovic L, Zandberg DP, Ferris RL. (2023). Improving head and neck cancer therapies by immunomodulation of the tumour microenvironment. *Nat Rev Cancer,* 23(3):173-188.
40. Chen X, Chen L, Kurten CHL, Jabbari F, Vujanovic L. et al. (2022). An individualized causal framework for learning intercellular communication networks that define microenvironments of individual tumors. *PLoS Comput Biol*, 18(12):e1010761.

41. Aggarwal C, Prawira A, Antonia S, Rahma O, Tolcher A. et al. (2022). Dual checkpoint targeting of B7-H3 and PD-1 with enoblituzumab and pembrolizumab in advanced solid tumors: interim results from a multicenter phase I/II trial. *J Immunother Cancer*, 10(4).
42. Ferris RL, Spanos WC, Leidner R, Goncalves A, Martens UM. et al. (2021). Neoadjuvant nivolumab for patients with resectable HPV-positive and HPV-negative squamous cell carcinomas of the head and neck in the CheckMate 358 trial. *J Immunother Cancer*. 9(6).
43. Cohen EEW, Bell RB, Bifulco CB, Burtness B, Gillison ML. et al. (2019). The Society for Immunotherapy of Cancer consensus statement on immunotherapy for the treatment of squamous cell carcinoma of the head and neck (HNSCC). *J Immunother Cancer*, 7(1):184.
44. Wang Q, Yang KL, Zhang Z, Wang Z, Li C. et al. (2021). Characterization of Global Research Trends and Prospects on Single-Cell Sequencing Technology: Bibliometric Analysis. *J Med Internet Res*, 23(8):e25789.
45. Peltanova B, Raudenska M, Masarik M. (2019). Effect of tumor microenvironment on pathogenesis of the head and neck squamous cell carcinoma: a systematic review. *Mol Cancer*, 18(1):63.
46. Joyce JA, Pollard JW. (2009). Microenvironmental regulation of metastasis. *Nat Rev Cancer*, 9(4):239-252.
47. Fridman WH, Pages F, Sautes-Fridman C, Galon J. (2012). The immune contexture in human tumours: impact on clinical outcome. *Nat Rev Cancer*, 12(4):298-306.
48. Elmusrati A, Wang J, Wang CY. (2021). Tumor microenvironment and immune evasion in head and neck squamous cell carcinoma. *Int J Oral Sci*, 13(1):24.
49. Ribas A, Wolchok JD. (2018). Cancer immunotherapy using checkpoint blockade. *Science*, 359(6382):1350-1355.
50. Postow MA, Callahan MK, Wolchok JD. (2015). Immune Checkpoint Blockade in Cancer Therapy. *J Clin Oncol*, 33(17):1974-1982.
51. Abril-Rodriguez G, Ribas A. (2017). SnapShot: Immune Checkpoint Inhibitors. *Cancer Cell*, 31(6):848-e1.
52. Zandberg DP, Strome SE. (2014). The role of the PD-L1: PD-1 pathway in squamous cell carcinoma of the head and neck. *Oral Oncol*, 50(7):627-632.
53. Deng WW, Mao L, Yu GT, Bu LL, Ma SR. et al. (2016). LAG-3 confers poor prognosis and its blockade reshapes antitumor response in head and neck squamous cell carcinoma. *Oncoimmunology*, 5(11):e1239005.
54. Zhou Q, Munger ME, Veenstra RG, Weigel BJ, Hirashima M. et al. (2011). Coexpression of Tim-3 and PD-1 identifies a CD8+ T-cell exhaustion phenotype in mice with disseminated acute myelogenous leukemia. *Blood*, 117(17):4501-4510.
55. Jie HB, Srivastava RM, Argiris A, Bauman JE, Kane LP, Ferris RL. (2017). Increased PD-1(+) and TIM-3(+) TILs during Cetuximab Therapy Inversely Correlate with Response in Head and Neck Cancer Patients. *Cancer Immunol Res*, 5(5):408-416.
56. Chen Y, Ding X, Bai X, Zhou Z, Liu Y. et al. (2023). The current advances and future directions of PD-1/PD-L1 blockade in head and neck squamous cell carcinoma (HNSCC) in the era of immunotherapy. *Int Immunopharmacol*, 120:110329.
57. Zolkind P, Uppaluri R. (2017). Checkpoint immunotherapy in head and neck cancers. *Cancer Metastasis Rev*, 36(3):475-489.
58. Okuyama K, Naruse T, Yanamoto S. (2023). Tumor microenvironmental modification by the current target therapy for head and neck squamous cell carcinoma. *J Exp Clin Cancer Res*, 42(1):114.

Cite this article: Miao R., Ma W., Liu S. (2023). Fundamental Cognizance and Scholarly Exploration of Immune-Related Notions in Head and Neck Squamous Cell Carcinoma (SCC) From 2012-2022: A Bibliometric Analysis. *Clinical Case Reports and Studies*, BioRes Scientia Publishers. 3(4):1-18. DOI: 10.59657/2837-2565.brs.23.077

Article History: **Received:** October 04, 2023 | **Accepted:** October 18, 2023 | **Published:** October 26, 2023