HUMAN VACCINES & IMMUNOTHERAPEUTICS
2025, VOL. 21, NO. 1, 2469403
https://doi.org/10.1080/21645515.2025.2469403

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RESEARCH ARTICLE

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Global research trends of immunosenescence and immunotherapy: A bibliometric study

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ABSTRACT

Immunosenescence refers to the gradual decline in immune system function with age, increasing susceptibility to infections and cancer in the elderly. The advent of novel immunotherapies has revolutionized the field of cancer treatment. However, the majority of patients exhibit poor re-sponses to immunotherapy, with immunosenescence likely playing a significant role. In recent years, significant progress has been made in understanding the interplay between immunosenescence and immunotherapy. Our research aims to explore the prospects and development trends in the field of immunosenescence and immunotherapy using a bibliometric analysis. Relevant articles were collected from the Web of Science Core Collection (WoSCC) (retrieved on July 20, 2024). Primary bibliometric characteristics were analyzed using the R package "Biblio-metrix," and keyword co-occurrence analysis and visualization were conducted using VOSviewer. A total of 213 English-language original research and review articles spanning 35 years were re-trieved for bibliometric analysis. There was a surge in publications in this field starting in 2017. The United States and China contributed the most articles. Frontiers in Immunology was the most productive journal, while the University of California System was the highest contributing institution. Besse Benjamin from France emerged as the most influential researcher in this field. Popular keywords included "nivolumab," "T cells," "dendritic cells," and "regulatory T cells." The "immunosenescence-associated secretory phenotype" has become a new hotspot, with immune checkpoint inhibitors remaining a central theme in this domain. The field of immunosenescence and immunotherapy is entering a phase of rapid development and will continue to hold significant value in future research.

ARTICLE HISTORY
Received 10 October 2024
Revised 31 January 2025
Accepted 15 February 2025

KEYWORDS
Immunosenescence; immunotherapy; bibliometric analysis; cancer; immune checkpoint inhibitors

Introduction

The concept of immunosenescence, first introduced in the 1960s, refers to the gradual decline in immune system function with age.[1] Aging itself is a natural physiological process, often associated with the loss of homeostasis within the organism, leading to negative health consequences.[2] Physiological changes during aging are particularly prominent in the immune system, resulting in a decline in immune function. Immunosenescence has since become a central focus of research in geriatrics and oncology. It is linked to higher rates of chronic diseases and mortality in the elderly, increasing their susceptibility to cancer. This decline in immune function impairs the body's ability to defend against pathogens and allows tumor cells to evade immune surveillance, facilitating tumor development and leading to higher rates of treatment failure and recurrence.[3,4]

In recent years, immunotherapy has become a pivotal area of oncology research, with its clinical efficacy gradually being recognized. Tumor immunotherapy primarily includes immune checkpoint inhibitors (ICIs), active immunotherapy, antibody-targeted therapy, adoptive cell transfer, cytokine therapy, and bispecific T-cell engagers.[5,6] Innovative immunotherapies, such as ICIs, have revolutionized cancer treatment. However, with the increasing human lifespan and the growing issue of global aging, notable differences have been observed in the response of elderly patients to ICI treatment compared to younger patients, with immunosenescence identified as a key factor.[7–10] Research indicates that immunosenescence alters the immune regulation within the tumor microenvironment, leading to decreased efficacy of ICIs and a higher incidence of adverse events.[11–13] Research on immunosenescence in the context of immunotherapy not only holds the potential to optimize current cancer treatment protocols but also provides theoretical support for developing new personalized treatment strategies, thus advancing precision medicine.

Bibliometrics has become an essential methodology for systematically assessing research domains of interest to scholars. It leverages statistical analysis and visualization techniques to quantitatively examine these domains, uncovering

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Supplemental data for this article can be accessed on the publisher's website at https://doi.org/10.1080/21645515.2025.2469403

research evolution and developmental trends.[14] Over the past few decades, there has been a significant surge in studies on immunosenescence.[15] However, a systematic evaluation of immunosenescence and immunotherapy remains lacking. To address this gap, we utilize the Web of Science Core Collection (WoSCC) databases in this study. We retrieved bibliometric data pertaining to immunosenescence and immunotherapy (including annual articles, countries/regions, authors, institutions, journals, references, and keywords) and performed descriptive statistical analyses. Additionally, we utilized the Bibliometrix R package and VOSviewer to map the knowledge landscape, providing a structured overview of the field. Overall, this study aims to examine the current landscape, research hotspots, and emerging trends in immunosenescence and immunotherapy. Specifically, we seek to identify key trends at the intersection of immunosenescence and immunotherapy, elucidate the research priorities and the evolving trends in research focus within this field, and provide insights into active research directions that may lead to future breakthroughs.

Methods

Data sources and search strategy

As one of the most extensive academic databases, Web of Science (WoS) includes over 12,000 high-quality journals and comprehensive citation records.[16] Thus, WoS was selected as the target database for this study. On July 20, 2024, a literature search was conducted, and relevant publications since 1990 were exported to the Web of Science Core Collection database (WoSCC). The search strategy was set as follows: [topic search = ("immunosenescence" OR "immune senescence" OR "immune aging" OR "aging immune" OR "immune ageing" OR "ageing immune" OR "immunoageing" OR "immune system aging" OR "immune system senescence") AND ("immunotherapy" OR "immune therapy" OR "immunotherapies" OR "immunotherapeutic" OR "immunotherapeutics")]. The inclusion criteria were as follows: only "articles" and "reviews" published in English were considered, with the search conducted up to July 20, 2024. Documents were excluded based on the following criteria: 1) conference abstracts, editorials, early access articles, corrections, letters, or preprints; 2) documents not addressing both immunosenescence and immunotherapy; 3) unpublished documents or those lacking sufficient information. The workflow of this study is illustrated in Figure 1. A total of 248 articles were initially retrieved, and after applying the exclusion criteria, 213 articles were included in the final analysis. The results were saved in plain.txt format for further study, including complete records and cited references.

Software tools and related functions

The software tools used for bibliometric analysis were the Bibliometrix R package and VOSviewer.[17,18] The Bibliometrix R package was primarily used for quantitative

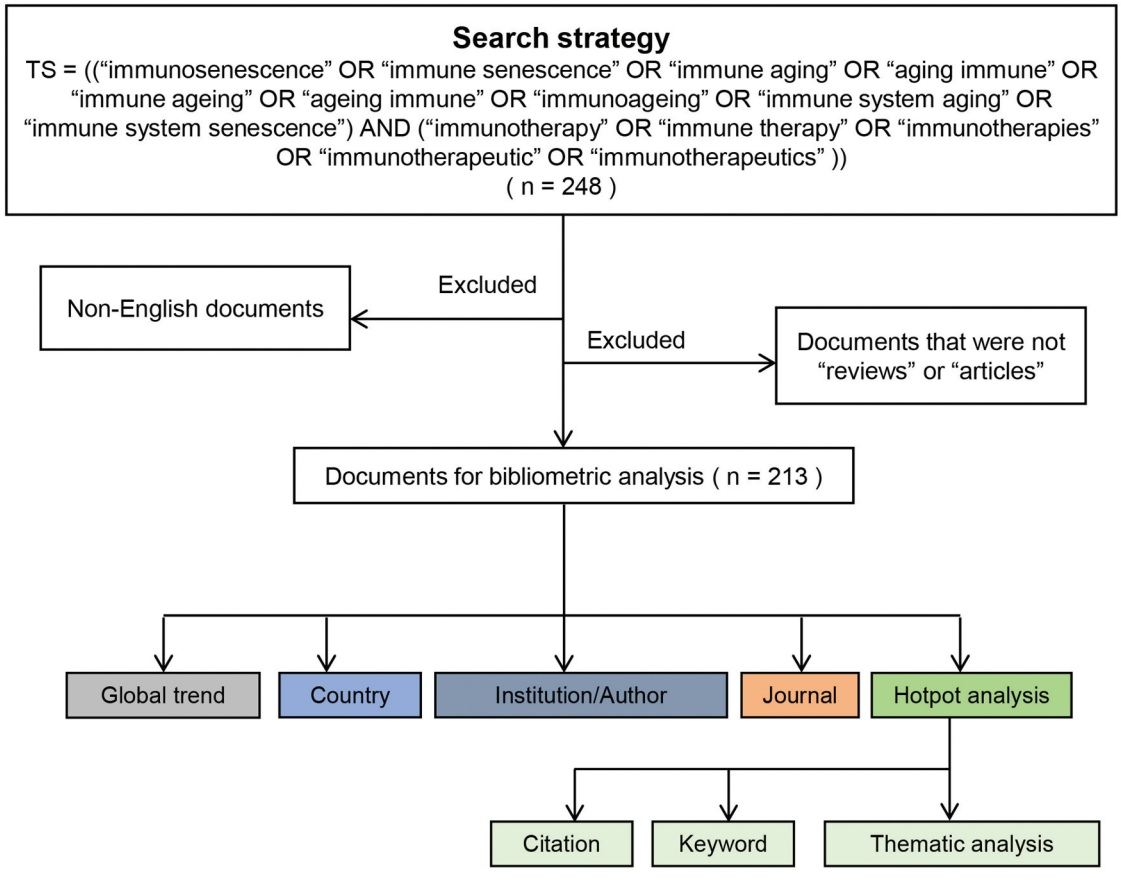

Figure 1. Workflow of the study.

analysis. We utilized the Bibliometrix package in R to extract and analyze basic publication information, such as publication trends, citation counts, the most productive or influential countries, institutions, authors, and the most popular journals. Additionally, we employed the Bibliometrix R's Thematic map to plot theme distribution and Factorial analysis to categorize research themes via dimensionality reduction. VOSviewer was used as an effective tool for keyword co-occurrence analysis. This study used co-authorship analysis to reveal the relationships between different keywords and visualized the network over a time span by adding a temporal overlay function. An overview of the bibliometric process is shown in Figure 1.

Results

Global publication trends and key contributors on immunosenescence and immunotherapy

As of July 20, 2024, 213 academic articles on immunosenescence and immunotherapy were retrieved from the WoSCC database, covering the period from 1990 to 2024. These publications were selected for detailed analysis, with 50.9% ($n = 109$) as original research articles and 49.1% ($n = 104$) as review articles. Figure 2(a) depicts the annual and cumulative publication numbers in the field of immunosenescence and immunotherapy. Over the past three decades, interest in the relationship between immunosenescence and immunotherapy has grown substantially, evidenced by an annual growth rate of 7.84%. Before 2016, the annual publication volume was relatively low, with the cumulative publications steadily increasing from 1 in 1990 to 60 in 2016. Notably, from 2017 to 2024, publication output increased rapidly, culminating in a cumulative total of 213 publications by 2024. Figure 2(b) shows the average annual citations of these publications, peaking in 2019, indicating groundbreaking studies that year, potentially explaining the slight peaks in publication numbers from 2020 to 2022. The lower number of publications recorded for 2024 likely reflects the time lag between publication and database inclusion. As time progresses, newer publications will be fully indexed and garner more citations, leading to more complete and accurate future data.

According to publication numbers shown in the national distribution map (Figure 2(c)) and bar chart (Figure 2(d)), the top four countries are the United States ($n = 63$, 29.6%), China ($n = 36$, 16.9%), Italy ($n = 25$, 11.7%), and France ($n = 16$, 7.5%). Additionally, we analyzed collaborative relationships between countries (Supplementary Figure S1). Our analysis reveals that the leading publishing countries have established close cooperative relationships. The United States, in particular, has formed strong collaborations with China, Italy, the United Kingdom, and Germany.

Figure 2(e) presents the publication output of various research institutions from different countries in major journals. The left side indicates the source countries of the publications, the middle represents the research institutions, and the right side shows the journals where the articles were published. The flow and thickness of the lines reflect the quantity and distribution of publications from countries to institutions to journals. For instance, research in the United States is primarily conducted by institutions such as the University of California system, the National Institutes of Health (NIH), the University of Texas system, and UT MD Anderson Cancer Center. In France, research is concentrated in six institutions: UNICANCER, Gustave Roussy, Université Paris Cité, Université Paris-Saclay, Institut National de la Santé et de la Recherche Médicale (INSERM), and Assistance Publique – Hôpitaux de Paris (APHP). The European Journal of Cancer, Journal of Geriatric Oncology, and Frontiers in Immunology are the most frequent publication venues for these countries and their affiliated institutions.

A total of 421 institutions have conducted research on immunosenescence and immunotherapy. The top 22 institutions are listed in Supplementary Table S1 (including KU Leuven, Nantong University, Sichuan University, and Sun Yat-sen University due to the same number of publications, leading to 22 institutions being ranked). Among these, eight institutions are from the United States, six from France, five from China, and one each from Finland, the United Kingdom, and Belgium. The University of California System ranks first with the highest output of 26 publications. A total of 1380 authors contributed to research on immunosenescence and immunotherapy. Supplementary Table S2 lists the top ten most productive authors. Specifically, Besse Benjamin has authored six publications (H-index = 5, G-index = 6, M-index = 0.625, total citations = 208), Chaput Nathalie has contributed four publications (H-index = 4, G-index = 4, M-index = 0.5, total citations = 151), and Lage Agustin has five publications (H-index = 4, G-index = 5, M-index = 0.364, total citations = 80). These authors are among the most influential in the field, with their significant academic contributions guiding the current research landscape. Additionally, we examined collaboration relationships among authors (Supplementary Figure S2). In the co-authorship cluster network, 44 authors are divided into ten clusters. The size of the nodes represents the number of publications by each researcher, while the color of the nodes indicates clusters classified by the strength of collaboration. These clusters are dispersed, with no cooperation between different clusters, forming no large interaction network. Given the relatively recent development of research in immunosenescence and immunotherapy, further collaboration between institutions and authors is necessary.

Top journals and highly cited articles in immunosenescence and immunotherapy

Research articles on immunosenescence and immunotherapy were published across 131 academic journals. Figure 3(a) shows the ten academic journals that published the most articles in this field, accounting for 30.5% of the total publications (65 out of 213 articles). Among these, Frontiers in Immunology had the highest number of publications with 13 articles. Immunity & Aging and the International Journal of Molecular Sciences each published nine articles. The Journal of Immunology had the highest citation number, totaling 831 citations (Figure 3(b)). Table 1 lists the ten most frequently cited academic articles exploring the relationship between immunosenescence and immunotherapy. The citation counts for these top ten articles

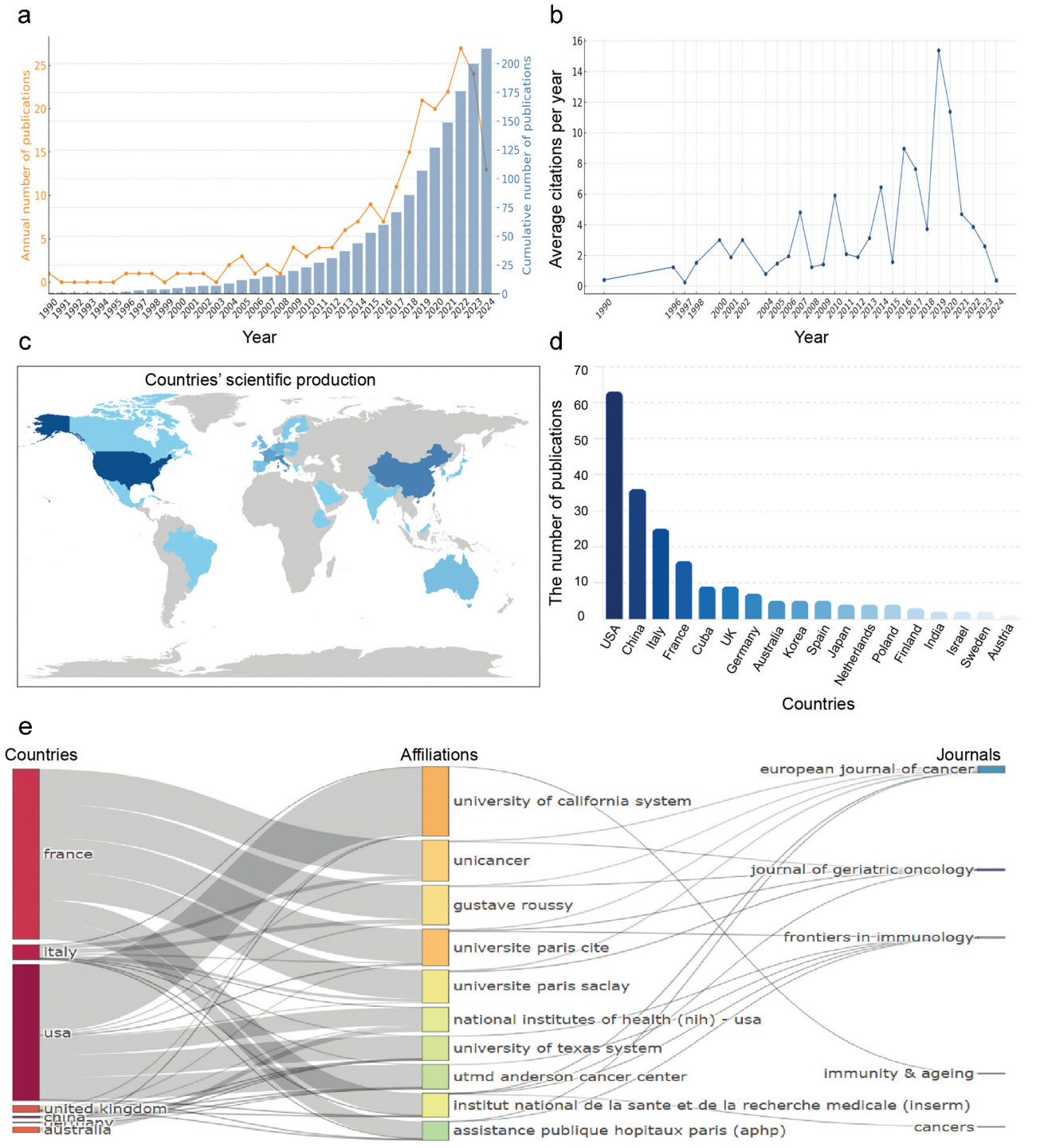

Figure 2. Global publication trends on immunosenescence and immunotherapy: (a) the annual number and the cumulative number of publications. (b) The average citations per year. (c) The national distribution map based on the article output. (d) The top 18 countries with the most publications. (e) Three-field plot of counties, affiliations and journals. The left section (in red) represents the source countries of the publications, the middle section (in green) represents the research affiliations, and the right section (in blue) represents the journals where the articles were published. The flow and thickness of the lines indicate the quantity and distribution of publications between countries, affiliations and journals.

range from 148 to 495. The article titled "Paradoxical effects of obesity on T cell function during tumor progression and PD-1 checkpoint blockade," published in 2019 in Nature Medicine, received the most citations, totaling 495. This highly cited article primarily describes how obesity leads to increased immunosenescence, tumor progression, and PD-1-mediated T cell dysfunction, highlighting obesity as a biomarker for certain cancer immunotherapies.[19] In addition, we further analyzed the key findings of the research articles, and Supplementary Table 3 lists the top 20 most influential research articles in this field. The citation counts of these articles range from 33 to 495. These studies are limited to primary research, which

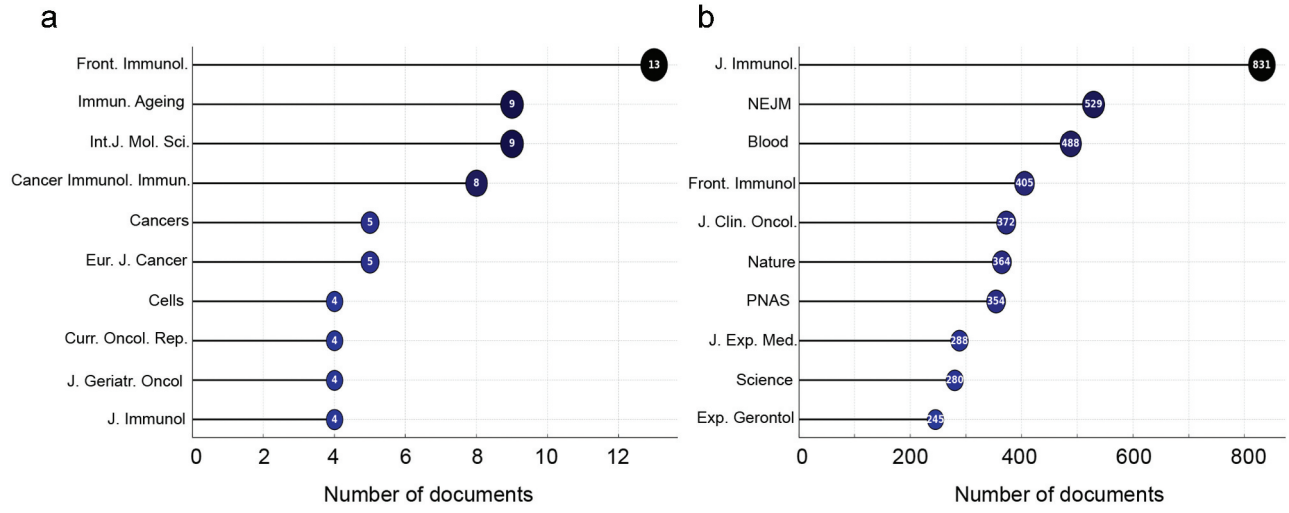

Figure 3. Top ten journals with most articles (a) and citations (b) about immunosenescence and immunotherapy.

Table 1. The top ten highest cited articles.

Rank	Title	Type	First Author	Journal	Year	Citations
1	Paradoxical effects of obesity on T cell function during tumor progression and PD-1 checkpoint blockade	Article	Ziming Wang	Nature Medicine	2019	495
2	Immunosenescence and its hallmarks: How to oppose aging strategically? A review of potential options for therapeutic intervention	Review	Anna Aiello	Frontiers in Immunology	2019	414
3	Cytokine Storm in COVID-19—Immunopathological Mechanisms, Clinical Considerations, and Therapeutic Approaches: The REPROGRAM Consortium Position Paper	Review	Sonu Bhaskar	Frontiers in Immunology	2020	333
4	Therapy of type 1 diabetes with CD4+CD25highCD127− regulatory T cells prolongs survival of pancreatic islets — Results of one year follow-up	Article	Natalia Marek-Trzonkowska	Clinical Immunology	2014	277
5	Can physical activity ameliorate immunosenescence and thereby reduce age-related multi-morbidity?	Review	Niharika A. Duggal	Nature Reviews Immunology	2019	249
6	Comparison of efficacy of immune checkpoint inhibitors (ICIs) between younger and older patients with cancer	Review	Takashi F. Nishijima	Cancer Treatment Reviews	2016	213
7	Immunosenescence: a key player in cancer development	Review	Jian Lian	Journal of Hematology & Oncology	2020	205
8	The concept of immune surveillance against tumors: The first theories	Review	Domenico Ribatti	Oncotarget	2017	188
9	Phase I study of recombinant human interleukin-7 administration in subjects with refractory malignancy	Article	Claude Sportes	Clinical Cancer Research	2010	159
10	Immunosenescence: deficits in adaptive immunity in the elderly	Review	Fabio T. Hakim	Tissue Antigens	2007	158

provides a clearer understanding of the current research achievements in the fields of immunosenescence and immunotherapy.

Research hotspot

Citation burst analysis of references

We performed a references publication year spectroscopy analysis (Supplementary Figure S3). The black line represents the number of cited references per year, whereas the red line indicates the deviation from the five-year median. The figure shows a significant increase in citations since the 1970s, coinciding with the period when the term "immunosenescence" was defined. Citation frequency increased notably after 2000, highlighting the growing attention and citations of research related to immunosenescence and immunotherapy in recent years. The top 25 most-cited references are listed in Supplementary Table S4. The most-cited reference is the article by Martin Reck et al.[20] titled "Pembrolizumab versus Chemotherapy for PD-L1-Positive Non-Small-Cell Lung Cancer."

Keyword occurrence and co-occurrence analysis

A total of 1376 keywords were identified in this study (Supplementary Table S5). Figure 4 displays the top 22 keywords ranked by frequency (including "cell lung-cancer," "older-adults," and "peripheral-blood," each appearing 11 times). Among these, "immunosenescence" had the highest frequency, appearing 36 times. In the top 20 keywords, "nivolumab" ($n = 26$) was the only monoclonal antibody, "docetaxel" ($n = 16$) was the only chemotherapy drug, and "T cells" ($n = 26$), "dendritic cells" ($n = 19$), "regulatory T cells" ($n = 17$), and "lymphocytes" ($n = 12$) were the cell types listed, with T cells and regulatory T cells being subsets of lymphocytes. "Cell lung cancer" ($n = 11$) was the only cancer type to appear in the ranking.

Based on bibliometric principles and Price's law,[21] a threshold frequency of five was selected to focus on statistically significant and impactful keywords. As a result, the co-occurrence analysis included 101 keywords that appeared more than five times. The network of these keywords is depicted in Figure 5(a). In this figure, the node size represents keyword frequency, the color indicates

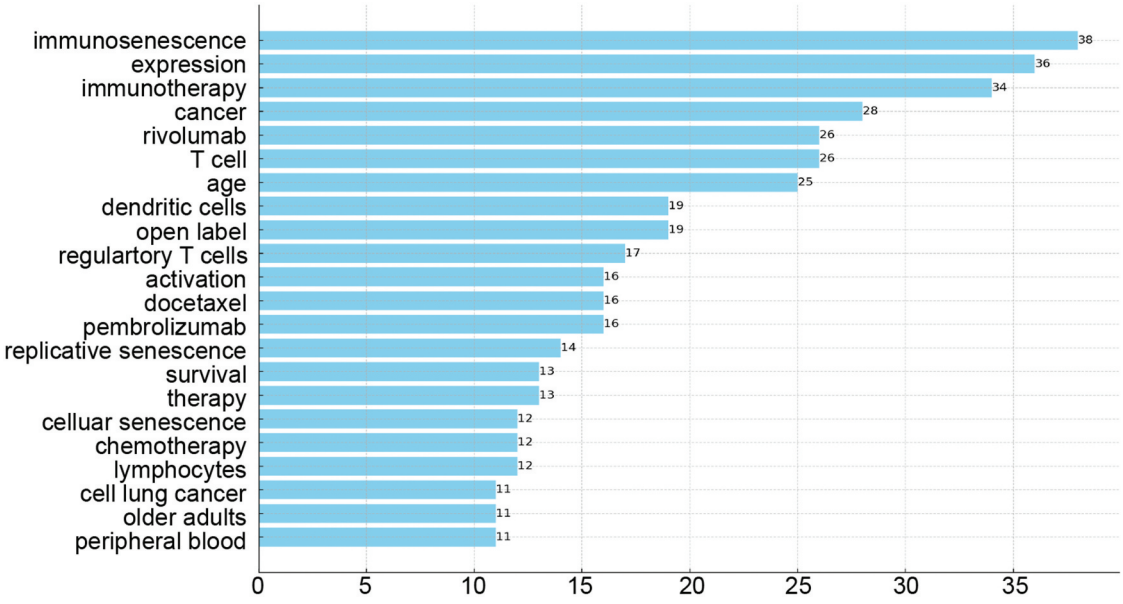

Figure 4. The top 22 most popular keywords on immunosenescence and immunotherapy.

keyword clusters, and the distance between nodes signifies the strength of their relationships. Keywords with closer relationships are grouped into the same cluster. The 101 keywords are divided into four clusters. The first cluster (red, 37 keywords) focuses on specific components and functions of the immune system, including "dendritic cells," "regulatory T cells," "T cells," "natural killer cells," "CD8(+) T cells," and "immune system." It also covers age-related diseases and infection risks like "infection," "COVID-19," and "influenza vaccine." The second cluster (green, 31 keywords) includes widely used "immune checkpoint inhibitors" like "nivolumab," "pembrolizumab," "ipilimumab," and "atezolizumab." This cluster also contains keywords related to cancer types, such as "cell lung cancer," "melanoma," "advanced melanoma," and "non-small cell lung cancer." The third cluster (blue, 19 keywords) focuses on treatment and efficacy, with keywords such as "therapy," "survival," and "prognosis." Additionally, keywords like "T-cells," "inflammation," and "biomarker" are also included in this cluster. The fourth cluster (yellow, 14 keywords) includes keywords related to the immune microenvironment and vaccine research, such as "vaccination," "tumor microenvironment," "mouse model," and "suppressor-cells." "Alzheimer's disease" is the only non-cancer-related disease that appears in this cluster.

Figure 5(b) presents the time-overlapping analysis network of these co-occurring keywords. The colors ranges from dark blue to light green to bright yellow, representing the average active years of these keywords that have drawn researchers' attention. Research around 2016 mainly focused on "cytokines/cytokine production," "dendritic cells," "regulatory T cells," and "natural killer cells." After 2018, the focus shifted to "T cell" and "CD8(+) T cells." Recently, topics such as "senescence-associated secretory phenotype" have gained more prominence.

Thematic analysiis

A thematic map was utilized to visualize and interpret themes and trends within a research field. By integrating factors such as citations, keyword frequencies, and co-occurrence relationships, we constructed a two-dimensional map that distributes different themes into four quadrants based on their centrality and density. As illustrated in Figure 6(a), motor themes represent highly central and dense topics, indicating well-developed and important themes, such as "nivolumab," "immunosenescence," and "age." Niche themes are highly dense but less central, representing mature yet relatively isolated topics. Terms related to transplantation, such as "bone marrow transplantation," "versus host disease," and "hematopoietic stem cells," fall into this category. Emerging or declining themes are characterized by low density and centrality, representing new or marginal topics, such as "vaccination," "protein," and "dysfunction." Basic themes have low density but high centrality, serving as bridging or interdisciplinary topics, with keywords such as "immunotherapy," "cancer," "immune response," "cytokine production," "age-related changes," "replicative senescence," "cellular senescence," and "peripheral blood."

Factorial analysis is a dimensionality reduction technique that extracts principal factors from variables to reduce data dimensions, thereby revealing underlying patterns and themes within a research field. It aids in understanding the intrinsic structure and relationships within the data. By categorizing these keywords into four distinct topics, we can explain over 60% of the research (Figure 6(b)). The identified topics include those involving immune checkpoint inhibitors, such as "nivolumab," "pembrolizumab," "ipilimumab," and "atezolizumab" (green); those associated with cellular aging processes, including "replicative senescence," "cellular senescence," "senescence-associated secretory phenotype," and "gene expression" (blue); those concerning patient demographics and specific diseases, such as "elderly patients" and "cell lung cancer" (purple); and the largest topic category (red), which encompasses a broad range of terms, including various cell types, experimental models, infection and inflammation, vaccines, and therapy-related terms (Supplementary Figure S4).

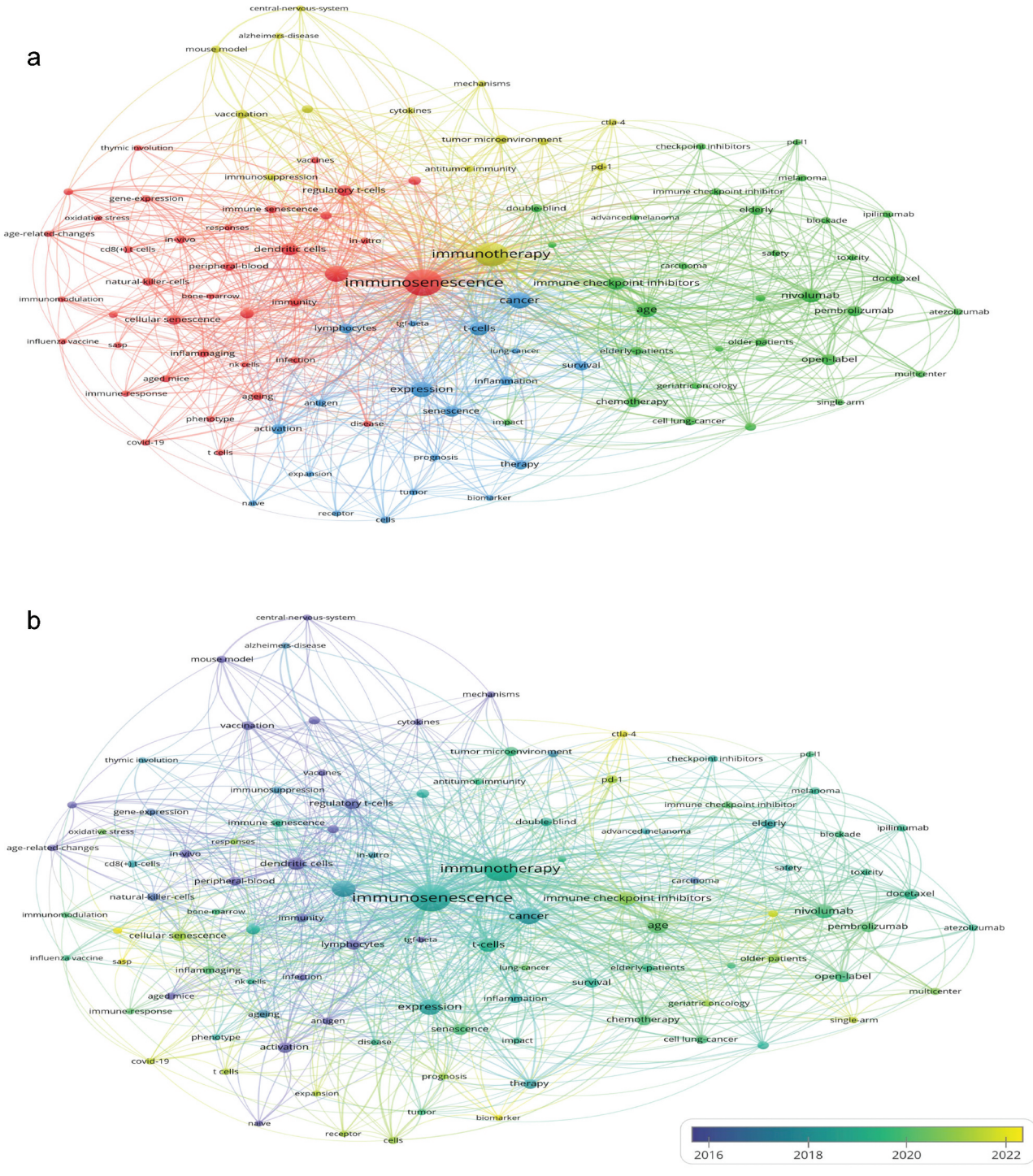

Figure 5. Keywords analysis on immunosenescence and immunotherapy. (a) Keyword co-occurrence network. (b) Keyword co-occurrence plus time-overlapping network.

Discussion

Bibliometric analysis has become a crucial tool for evaluating trends and progress in numerous academic disciplines. Over the past three decades, extensive research has delved into the intricate relationship between immunosenescence and immunotherapy.[15,22] The inaugural article in this domain was published in 1990 by Shupeng Ho et al. from the United States.[23] They assessed the function of natural killer and lymphokine-activated killer cells in young and old mice in vitro and evaluated the impact of exogenous recombinant human IL-2 on tumor-bearing mice of different ages. Their findings revealed a significant reduction in the function of natural killer cells in older mice, suggesting that age-related immune function decline could be a critical factor in tumor pathogenesis and response to immunopharmacological interventions. Since then, there has been a growing interest among researchers in this field. Prior to 2016, the annual publication volume remained relatively low, with fewer than ten papers published

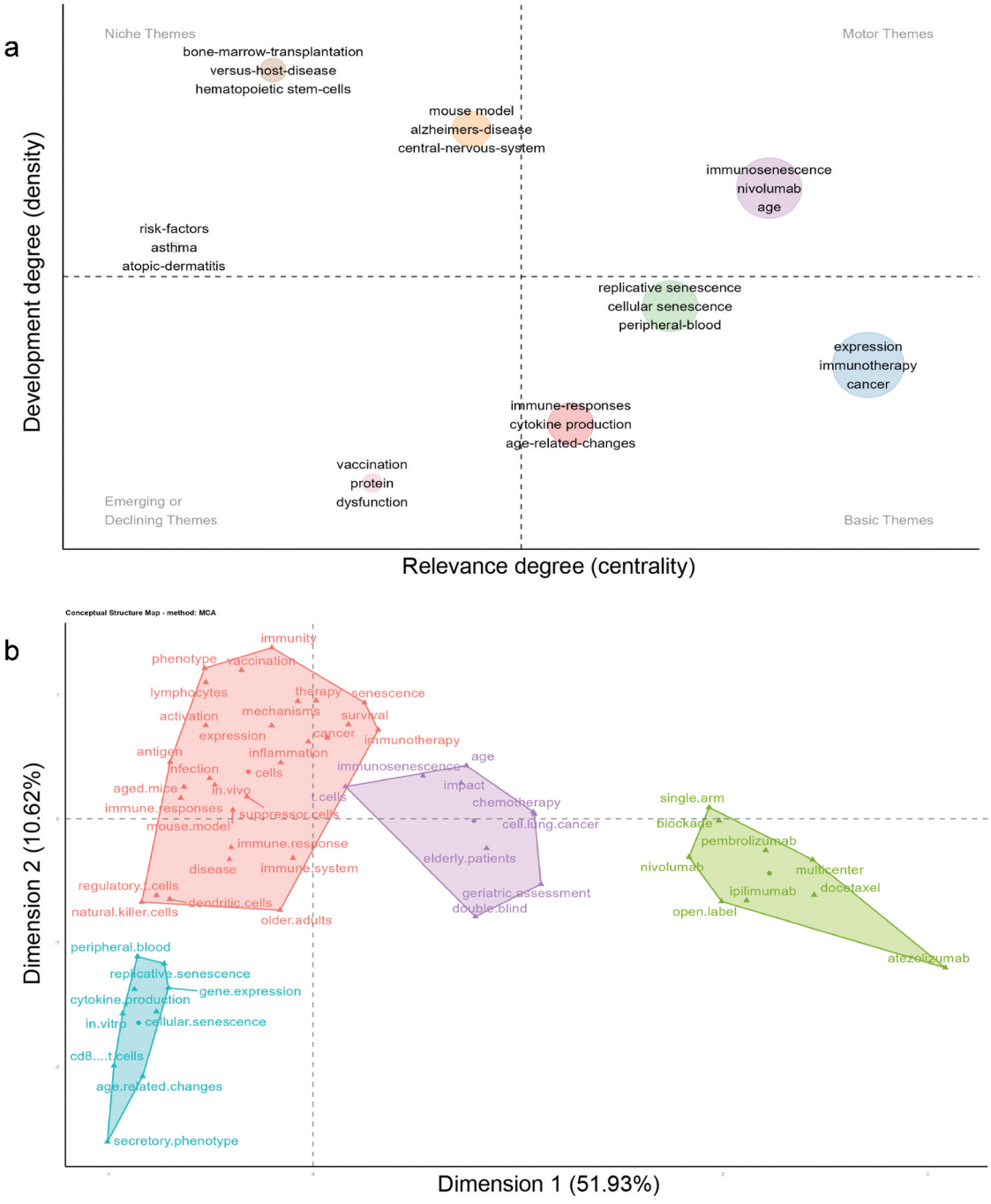

Figure 6. Thematic analysis on immunosenescence and immunotherapy. (a) Thematic map. (b) Factorial analysis.

each year. However, since 2017, the annual publication output on immunosenescence and immunotherapy has significantly increased, averaging over 20 papers per year. This surge in research activity is closely linked to major breakthroughs in these areas. The FDA approval of PD-1 inhibitors nivolumab and pembrolizumab in 2014, followed by the approval of the PD-L1 inhibitor atezolizumab in 2016,[24] marked a pivotal milestone in cancer immunotherapy. These approvals not only transformed treatment strategies but also significantly increased investment and research efforts. As these therapies became more widely applied in clinical practice, funding and innovation in the field accelerated further. Despite these breakthroughs, immunotherapy continues to face challenges, particularly in elderly populations, where immunosenescence is considered a key factor influencing the efficacy of ICIs.[25] Consequently, this issue has become a major research focus in recent years, leading to a rapid expansion of related studies. This trend highlights the dynamic and rapidly evolving nature of the field.

Immunotherapy has demonstrated considerable promise in cancer treatment, yet its response rate remains relatively low, at approximately 20%.[26,27] To enhance treatment response rates and patient outcomes, researchers have investigated the underlying mechanisms responsible for patient response

variability.[28] Numerous studies have demonstrated that immunosenescence is a pivotal factor in this process.[29–32] Consequently, extensive research has been conducted on the role of immunosenescence within the context of immunotherapy. Specifically, recent studies have discovered that immunosenescence disrupts the immune regulation of the tumor microenvironment, resulting in reduced efficacy of ICIs and increased adverse events in cancer patients.[33,34] Therefore, targeting and reversing immunosenescence could potentially enhance the effectiveness of immunotherapy in elderly cancer patients. In summary, bibliometric analysis has revealed rapid development trends and promising future prospects in the field of immunosenescence and immunotherapy research.

In the realm of immunosenescence and immunotherapy, the top four countries contribute 65.7% of the total publications, with the United States at the forefront. This dominance is evident not only in the publications but also in the breadth of its international collaboration network. The United States' strong economic power and substantial healthcare investment provide robust support for its research institutions, ensuring its leading position in global scientific research. Although China ranks second in publications, its research concentration remains relatively low, with only four universities among the top 22 research institutions. This suggests that China still has considerable room for improvement in terms of research output and impact.

Despite the involvement of 1,380 authors, Besse Benjamin from France emerges as the most prominent researcher. He has long been dedicated to clinical research on non-small cell lung cancer (NSCLC) and has published numerous reviews and original research papers on immunotherapy and immunosenescence.[8–35–41] Besse has established a strong collaboration with Chaput Nathalie, the second most prominent author in this field, resulting in many influential coauthored studies. However, co-authorship analysis reveals that researchers are dispersed across multiple independent clusters, lacking inter-cluster collaboration. This dispersion not only limits the depth and breadth of research but also hinder knowledge dissemination and innovation. To advance this field, strengthening collaborative relationships is imperative.

In terms of journals, Frontiers in Immunology leads in the number of published articles, indicating its extensive influence. However, despite a lower number of articles, the Journal of Immunology boasts the highest citation count, underscoring the significant academic impact and recognition of its research. Highly cited article, such as the one published in Nature Medicine,[19] highlights the critical role of obesity in immunosenescence and cancer immunotherapy, further demonstrating the importance of high-impact journals in advancing the frontiers of this field.

Since the definition of "immunosenescence" in the 1970s, the citations of related research has significantly increased, especially after 2000, particularly after 2000, underscoring the importance and growing academic influence of this field. Through the co-occurrence analysis of 1376 keywords, we identified research hotspots and trends in immunosenescence and immunotherapy. The high frequency of keywords and clustering results reflect several pivotal research directions, including immune system function, the application of ICIs, treatment outcomes, and the immune microenvironment (TME). In tumor immunology research, the mechanisms of tumor immune evasion have become a key focus. In line with our findings, some researchers have examined novel cancer mechanisms at the molecular level, including the pathways governing cancer cell apoptosis and the role of inflammatory signaling in both cancer immune evasion and immunosenescence.[42,43] Moreover, the critical role of the TME in modulating immunotherapeutic efficacy has gained increasing recognition. Studies indicate that TME can influence tumor progression and immune responses by inducing epithelial-to-mesenchymal transition (EMT) and reshaping the inflammatory milieu.[44] Further keyword analysis reveals that "T cell" and "CD8(+) T cells" have attracted heightened attention in recent years. Consequently, many scholars have delved into the heterogeneity, differentiation pathways, and functions of cytotoxic T lymphocytes (CTLs) in cancer immunity.[45] These findings not only shed new light on the molecular mechanisms underlying tumor immune evasion but also open up new avenues for cancer immunotherapy.

Notably, post-2019, there was a significant surge in COVID-19-related research,[46] further underscoring the close relationship between immunosenescence and infection risk.[47,48] Studies have demonstrated that the elderly are more susceptible to COVID-19 and experience higher disease severity,[49,50] shifting research focus toward vaccine development and immune response mechanisms.[51] This trend indicates that immunosenescence research plays a critical role in infection risk management and vaccine development.

Thematic analysis enables the identification of primary research themes and development trends in immunosenescence and immunotherapy. It reveals that immune checkpoint inhibitors and immunosenescence are prominent research hotspots,[7–52,53–54] garnering extensive attention for their applications and mechanisms. As research deepens, these fields are anticipated to continue spearheading scientific exploration and clinical applications. Niche themes such as bone marrow transplantation and graft-versus-host disease, though significant in specific studies, exhibit limited interaction with other research areas. Emerging themes such as "vaccine" has gained rapid importance in the context of COVID-19. Vaccine research, particularly in addressing emerging infectious diseases like COVID-19, demonstrates significant potential and developmental prospects.[55,56] Basic research themes such as "immunotherapy," "cancer," and "immune response" act as bridges across multiple fields. These foundational studies not only provide a robust theoretical framework for understanding the mechanisms of immunosenescence and immunotherapy but also offer critical support for various clinical applications. Factorial Analysis further confirms these thematic classifications. Overall, thematic analysis offers a comprehensive perspective, aiding our understanding of the current status and future directions of research on immunosenescence and immunotherapy.

This study has certain limitations. First, we focused exclusively on English-language literature, potentially overlooking significant findings in non-English studies.

Considering the global nature of research, future studies should include multi-language literature to ensure a more comprehensive analytical perspective. Secondly, although keyword co-occurrence and thematic analysis revealed current research hotspots and trends, the results are dependent on the analytical tools and algorithms employed. Despite their robustness, these tools may introduce biases or limitations that affect the interpretation of results. Furthermore, as an emerging research area, the literature on immunosenescence and immunotherapy remains relatively sparse. This limitation may restrict our comprehensive understanding of the field. As research progresses and more findings are published, our understanding will become more complete and nuanced.

Conclusion

Since 1990, global research in immunosenescence and immunotherapy has significantly increased. A bibliometric analysis of 213 academic articles has identified research hotspots and development trends in this field. The United States leads this field, with substantial contributions from institutions such as the University of California system. Core research hotspots include immune cells and ICIs, underscoring their pivotal role in cancer immunotherapy. Additionally, the COVID-19 pandemic has further highlighted the close relationship between immunosenescence and infection risk, accelerating vaccine research. However, this field still requires greater interdisciplinary and international collaboration to enhance overall research quality and impact. Future studies should focus on the role of immunosenescence in cancer management, infection control, and personalized treatment to improve the quality of life for the elderly.

Disclosure statement

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

Funding

The work was supported by Beijing Natural Science Foundation [L244031].

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Wei Cui, MD, is the Director of the Clinical Laboratory Department at the Cancer Hospital, Chinese Academy of Medical Sciences, and Chair-Elect of the Chinese Society of Laboratory Medicine. Her research focuses on the clinical application of biomarkers. She has led over 20 national projects and published 200+ papers. Prof. Cui also serves as Deputy Editor-in-Chief of the Chinese Journal of Laboratory Medicine and is a committee member of the ISLH Cellular Analysis & Flow Cytometry Committee.

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