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Global research trends in CAR-T cell therapy for glioblastoma: a bibliometric and visualized analysis

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Abstract

Background Glioblastoma (GBM) is the most aggressive and lethal primary malignant brain tumor in adults, characterized by extensive heterogeneity and a profoundly immunosuppressive microenvironment. Despite advances in surgery, radiotherapy, and chemotherapy, therapeutic outcomes remain poor. Chimeric antigen receptor (CAR)-T cell therapy has shown remarkable efficacy in hematologic malignancies and is now being explored for solid tumors such as GBM. Given the expanding research landscape, a systematic understanding of global trends and hotspots in this domain is urgently needed.

Methods We conducted a comprehensive bibliometric and visualized analysis of publications related to CAR-T cell therapy in GBM from inception to December 31, 2024, using the Web of Science Core Collection. CiteSpace was used to analyze publication trends, country and institutional collaboration, author impact, journal co-citation, reference networks, and keyword co-occurrence, clustering, and bursts.

Results A total of 303 relevant publications were included. Annual outputs showed rapid growth beginning in 2015, with the United States and China leading in productivity and collaboration. Influential authors such as Christine E. Brown and Donald M. O'Rourke were identified as core contributors. Neuro-Oncology and Clinical Cancer Research emerged as key publishing and co-cited journals. Co-citation and keyword analysis revealed a shift from early focus on single-antigen CAR designs (e.g., IL13Rα2, EGFRvIII) toward dual-target constructs, "armored" CAR-T cells, and combinatorial immunotherapies. Recent research hotspots included immunomodulation, precision medicine, and novel delivery platforms such as nanoparticles and oncolytic viruses.

Conclusions This study maps the evolving scientific landscape of CAR-T cell therapy in GBM, highlighting key contributors, institutional collaboration, and emerging research frontiers. The transition from basic antigen targeting to multifunctional, immune-enhancing strategies reflects a maturing field with increasing translational focus. Our findings offer valuable insights that can inform strategic funding allocation by identifying high-impact institutions and authors, optimize clinical trial design by



highlighting emerging combinatorial and delivery strategies, and guide novel target discovery through analysis of co-cited references and keyword bursts. By revealing global collaboration networks and thematic shifts, this study also supports the development of interdisciplinary research frameworks in CAR-T therapy for GBM.

Keywords Glioblastoma, CAR-T cell therapy, Bibliometric analysis, Immunotherapy, Research trends

1 Introduction

Glioblastoma (GBM) is the most common and lethal primary malignant brain tumor in adults, classified as grade IV astrocytoma by the World Health Organization [1]. Despite aggressive treatment involving maximal safe surgical resection followed by radiotherapy and concurrent temozolomide chemotherapy, the prognosis remains dismal, with a median survival of approximately 12 to 15 months and a five-year survival rate of less than 10% [2]. This poor outcome is largely attributed to the highly infiltrative nature of GBM, its pronounced inter- and intra-tumoral heterogeneity, and the profound immunosuppressive tumor microenvironment, which together enable tumor recurrence and resistance to conventional therapies.

The emergence of chimeric antigen receptor (CAR)-T cell therapy has revolutionized cancer treatment, particularly in hematologic malignancies such as B-cell leukemia and lymphoma, where it has demonstrated durable responses and led to multiple FDA-approved products [3–5]. CAR-T cells are genetically engineered T lymphocytes capable of recognizing tumor-associated antigens independently of MHC restriction, providing potent cytotoxicity even in immunologically “cold” tumors [6, 7]. Inspired by this success, researchers have increasingly focused on extending CAR-T therapy to solid tumors, including GBM. Several GBM-specific targets have been identified, such as IL13R α 2, EGFRvIII, HER2, and B7-H3 [8–16]. Early-phase clinical trials have confirmed the feasibility and relative safety of intracavitary or intraventricular CAR-T cell infusion, though therapeutic efficacy remains variable and often transient [11, 17]. However, unlike hematologic malignancies, CAR-T cells face substantial challenges in treating solid tumors such as GBM. One major limitation is the poor penetrability of CAR-T cells into the tumor mass, largely due to the physical barriers posed by the dense extracellular matrix, abnormal vasculature, and blood–brain barrier (BBB) [18]. In addition, the immunosuppressive tumor microenvironment, enriched with regulatory T cells, myeloid-derived suppressor cells, and inhibitory cytokines, further impedes T cell infiltration and persistence. As a result, conventional intravenous administration often leads to inadequate intratumoral accumulation of CAR-T cells. To overcome these barriers, researchers have explored locoregional delivery methods, such as intracavitary or intraventricular infusion, which allow direct delivery of CAR-T cells into the resected tumor cavity or cerebrospinal fluid, thereby bypassing systemic barriers and enhancing local exposure.

Multiple factors hinder the clinical translation of CAR-T therapy in GBM, including limited trafficking and persistence of T cells in the brain, antigen escape mechanisms, heterogeneous expression of target antigens, and robust immunosuppressive mechanisms involving regulatory T cells, myeloid-derived suppressor cells, and inhibitory cytokines such as TGF- β [19–21]. In particular, the BBB poses a significant obstacle for intravenously infused CAR-T cells, limiting their penetration into the central nervous system and reducing therapeutic efficacy. This has prompted the development

of alternative delivery strategies, such as intracavitary or intraventricular infusions, to bypass the BBB and achieve more effective local exposure of CAR-T cells within the tumor environment [19]. To address these challenges, ongoing studies have explored novel CAR designs (e.g., bispecific or “armored” CARs), combinatorial immunotherapy strategies, local delivery approaches, and modulation of the tumor microenvironment [22, 23]. The field is rapidly evolving, with increasing academic and industrial investment.

Given the expanding volume of literature and growing complexity of research directions, there is a critical need to systematically map the global landscape of CAR-T cell therapy research in GBM. Bibliometric analysis, a method combining quantitative evaluation with visualization techniques, offers a powerful tool to uncover publication trends, research hotspots, influential contributors, and collaboration networks. It enables researchers, clinicians, and policy-makers to identify emerging frontiers, guide funding priorities, and support evidence-based decision-making.

Therefore, this study aimed to perform a comprehensive bibliometric and visualized analysis of global publications related to CAR-T cell therapy in glioblastoma. Using CiteSpace, we systematically examined annual publication output, country and institutional collaboration patterns, author productivity and co-citation relationships, core journals and references, and the evolution of key research themes over time. By providing an in-depth overview of the knowledge structure and development trajectory of this field, our findings are expected to inform future research directions, foster cross-institutional collaboration, and support the design of more effective immunotherapeutic strategies for this devastating disease.

2 Materials and methods

2.1 Data source and search strategy

All bibliometric data were retrieved from the Web of Science Core Collection (WoSCC) on March 11, 2025. The search was conducted using the following topic terms: TS=(“glioblastoma” OR “GBM” OR “glioblastoma multiforme”) AND (“CAR-T cell” OR “chimeric antigen receptor T cell” OR “CAR T-cell therapy” OR “CAR-T immunotherapy” OR “CAR T-cell immunotherapy” OR “chimeric antigen receptor T-cell immunotherapy”)*.

The timespan was set from database inception to December 31, 2024, with results limited to articles and review articles in English. After removing duplicates, two reviewers independently screened the titles and abstracts to exclude irrelevant records, such as those not related to glioblastoma or not focused on CAR-T cell therapy. Discrepancies were resolved through discussion. In cases where relevance was uncertain based on title and abstract, full-text review was conducted. Only articles specifically addressing CAR-T cell therapy in the context of glioblastoma were retained for analysis. A total of 303 publications were included for analysis. The literature screening process is detailed in Fig. 1.

2.2 Bibliometric analysis and visualization

Bibliometric analysis and visualization were conducted using CiteSpace (version 6.2.R6) [24]. This software was employed to construct networks of co-authorship, institutional collaboration, keyword co-occurrence, reference co-citation, and journal citation

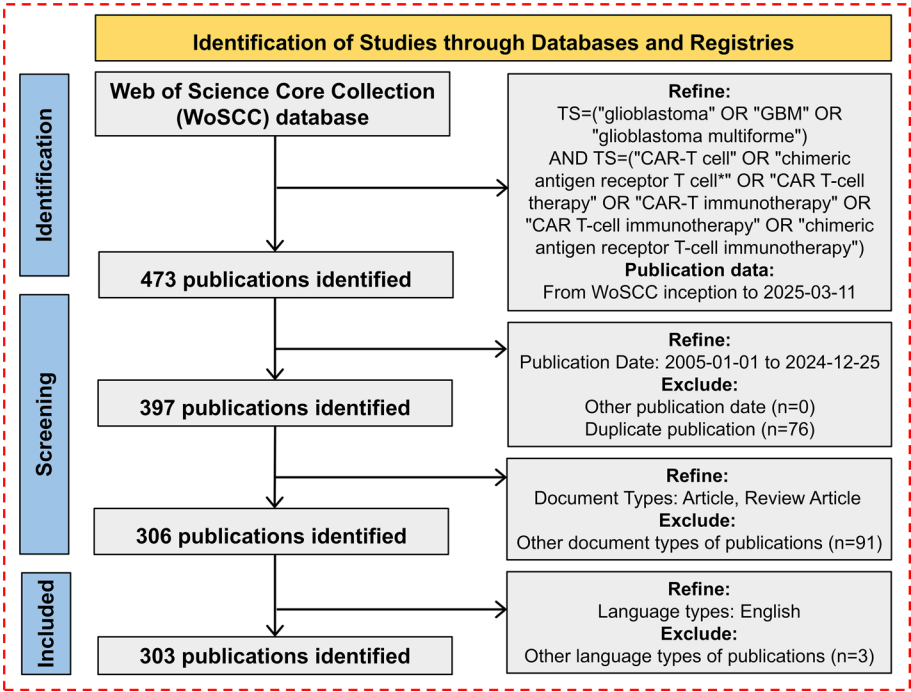


Fig. 1 Flowchart of the literature screening and selection process. A total of 473 publications were initially retrieved from the WoSCC database. After removing duplicates, filtering by publication date, document type, and language, 303 publications were finally included in the bibliometric analysis

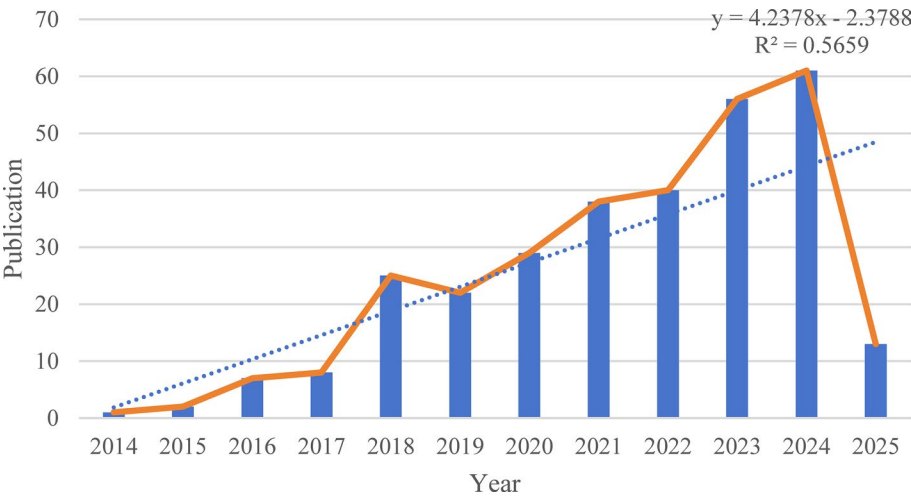


Fig. 2 Annual publication trends of research on CAR-T cell therapy for glioblastoma from 2014 to early 2025. The number of publications shows a continuous increase, peaking in 2024

relationships. Clustering, burst detection, timeline, and timezone views were used to identify research hotspots and evolving trends.

3 Results

3.1 Annual publication trends

The annual number of publications related to CAR T cell therapy in GBM showed a significant upward trend from 2014 to 2024 (Fig. 2). While there were minimal publications prior to 2016, a marked increase occurred starting in 2018, with annual output rising

from fewer than 10 papers to over 25 in that year. Although a slight decline was observed in 2019, the number of studies grew steadily from 2020 to 2022. Notably, publication activity peaked in 2024 with 63 articles, followed by 58 in 2023.

3.2 Global distribution and collaboration of countries/regions and institutions

Publications on CAR-T cell therapy in GBM originated from a wide range of countries/regions, with the United States and China leading in both productivity and international collaboration (Fig. 3A). The United States maintained long-standing partnerships with Germany, Australia, the United Kingdom, and Canada, while China's international collaboration network expanded significantly after 2018. Among the top 10 contributing countries/regions, the United States consistently ranked first throughout the study period. China showed the most notable growth in recent years, followed by steady contributions from Italy, Australia, and Germany (Fig. 3B). Collaboration network analysis confirmed that the United States and China occupied the most central positions in global collaboration networks, reflecting their pivotal influence on the research landscape (Fig. 3C). Institutional collaboration analysis further identified key research hubs, including the University of California System, Harvard University, the University of Pennsylvania, and Beckman Research Institute of City of Hope. A detailed list of the top 10 countries/regions and institutions based on publication volume is provided in Table S1.

3.3 Author collaboration and influence

The author co-authorship network (Fig. 4A) revealed several prominent clusters of collaboration in CAR-T cell therapy research for glioblastoma. Christine E. Brown emerged as the most central and productive author, forming strong collaborative links with Darya Alizadeh, Brenda Aguilar, Julie R. Ostberg, and Hideho Okada. Other notable contributors included Zev A. Binder, Behnam Badie, and Donald M. O'Rourke, who were involved in dense networks of inter-institutional cooperation. The author co-citation network (Fig. 4B) further identified highly influential researchers based on citation frequency. Christine E. Brown, Donald M. O'Rourke, Nabil Ahmed, and John H. Sampson

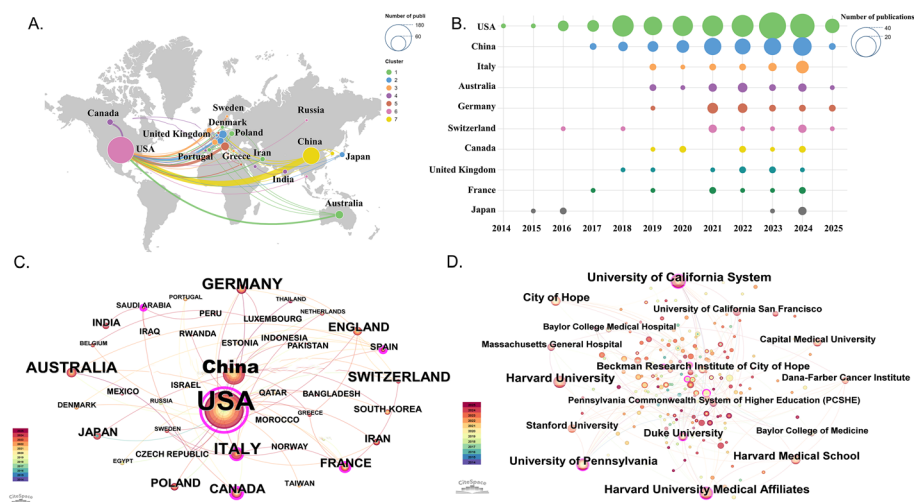


Fig. 3 Geographical and institutional distribution of publications. **A** International collaboration map of countries. **B** Top 10 productive countries over time. **C** Country co-authorship network. **D** Institutional collaboration network highlighting major contributors

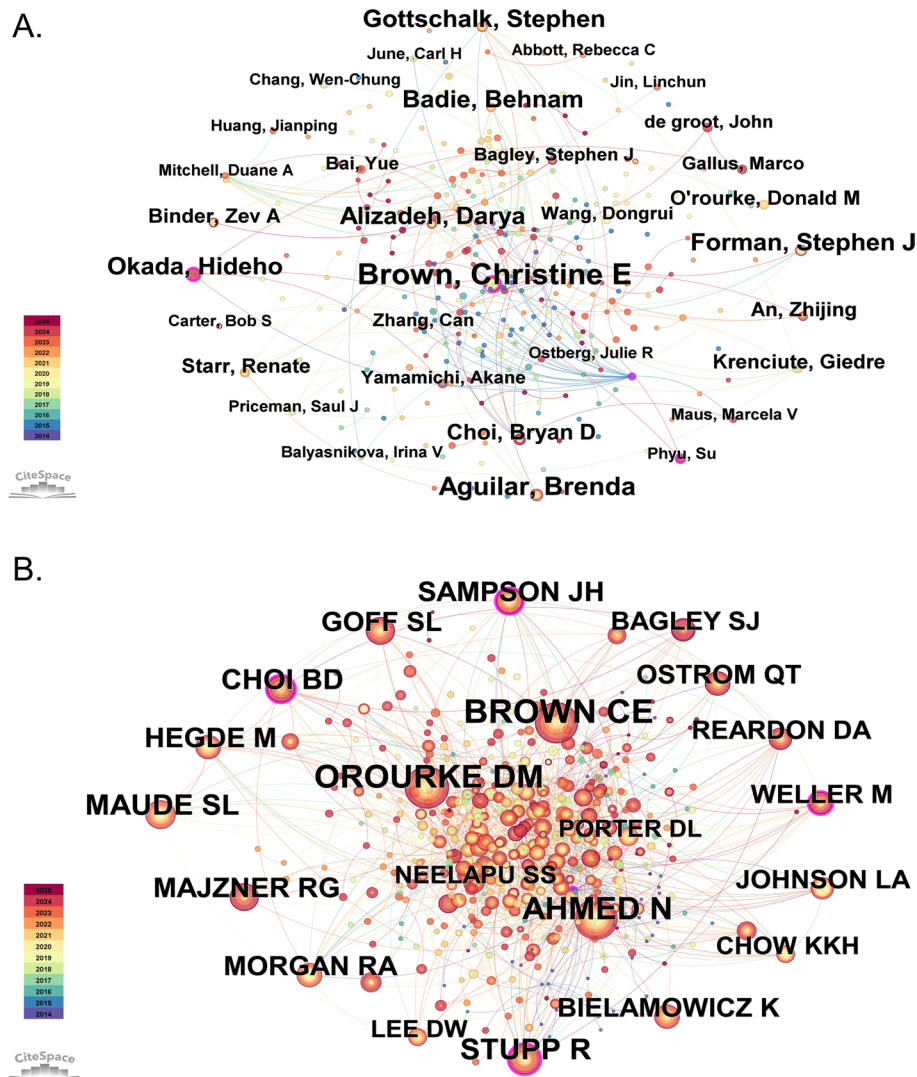


Fig. 4 Author collaboration and co-citation networks. **A** Co-authorship network of active authors. **B** Co-citation network of influential authors in the field

appeared as major knowledge contributors, evidenced by large node sizes and strong citation links. Stephen J. Bagley, Bryan D. Choi, and Marcela V. Maus were also frequently cited and contributed to shaping the field's foundational knowledge base. Table S2 listed the top 10 authors based on publication count and co-citation frequency.

3.4 Journal co-citation and citation pathways

The journal co-citation network (Fig. 5A) revealed that Neuro-Oncology, Clinical Cancer Research, and Science Translational Medicine were among the most frequently co-cited journals in the field of CAR-T cell therapy for glioblastoma. Other highly influential journals included Cancer Cell, Nature, Science, and The New England Journal of Medicine, reflecting the interdisciplinary nature of this research spanning oncology, immunology, and translational medicine. The dual-map overlay (Fig. 5B) demonstrated the disciplinary citation trajectories between citing and cited journals. The primary citation path flowed from molecular biology, immunology, and clinical medicine (on the left side) to genetics, health, and nursing-related journals (on the right). This indicated

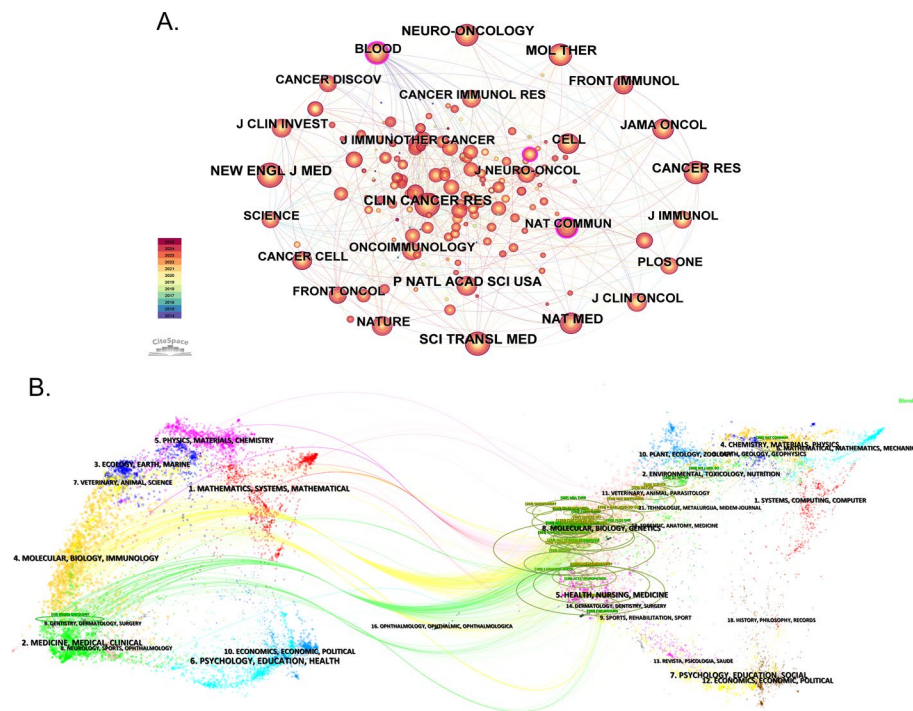


Fig. 5 Journal analysis. **A** Co-citation network of journals. **B** Dual-map overlay showing the disciplinary distribution of citing and cited journals

that researchers working on CAR-T cell therapy for glioblastoma primarily published in medical and immunological journals, while drawing foundational knowledge from broader biomedical and genetic research domains. Additional details on the top 10 publishing and co-cited journals are provided in Table S3.

3.5 Co-cited references and emerging research fronts

The co-citation network (Fig. 6A) revealed several highly influential references that formed the foundational knowledge base for CAR-T cell therapy in glioblastoma. Landmark publications by Christine E. Brown (2015, 2016, 2018), Donald M. O'Rourke (2017), and Nabil Ahmed (2017) were positioned at the center of the network, indicating their pivotal roles in advancing early clinical applications. Other frequently co-cited studies included works by Maude et al. (2014) and Johnson et al. (2015), which contributed to the conceptual transfer of CAR-T therapy from hematologic malignancies to solid tumors. Reference clustering (Fig. 6B) identified several thematic areas, notably including clusters related to “chimeric antigen receptor,” “tumor microenvironment,” “clinical trial,” and “T lymphocytes.” Recent clusters such as “central nervous system tumors” and “primary malignant brain tumors” reflected a growing focus on glioma-specific immunotherapeutic strategies. The modular structure and low silhouette values suggested interdisciplinary integration across immunotherapy, neuro-oncology, and cell engineering.

The top 25 references with the strongest citation bursts (Fig. 6C) highlighted key articles that gained rapid attention within short timeframes. The most prominent citation bursts were observed for Brown et al. (2015, Clin Cancer Res), Johnson et al. (2015, Sci Transl Med), and Maude et al. (2014, N Engl J Med), indicating their impact in shaping

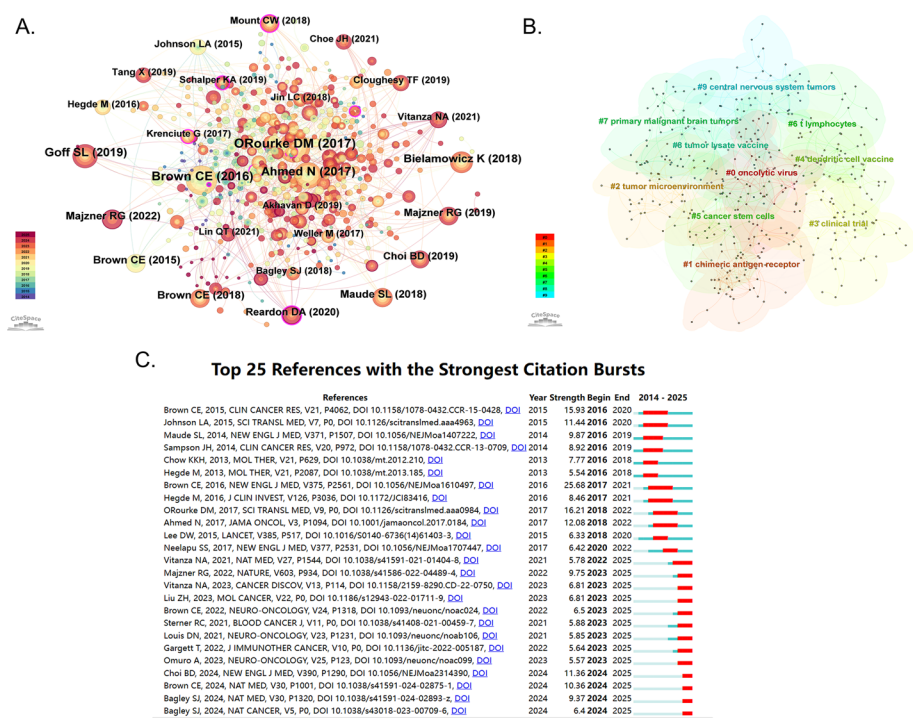


Fig. 6 Reference analysis. **A** Reference co-citation network. **B** Reference clustering by thematic topics. **C** Top 25 references with the strongest citation bursts between 2014 and 2025

the early research direction. In recent years, studies by Vitanza (2023), Bagley (2023), and Choi (2024) have shown strong bursts, underscoring emerging attention toward updated clinical trials, dual-target CARs, and intraventricular delivery strategies. Table S4 summarized the 10 most frequently co-cited references in this field.

3.6 Research hotspots and emerging trends

The keyword co-occurrence network (Fig. 7A) revealed that the most frequently occurring terms included glioblastoma, chimeric antigen receptor, expression, immunotherapy, and tumor microenvironment, reflecting the core research topics in this field. Terms such as IL13Rα2, B cells, adoptive immunotherapy, and blood–brain barrier also appeared frequently, suggesting a sustained focus on tumor-targeting strategies and delivery mechanisms. Keyword clustering analysis (Fig. 7B) identified ten major clusters. Among them, the most prominent included “#0 vaccines,” “#1 chimeric antigen receptor,” “#2 cancer stem cells,” and “#3 CD19.” These clusters corresponded to different research modules, ranging from early CAR constructs to advanced strategies involving dual-targeting and personalized neoantigen vaccines. Cluster #4 “IL13R alpha 2” and #5 “adoptive immunotherapy” emphasized GBM-specific target antigens and T cell-based therapy modalities. Citation burst analysis (Fig. 7C) highlighted keywords that gained sudden attention during specific periods. Earlier bursts focused on antitumor activity, therapy, and glioblastoma multiforme, while recent bursts included adaptive immunotherapy, radiotherapy, dendritic cells, classification, and identification, suggesting a shift toward combinatorial immunotherapy, precision medicine, and computational biomarker discovery.

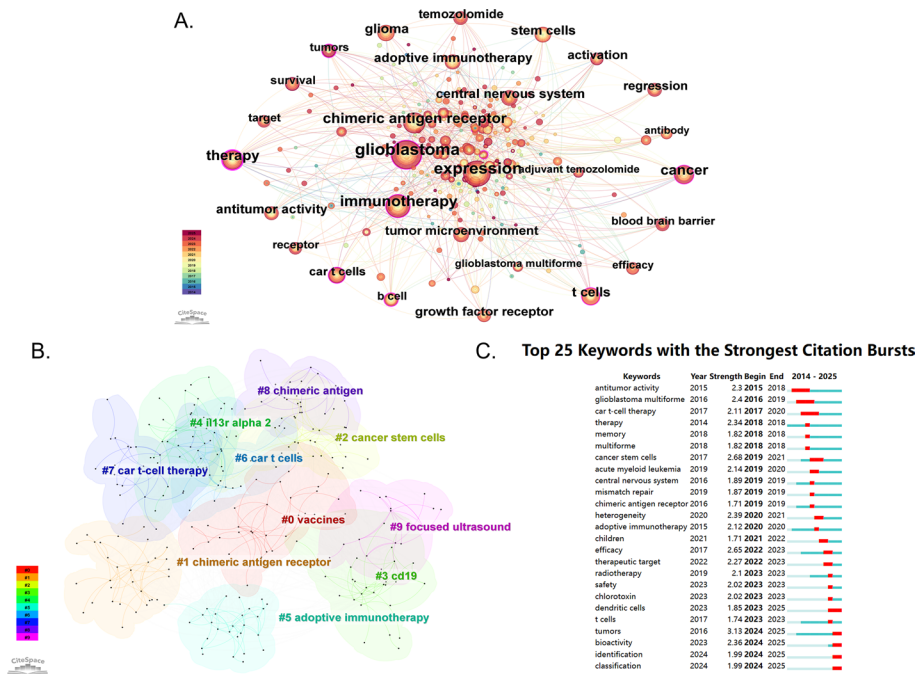


Fig. 7 Keyword analysis. **A** Keyword co-occurrence network highlighting core themes. **B** Keyword clustering map showing major research directions. **C** Top 25 keywords with the strongest citation bursts and their active periods

The timeline view of keyword clusters (Fig. 8A) further demonstrated the chronological emergence of research themes. For instance, chimeric antigen receptor and glioblastoma remained core topics throughout the period, while newer terms such as clinical trials, nanoparticles, and oncolytic virus appeared more frequently after 2020. The time-zone view (Fig. 8B) confirmed a progressive shift from foundational topics (e.g., expression, tumor microenvironment) toward translational research directions, including cell engineering, recombinant antigens, and vaccine delivery systems.

4 Discussion

4.1 Accelerated growth and global contributions in CAR-T research for GBM

Over the past decades, CAR-T cell therapy research for GBM has undergone a remarkable expansion. Our bibliometric analysis identified a distinct surge in publication volume beginning in 2015, coinciding with the initiation of first-in-human clinical trials targeting IL13R α 2 and EGFRvIII [16, 25]. This growth reflects a paradigm shift in neuro-oncology, moving from conventional therapies to immunotherapeutic approaches inspired by the success of CAR-T cell treatments in hematologic malignancies.

The United States and China were the most prolific contributors, not only in terms of publication output but also in establishing extensive international collaborations. Institutions such as the University of Pennsylvania, City of Hope National Medical Center, and Fudan University emerged as global hubs driving innovation. Notably, the collaborative network revealed that United States researchers occupied central nodes, indicating leadership in trial design, antigen discovery, and translational application. This global momentum mirrors the increasing clinical relevance of CAR-T therapy in GBM, international research synergy has become indispensable for advancing CAR-T therapy, enabling cross-validation of findings and multicenter trial enrollment.

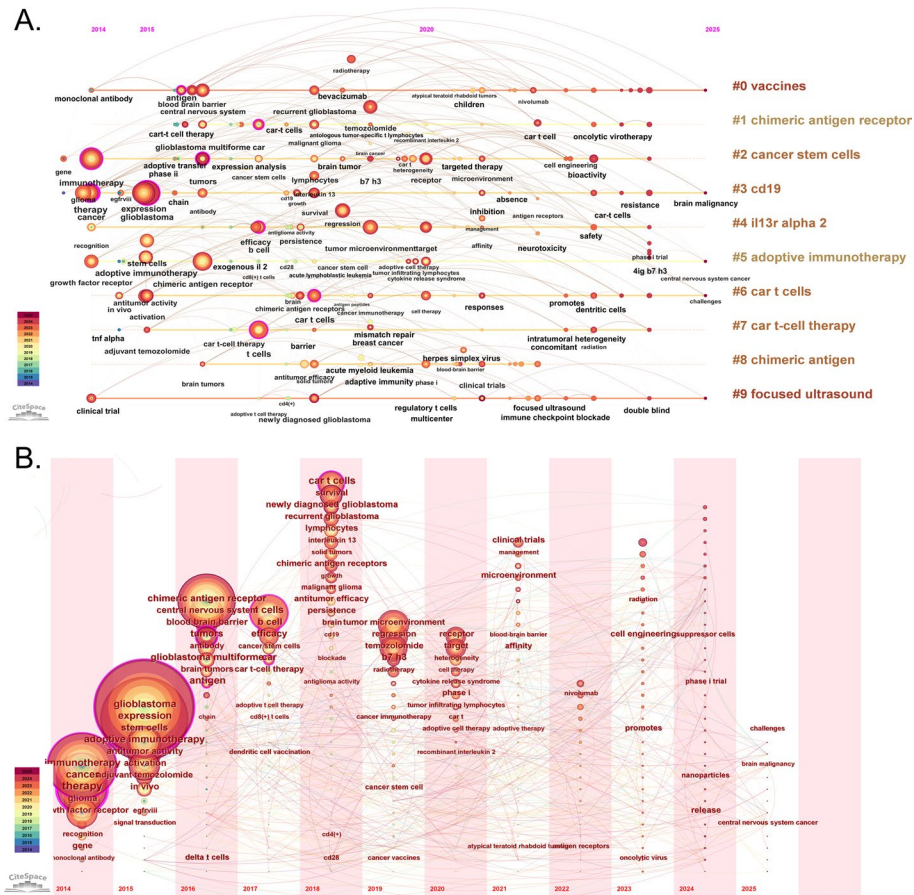


Fig. 8 Temporal evolution of research topics. **A** Timeline view of major keyword clusters. **B** Time-zone view showing the chronological emergence and development of major topics in the field

4.2 Influential authors and journals reflecting the evolution of scientific leadership

The author co-authorship and co-citation networks provide valuable insights into the scholarly backbone of this field. Christine E. Brown, Donald M. O'Rourke, and Zev A. Binder were identified as leading contributors, with high citation frequency and centrality scores. These individuals not only spearheaded landmark clinical trials but also contributed to preclinical innovations such as dual-target CARs, armored constructs, and regional delivery strategies.

Prominent journals such as Neuro-Oncology, Clinical Cancer Research, and Science Translational Medicine ranked among the most frequently co-cited, reflecting the multidisciplinary nature of this field at the intersection of immunology, oncology, and neurobiology. The dual-map overlay of journal citation pathways revealed that publications primarily stem from molecular and clinical medicine disciplines, while drawing foundational knowledge from broader domains such as genetics and cellular biology. This underscores the translational bridge between basic research and clinical implementation. The dominance of these authors and journals not only establishes credibility but also shapes funding priorities, clinical trial frameworks, and future review standards in the field.

4.3 Shifting research hotspots: from antigen discovery to immunomodulatory strategies

Keyword co-occurrence, clustering, and burst analyses clearly illustrate a dynamic shift in research priorities over time in the field of CAR-T cell therapy for glioblastoma. Earlier studies were heavily concentrated on fundamental themes such as “chimeric antigen receptor,” “expression,” and “tumor microenvironment.” These keywords dominated between 2015 and 2018, reflecting an initial phase where research focused primarily on the design of CAR constructs, identification of glioblastoma-specific antigens (e.g., IL13R α 2, EGFRvIII, HER2), and early-phase clinical trials testing their safety and feasibility. Notably, this period saw pioneering efforts by Brown et al. (2015, 2016) and O’Rourke et al. (2017), which introduced single-target CAR-T cells administered via intracavitary or intravenous routes. While these studies demonstrated acceptable safety profiles, they were limited by short-lived responses due to antigen loss, insufficient trafficking across the blood–brain barrier BBB, and rapid functional exhaustion of infused T cells. In addition to conventional single-antigen CARs, several innovative CAR architectures have been developed to enhance efficacy and overcome antigen escape. Among them, dual-CAR systems express two separate CAR constructs targeting different antigens, providing flexibility in tumor recognition and reducing the likelihood of immune escape [26, 27]. Alternatively, tandem-CARs (TanCARs) combine two antigen-binding domains in a single CAR molecule, allowing simultaneous recognition of multiple targets [28]. These approaches are particularly valuable in GBM, where antigen heterogeneity remains a major challenge. For instance, intrathecal delivery of bivalent CAR-T cells targeting EGFR and IL13R α 2 has shown encouraging activity in recurrent GBM patients [10]. Moreover, armored CARs are engineered to secrete immunostimulatory cytokines (e.g., IL-12, IL-18) or express dominant-negative receptors to resist immunosuppressive signals in the tumor microenvironment [29]. Such multifunctional designs aim to improve T cell persistence and functionality in hostile CNS conditions.

As visualized in the cluster timeline and citation burst detection, the field has since evolved rapidly toward immunomodulatory strategies that address the intrinsic limitations of the GBM microenvironment. Starting around 2019, there was a noticeable emergence of keywords such as “adaptive immunotherapy,” “dendritic cells,” “checkpoint blockade,” “TGF- β ,” and “vaccines.” This evolution highlights an increasing awareness of the need to remodel the hostile tumor immune contexture characterized by dense infiltration of regulatory T cells, myeloid-derived suppressor cells (MDSCs), and pro-tumor cytokines into an environment that supports T cell survival and cytotoxicity. These findings are consistent with ongoing trials incorporating combinatorial regimens such as CAR-T cells plus PD-1/PD-L1 inhibitors or the use of engineered “armored CARs” that secrete immunostimulatory cytokines like IL-12 or IL-18 to counteract immunosuppression [30–32].

Moreover, newer clusters like “nanoparticles,” “oncolytic virus,” and “biomarker discovery” that emerged in 2021–2024 point to an interdisciplinary convergence of synthetic biology, biomaterials science, and systems immunology in the development of CAR-T therapies. For example, CAR-T cells loaded into biodegradable hydrogels or co-delivered with viral vectors are being investigated to enhance local retention, mitigate systemic toxicity, and achieve sustained release [33–35]. These novel approaches reflect a strategic shift in therapeutic design from simply delivering tumor-killing cells to orchestrating an immunological transformation within the tumor microenvironment. Furthermore,

logic-gated CAR-T strategies have recently emerged as a promising direction to enhance tumor specificity while minimizing off-target toxicity. Choe et al. introduced SynNotch-CAR T cells that respond to tumor antigen combinations, thereby overcoming challenges related to antigen heterogeneity and CAR-T persistence in GBM [36]. Similarly, Simic et al. engineered tissue-sensing T cells capable of recognizing the brain microenvironment and delivering therapeutic payloads with high spatial precision [37]. These innovations exemplify the shift toward next-generation CAR designs that integrate contextual sensing and programmable logic for safer and more effective immunotherapy in GBM.

Importantly, our analysis also revealed emerging focus on personalized and precision strategies, with burst keywords like “classification,” “identification,” and “transcriptomics” suggesting the integration of omics-based profiling to stratify patients based on antigen expression or immune infiltration patterns. This opens the door for the development of patient-specific CAR-T therapies tailored to tumor molecular signatures, potentially overcoming the challenge of intratumoral heterogeneity that has plagued single-antigen approaches [38, 39].

In summary, the evolution of research hotspots in CAR-T therapy for GBM, as revealed by bibliometric visualization, mirrors the clinical realization that success in solid tumors requires more than target recognition. It demands a multifaceted strategy to penetrate, persist, and function within a suppressive and genetically unstable microenvironment. Our study not only quantifies this transformation but also positions it within a broader translational framework, highlighting the expanding interface between immunoengineering, neuro-oncology, and computational biology.

4.4 Limitations of current literature and challenges in CAR-T implementation

Despite promising advances, several limitations persist in both research methodology and clinical application. First, bibliometric studies are inherently limited by their reliance on indexed publications, which may overlook unpublished or negative trial results. Additionally, our analysis focused on metadata rather than full-text content, making it difficult to differentiate between studies addressing primary versus recurrent GBM, or those using autologous versus allogeneic T cells. Additionally, our analysis was limited to publications indexed in the WoSCC and restricted to English-language articles, which may introduce database and language bias. As a result, relevant studies published in non-English journals or indexed exclusively in Scopus, PubMed, or other regional databases may have been omitted. While WoS remains one of the most widely used sources for bibliometric analysis due to its structured metadata and citation tracking capabilities, future studies could benefit from cross-validation across multiple databases to ensure a more comprehensive and balanced perspective.

Clinically, CAR-T therapy for GBM continues to face biological and logistical hurdles. As noted in Begley et al., antigen heterogeneity remains a formidable barrier, with target loss often occurring after treatment. Furthermore, the immunosuppressive tumor microenvironment, characterized by regulatory T cells, TAMs, and inhibitory cytokines such as TGF- β , limits T cell infiltration and function. Locoregional delivery (e.g., intraventricular infusion) has improved CNS access, but neurotoxicity and pseudo-progression complicate treatment evaluation [40, 41]. The scalability of personalized CAR-T manufacturing is another unresolved issue. While autologous approaches reduce

rejection risk, they prolong production time, whereas off-the-shelf allogeneic products risk immune incompatibility and reduced persistence.

4.5 Future research directions and opportunities for innovation

The future of CAR-T cell therapy for glioblastoma lies in overcoming its current biological and technical constraints through integrated, multi-pronged innovations. One major direction is the refinement of CAR design to address antigen heterogeneity, such as through bispecific or multispecific CARs capable of targeting multiple tumor antigens simultaneously. This strategy may reduce the likelihood of antigen escape and improve tumor coverage. Simultaneously, modulating the tumor microenvironment remains critical. Efforts to engineer CAR-T cells with intrinsic immunomodulatory properties such as armored CARs that secrete cytokines (e.g., IL-18) or express dominant-negative TGF- β receptors have shown promise in preclinical models and are now entering clinical evaluation [42–44]. These approaches aim to improve CAR-T cell persistence and activity in the immunosuppressive central nervous system niche of GBM.

In addition, research is increasingly exploring novel delivery platforms, such as biomaterial-based scaffolds or intracavitary depot systems, to localize and sustain CAR-T cell activity post-surgery. Precision medicine technologies like single-cell transcriptomics and spatial proteomics may facilitate the development of predictive biomarkers for patient stratification and target selection, enhancing therapeutic specificity. Moreover, while most published trials have been limited to early-phase safety assessments, future studies should focus on randomized controlled trials that compare CAR-T cell therapy with existing standard-of-care treatments. These directions, reflected in emerging bibliometric trends such as bursts in keywords related to "nanoparticles," "biomarkers," and "clinical translation," underscore the evolving complexity and translational potential of CAR-T therapy in GBM.

Another important dimension in the evolution of CAR-T cell therapy for GBM is the distinction between autologous and allogeneic approaches. Autologous CAR-T cells, derived from the patient's own T cells, have the advantage of low immunogenicity but are associated with longer production times and variability in T cell quality, an especially critical issue in heavily pretreated GBM patients. In contrast, allogeneic "off-the-shelf" CAR-T cells are generated from healthy donors and engineered to reduce graft-versus-host disease (GvHD) risk, offering scalability and reduced manufacturing time [45]. However, they may face rejection by the host immune system and have limited persistence.

Furthermore, the field has witnessed the emergence of in vivo CAR-T technologies, where CAR constructs are delivered directly into the patient via viral or non-viral vectors, allowing in situ T cell reprogramming [46]. This strategy bypasses ex vivo manipulation and may accelerate therapy accessibility, but safety and transduction efficiency remain key concerns. As such, the distinction between ex vivo and in vivo CAR-T platforms is gaining attention, with several preclinical studies and early-phase trials underway to evaluate their feasibility in solid tumors including GBM.

5 Conclusions

In summary, our bibliometric and visualized analysis delineates the dynamic evolution of CAR-T cell therapy research in glioblastoma. From early-phase clinical feasibility studies to advanced engineering of multifunctional CAR constructs, the field has demonstrated both intellectual vitality and translational ambition. Our findings corroborate clinical observations, identify key contributors and collaborations, and anticipate the next wave of innovation in GBM immunotherapy. By mapping the landscape of this emerging field, we hope to support more informed and strategic decision-making for researchers, clinicians, and funding agencies working to transform CAR-T therapy from a promising concept into a clinically transformative treatment for GBM.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1007/s12672-025-03285-6>.

Additional file 1: Table S1. The top 10 countries/regions and institutions contributing to CAR T cell therapy for GBM research based on publication count.

Additional file 2: Table S2. Top 10 authors and co-cited authors in CAR T cell therapy for GBM research.

Additional file 3: Table S3. Top 10 journals and co-cited journals in CAR T cell therapy for GBM research.

Additional file 4: Table S4. Top 10 highly co-cited references in CAR T cell therapy for GBM research.

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Not applicable.

Author contributions

Jian Li and Lichun Lu designed the study, conducted the literature search, and performed the data analysis. Yu Duan, Guohui Huang, Xuhao Fang, and Yao Deng contributed to data collection, visualization, and interpretation. Feng Tang provided critical revisions. Feng Jiang and Dongwei Dai supervised the project and revised the manuscript critically for important intellectual content. All authors read and approved the final manuscript.

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Data availability

The data supporting the findings of this study are publicly available from the WoSCC database. The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable. This study is a bibliometric analysis based on publicly available data from the WoSCC and does not involve human participants, animals, or identifiable personal data. Therefore, ethical approval and informed consent were not required. Clinical trial number: not applicable.

Consent to publication

Not applicable.

Competing interests

The authors declare no competing interests.

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