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Research trends in anti-rabies virus monoclonal antibody: A bibliometric analysis

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ABSTRACT

Rabies is a fatal zoonotic infectious disease primarily caused by the rabies virus. Anti-rabies monoclonal antibody (mAb) is developed using modern genetic engineering technology. However, no bibliometric assessment has been conducted to evaluate the scientific progress in this area. A search of articles in the Web of Science (WoS) from January 1, 1991, to November 17, 2024, yielded 455 papers that were analyzed using various online analysis tools. The cumulative publications from 1991 to 2023 followed a linear distribution. The United States and China led this research initiative. Keywords were divided into two clusters, including "monoclonal-antibody" and "post-exposure prophylaxis." This systematic bibliometric analysis of the literature on anti-rabies monoclonal antibodies will help to reveal the internal relationship of the whole research and development network and promote the perfection of related research and development work to a considerable extent. This study not only delineates the historical trajectory and current status of mAb research but also provides valuable insights and concrete recommendations for future directions.

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Introduction

Rabies, is an infectious disease primarily invading the central nervous system, mainly caused by the rabies virus (RABV), a single-stranded RNA virus of the Lyssavirus genus.[1] Rabies, known as a highly fatal zoonotic disease, has an almost 100% fatality rate and causes 59,000 human deaths annually in over 150 countries.[2,3] Post-exposure prophylaxis (PEP) is considered the most effective strategy for preventing rabies by the World Health Organization (WHO).[4] Prompt and effective PEP can almost entirely prevent the onset of the disease.[3] PEP includes: 1. Effective washing of all wounds that occurred during exposure, 2. Prompt administration of rabies vaccine, and 3. Correct use of rabies immunoglobulins (RIGs) if indicated.[5] Available RIGs include equine rabies immunoglobulin (ERIG), and human rabies immunoglobulin (HRIG).

ERIG derived from the plasma of immunized horses may cause serious side effects and hypersensitivity reactions.[6] HRIG derived from the serum of immunized humans is considered safer than ERIG, but it is hindered by its high cost and the insufficiency of donors. Since rabies vaccines cannot provide comprehensive and timely protection, RIGs are limited due to supply, cost, and safety, monoclonal antibody (mAb) can be the best choice in rabies PEP.[6]

The mAb products are developed and produced using modern genetic engineering technology in recent decades. They can specifically bind to different antigenic sites on the surface glycoprotein (GP) of the RABV blocking the virus from binding to cell surface receptors, preventing the virus from invading cells, and ultimately being cleared by the human immune system. RABV GP has distinct antigenic sites (AS): I (a.a.226–231), II (IIa a.a.198–200, IIb a.a.34–42), III (a.a.330–338), IV (a single a.a.251), minor site a (a.a.342–343, otherwise referred to as G1), and G5 (a.a.261–264, also comprises as VI, a single a.a.264), which are potential sites of mAbs.[6]

Currently, the mAb products have been a major hotspot in the field of rabies prevention, which are considered to have the advantages of high purity, high affinity, high safety, and sustainable large-scale production, and has a good prospect for clinical application in PEP of rabies. Multiple anti-rabies mAb preparations are advancing in clinical research globally, with at least four antibody products already on the market: 1. Rabishield produced by the Serum Institute of India Pvt Ltd. was launched in 2017;[7] 2. TwinRab produced by the Zydus Lifesciences Ltd. was launched in 2019;[8] 3. Ormutivimab produced by North China Pharmaceutical Research and Development Co., Ltd. was launched in 2022.[9] 4. Zamerovimab/Mazorelvimab produced by Synermore Biologics (Suzhou) Co., Ltd. was launched in 2024.[10]

The research of mAb against RABV has been international from the beginning. The key phase III clinical studies of anti-rabies mAb were mainly carried out in India and China. Systematic bibliometric analysis of the literature on anti-rabies mAb will help to reveal the internal relationship of the whole research and development network and promote the improvement and perfection of related research and development work to a considerable extent.

As far as we know, there is no bibliometric study on mAb against RABV. Therefore, this study quantifies and analyzes the literature on mAb against RABV, to evaluate research trends.

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Methods

Data source and search strategy

The data used in this study were downloaded from the Web of Science Core Collection (WoSCC), Science Citation Index Expanded (SCI-E) database (https://webofknowledge.com/). The SCI – E database was retrieved through Peking University Online Library. Web of Science (WoS) is a widely used database in bibliometric studies in various research zones, which was chosen for our analysis because of its rigorous journal curation, historical depth, citation network integrity, and standardized data.

The data sources, selection, and extraction are listed in Table 1. The finalized and integrated retrieval strategy is "TS = (monoclonal or (monoclonal antibody) or (anti-rabies virus monoclonal antibody) or mab*) AND TS = (rabies)."

Our exclusion criteria were primarily based on the type of publication, language, and research topic. A comprehensive depiction of the entire screening process is presented in Figure 1. The data extraction was performed on 17 November 2024, to reduce database update bias.

Table 1. Data sources, selection, and extraction details.

Category	Specific standard requirement
Research database	Web of Science core collection
Citation indexes	SCI-E
Time span	1 January 1991 to 27 November 2024
Data extraction time	27 November 2024
Language	English
Document types	Article, Review
Sample size	4515
Data extraction	Export with records and citedreferences in BibTex format

Bibliometric analysis

Bibliometric analysis and plotting visualizations of countries, institutions, and keywords were performed by R 4.3.3 (© R Foundation for Statistical Computing, 2023). Country-level h-index values were directly extracted from WoS using its built-in analytical tools in selected articles. In network visualization and overlay visualization defined by co-occurrence frequency from all countries, authors, keywords and institutions. Nodes represent specific indicators and Node size corresponds to frequency. Edges (connections) indicate the strength of co-occurrence between pairs of nodes within the same publication, and edge thickness reflects connection strength. In the overlay visualization, the colors of the nodes represent their average year of occurrence.

Results

Publication trends

Publication trends are shown in Figure 2a. The most frequent year of publication was 2013 ($n = 24$, 5.3%), while the less frequent year of publication was 2001 ($n = 7$, 1.6%). The cumulative publications from 1991 to 2023 proved to follow a linear distribution, via regression analysis ($p < .001$) (Figure 2b). Each publication received an average of 1.64 citations per year, with the highest peak occurring in 2014 at 3.36 citations per publication (Figure 2c).

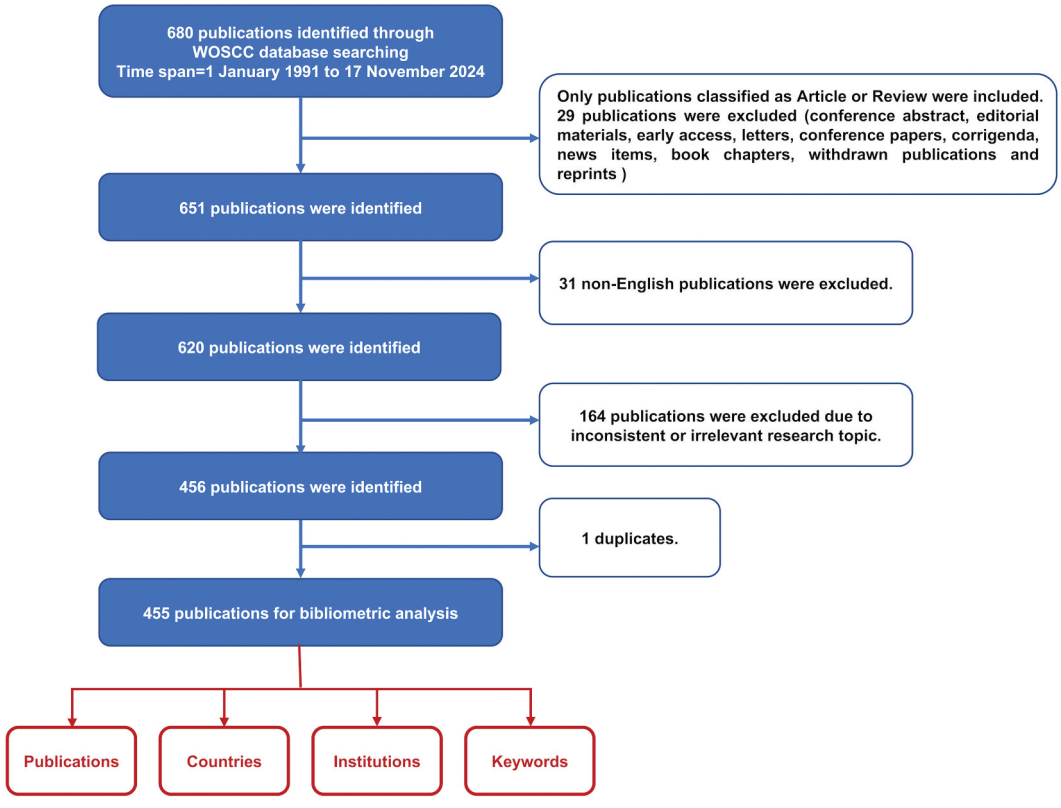


Figure 1. Literature screening procedures.

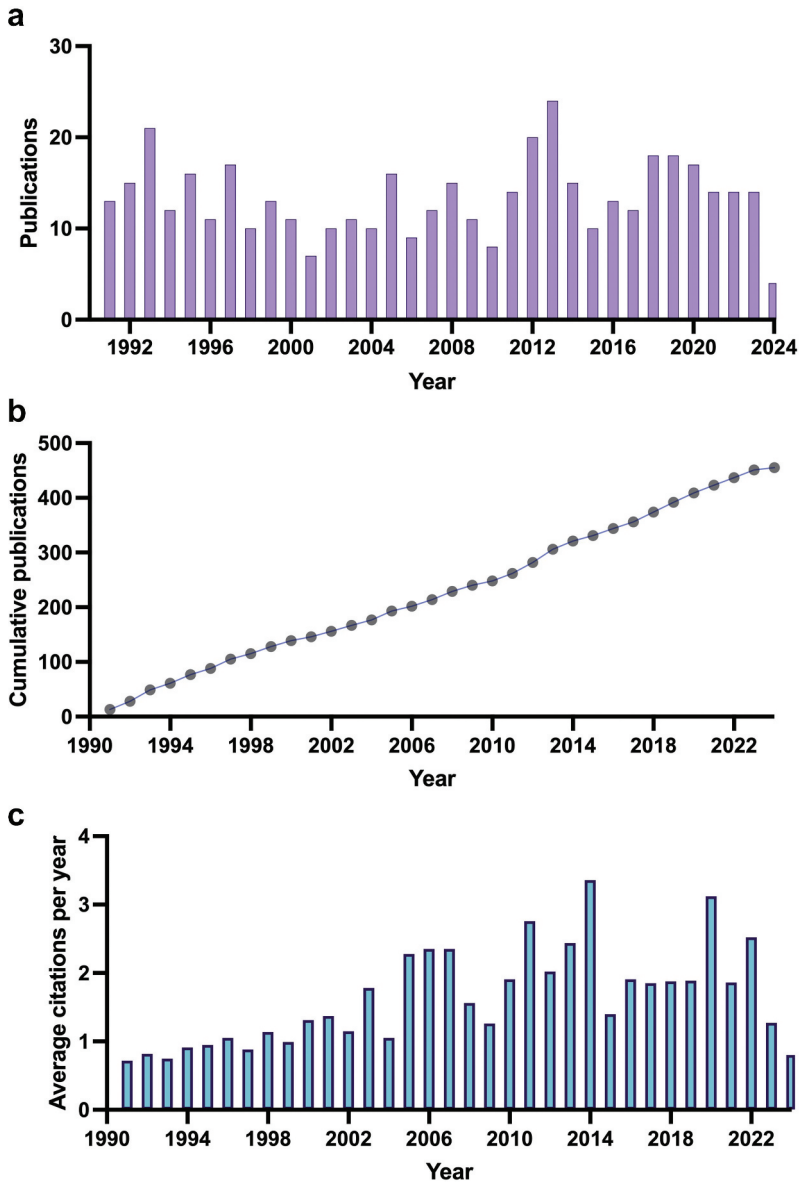


Figure 2. Publication trends in research. (a) Annual publication volume of global science Citation Index (SCI) studies. (b) The curves of the cumulative number of publications. (c) Annual average citations of studies.

Countries

A total of 52 countries/regions contributed to the global scientific output. The annual number of countries with production in anti-rabies mAb research increased to 52 in 2023. However, there was a dip in the number of contributing countries for 1991, with a total of 8.

The top-10 countries/regions in terms of publications are listed in Table 2. Among them, USA ($n = 90$), CHINA ($n = 63$) and JAPAN ($n = 36$) are the top three. Comparative map of the cumulative number of papers published in each country is shown in Figure 3a. The Top ten productive countries/regions ranked by the number of publications are shown in Table 2. Figure 3b shows the change in publications for the top ten countries, revealing that most countries showed consistently increasing publications. The top three countries/regions cited most were the USA, UNITED KINGDOM and FRANCE. Figure 3c highlights a strong collaboration between INDIA and the USA, CHINA and the USA, FRANCE and SWITZERLAND. The USA also has frequent collaborators with European countries, such as FRANCE, GERMANY, NETHERLANDS. The USA, FRANCE, and CHINA are the three central nodes.

Institutions

Five hundred and forty-eight institutions globally made contributions to publications. However, it is worth noting that only 12 of these institutions had over 10 publications. Table 3 displays the ten institutions with the most publications. *PASTEUR NETWORK*, was a global association with members from 25 countries, which had most publications. The other two hailing from the USA, three from CHINA, two from FRANCE, and the remaining two from JAPAN. Figure 4a displays the cumulative number of publications for the top three institutions over time. It is evident that these institutions keep the

Table 2. Top ten productive countries/regions by corresponding author ranked by the number of publications.

Country/Region	Count (percentage)	Total (citations)	Average Article Citations	H-index
USA	90 (19.78)	2673	29.7	40
CHINA	61 (13.41)	569	9.2	14
JAPAN	36 (7.91)	616	17.1	19
FRANCE	28 (6.15)	877	31.3	26
INDIA	24 (5.27)	380	15.8	14
UNITED KINGDOM	23 (5.05)	1054	45.8	22
BRAZIL	19 (4.18)	298	15.7	12
SOUTH AFRICA	14 (3.07)	372	26.6	13
CANADA	13 (2.86)	341	26.2	12
NETHERLANDS	12 (2.64)	689	57.4	14

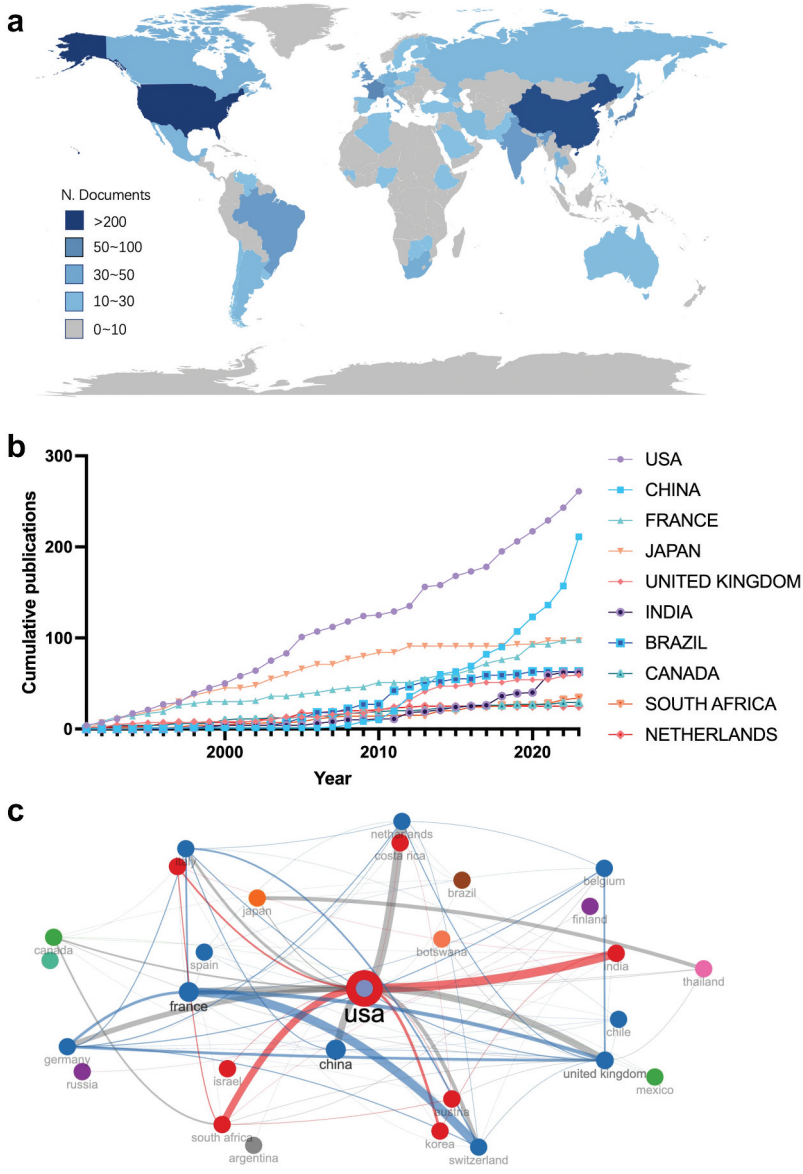


Figure 3. (a) Comparative map of the cumulative number of papers published in each country. (b) The change in publications for the top ten countries. (c) Cooperation networks in countries around the world.

increasing trend consistently. Notably, *PASTEUR NETWORK*, as a global association, exceed the *CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC)* and JEFFERSON UNIVERSITY in recent years. Network visualization (Figure 4b) revealed that there are only two central institutions: *PASTEUR NETWORK* and *the CDC*.

Journals

A total of 175 journals were involved in global publications. Table 4 showcases the top ten journals based on the number of publications. Among the top ten journals, the *VACCINE* leads with 36 publications, followed closely by *MICROBIOLOGY*

Table 3. Top-10 most productive institutions.

Ranking	Institutions	Count
1	PASTEUR NETWORK	59
2	CENTERS FOR DISEASE CONTROL AND PREVENTION	48
3	JEFFERSON UNIVERSITY	45
4	UNIVERSITE PARIS CITE	37
5	INSTITUT PASTEUR PARIS	36
6	KYOTO UNIVERSITY	28
7	OITA UNIVERSITY	25
8	JILIN UNIVERSITY	21
9	CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE (CNRS)	16
10	ACADEMY OF MILITARY MEDICAL SCIENCES – CHINA	15

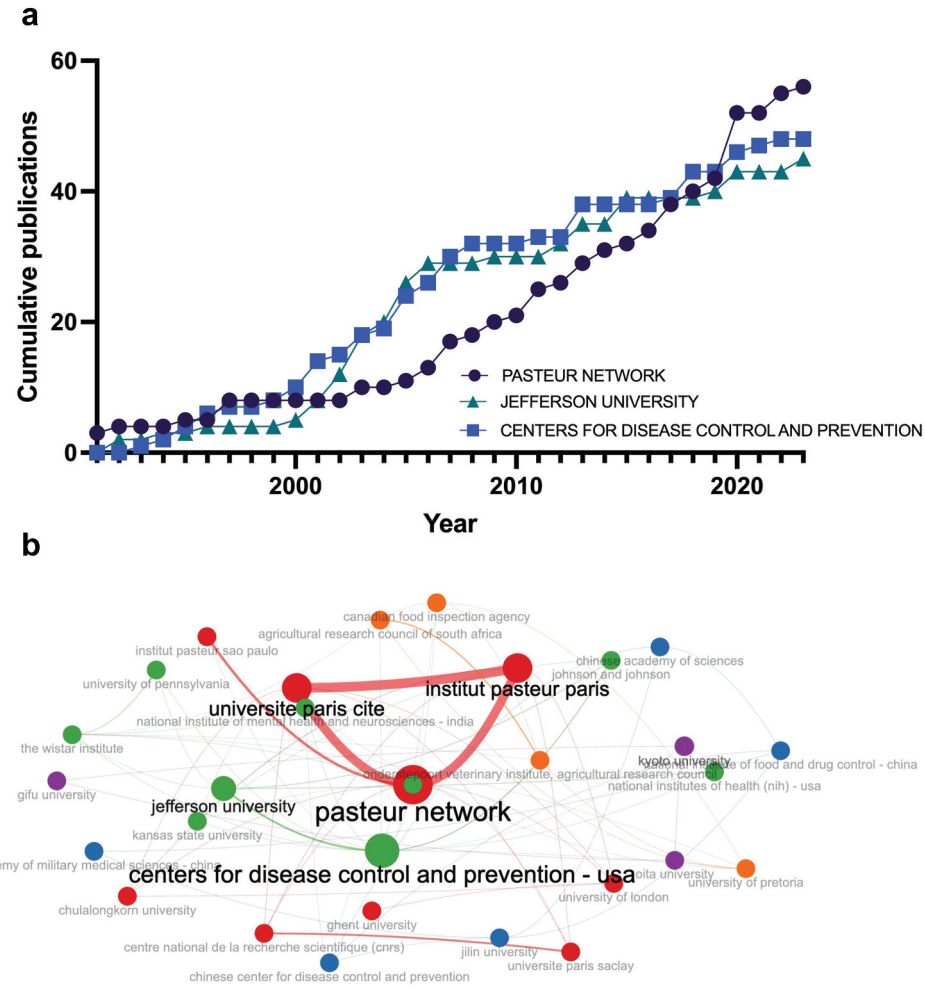


Figure 4. (a) The curves of the cumulative number of publications the top three institutions over time. (b) Cooperation networks in institutions around the world.

Table 4. Top-10 most productive journals in rabies monoclonal antibodies.

Ranking	Journals	Count
1	VACCINE	36
2	MICROBIOLOGY AND IMMUNOLOGY	25
3	JOURNAL OF VIROLOGY	19
4	VIRUS RESEARCH	16
5	JOURNAL OF GENERAL VIROLOGY	15
6	JOURNAL OF VIROLOGICAL METHODS	14
7	ARCHIVES OF VIROLOGY	11
8	PLOS ONE	10
9	VIRUSES-BASEL	10
10	BIOLOGICALS	9

AND IMMUNOLOGY ($n = 25$), and *JOURNAL OF VIROLOGY* ($n = 19$).

The publications of *VACCINE* are consistently growing over time, and most other journals have maintained a steady since 2010 (Figure 5a). According to Bradford's law, all journals were classified into zones 1–3, with 9 core source journals falling into zone 1 (Figure 5b).

JOURNAL of VIROLOGY, VACCINE, and *JOURNAL OF GENERAL VIROLOGY* are the top-3 most cited journals. Figure 5c displays the H-index of different journals, and both

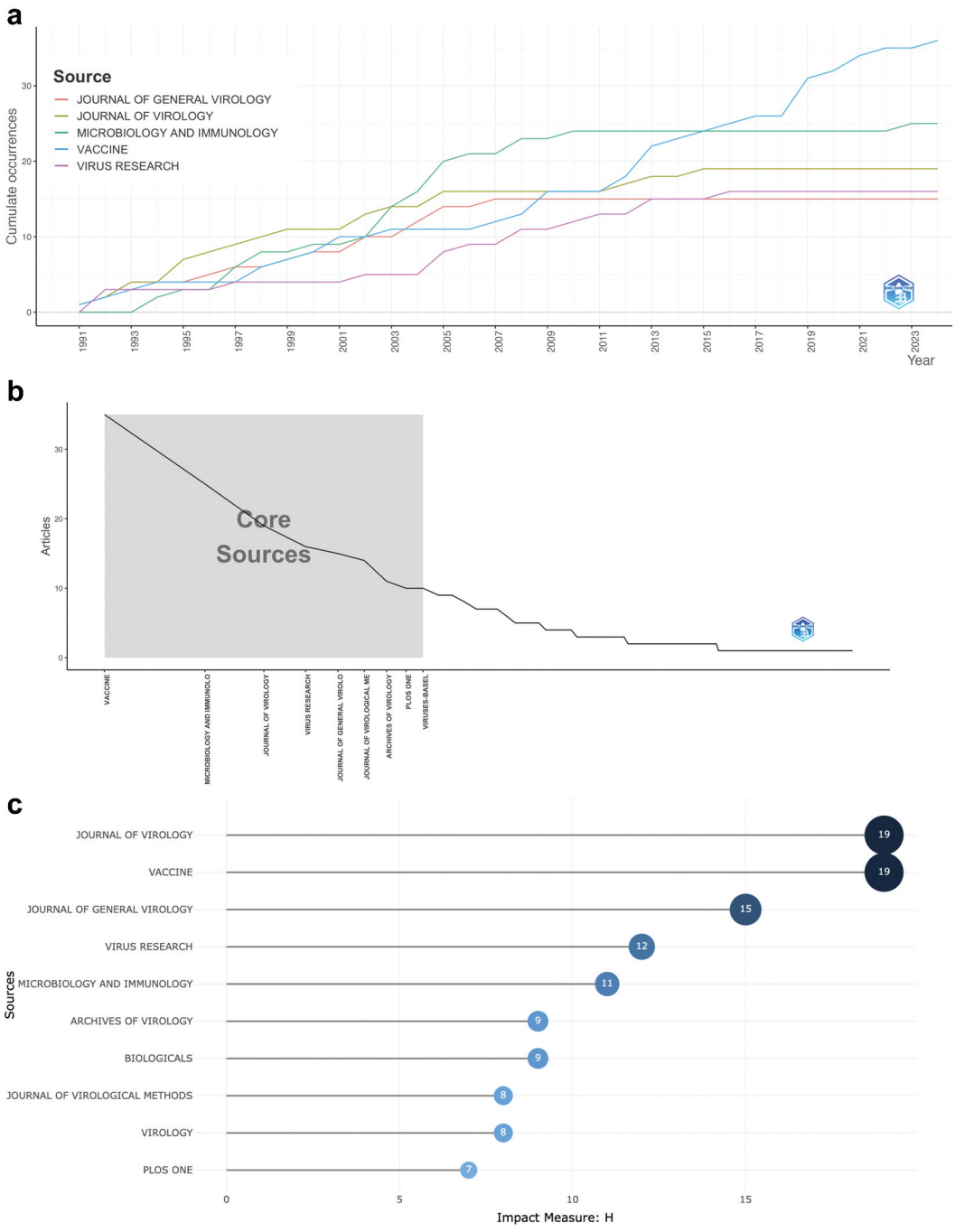


Figure 5. (a) The curves of the cumulative number of publications the top five journals over time. (b) Core sources by Bradford's law. (c) The H-index of the top ten journals.

JOURNAL of VIROLOGY and *VACCINE* showed the highest H-index.

A total of 180 publications had funding information. The top ten funding agencies are listed in Table 5. The United States Department of Health and Human Services of USA supported 38 studies, ranking the first. Within the ranking of top funding agencies, Top-three are all held by USA organizations, other three belong to the JAPAN, EUROPEAN UNION and CHINA held two respectively.

Authors citation

The number of single-author articles was 24. Of the 1905 authors, Rupprecht Charles E was the most prolific author (documents = 40, citations = 493), who keeps productively annually. Only nine authors had published at least ten studies. The top ten productive authors are shown in Table 6. Figure 6 shows the authors' collaboration network, revealing that Rupprecht Charles E was also in a central position regarding author collaboration.

Table 5. Top-10 related funding agencies.

Ranking	Funding Agencies	Count
1	UNITED STATES DEPARTMENT OF HEALTH HUMAN SERVICES	38
2	NATIONAL INSTITUTES OF HEALTH NIH	36
3	NIH NATIONAL INSTITUTE OF ALLERGY INFECTIOUS DISEASES NIAID	19
4	NATIONAL NATURAL SCIENCE FOUNDATION OF CHINA NSFC	17
5	EUROPEAN UNION EU	8
6	WELLCOME TRUST	7
7	GRANTS IN AID FOR SCIENTIFIC RESEARCH KAKENHI	5
8	JAPAN SOCIETY FOR THE PROMOTION OF SCIENCE	5
9	MINISTRY OF EDUCATION CULTURE SPORTS SCIENCE AND TECHNOLOGY JAPAN MEXT	5
10	NATIONAL KEY RESEARCH DEVELOPMENT PROGRAM OF CHINA	5

Table 6. Top-10 most productive authors.

Ranking	Authors	Articles (count)	Articles Fractionalized
1	RUPPRECHT CE	40	7.26
2	KAWAI A	27	5.91
3	DIETZSCHOLD B	17	3.59
4	MINAMOTO N	12	1.41
5	FLAMAND A	11	2.32
6	KOPROWSKI H	11	2.09
7	NIEZGODA M	11	1.64
8	NISHIZONO A	11	1.56
9	SCHNELL MJ	11	2.25
10	FOOKS AR	10	1.62

Keywords

Characteristics of the top ten most cited research articles are shown in Table 7. After eliminating meaningless terminology and consolidating synonymous expressions, singular and plural forms, and abbreviations and full names, the top ten high-frequency keywords are displayed in Figure 7a and the word cloud of top 30 high-frequency keywords is shown in Figure 7b. Monoclonal-antibody was the most used keyword ($n = 146$).

Figure 8a represents the co-occurrence of all keywords. The keywords were displayed in two clusters. The monoclonal-antibody and glycoprotein were central keywords of the bigger cluster. These key messages are concisely and succinctly sketched.

The top three keywords with Citation Bursts are shown in Figure 8b. The latest keywords are indicative, to some extent, of the current research frontiers and emerging trends. We also analyzed the trend topic and found that it was *noninferiority in 2021*, *vaccine* in 2019, and *immunogenicity* in 2018.

Discussion

Rabies is one of the most dangerous acute encephalitis caused by RABV infection. Currently, effective treatments are still lacking for rabies. The administration of passive immunity soon after exposure is essential to inhibit viral spread in the interval before sufficient immunity is developed in response to vaccination.[19]

Rabies mAb products have made considerable progress in the urgent PEP of rabies. The development of safe, effective, and affordable rabies mAb products was still the direction for

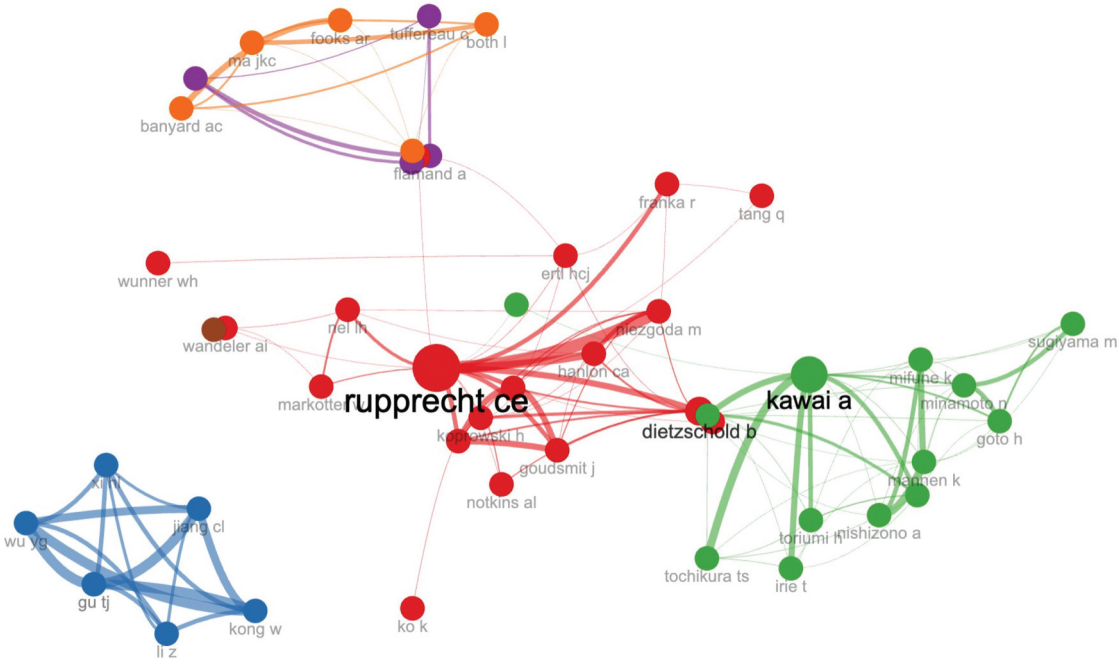


Figure 6. The authors' collaboration network.

Table 7. Top-10 most cited research articles.

Author	Descriptions	Total Citations	TC per Year	Year	JOURNAL
BAKKER ABH[11]	The study characterized one human MAb (CR57) strong neutralizing activity and broad specificity. It identified linear binding at antigenic site I on the RV glycoprotein through CR57 escape mutant analysis. Additionally, phage display identified another antibody (CR4098), targeting a distinct epitope (antigenic site III), which matched CR57's neutralizing strength and effectiveness against escape mutants. In summary, a new combination of Mab was found to potentially replace RIG.	53	4.51	2005	J VIROL
MARISSEN WE[12]	Researchers generated two potent rabies virus-neutralizing human monoclonal antibodies (MAbs), CR57 and CRJB, using human PER.C6 cells. CR57 escape mutants were partially neutralized by CRJB, while CRJB-resistant variants fully evaded CR57. The competition and escape profiles suggest that combining CR57 and CRJB in a MAb cocktail to replace traditional immunoglobulin preparations is inadvisable.	51	4.34	2005	J VIROL
BAKKER ABH[12]	The study report presents clinical data from two phase I trials of the monoclonal antibody cocktail CL184 against rabies. The trials included healthy adults from the USA and India and had two phases. First, participants received a single intramuscular dose of CL184 or placebo in a randomized, double-blind, dose-escalation trial. Second, CL184 (20 IU/kg) was administered alongside the rabies vaccine. In summary, CL184 shows promise as an alternative to RIG in post-exposure prophylaxis.	44	8.46	2008	VACCINE
GOUDSMIT J[13]	The study compared the CR57/CR4098 MAb cocktail and HRIG. When combined with a vaccine, the MAb cocktail protected Syrian hamsters from lethal rabies if given 24 hours after exposure, similar to HRIG results. These findings show that the CR57 and CR4098 human MAb cocktail is a safe and effective alternative to RIG for rabies postexposure.	41	4.79	2006	J INFECT DIS
SLOAN SE[14]	HuMAb 17C7 was the most promising antibody identified because it neutralized all rabies virus isolates tested. HuMAb 17C7 recognizes a conformational epitope on the rabies virus glycoprotein which includes antigenic site III. HuMAb 17C7 protected hamsters from a lethal dose of rabies virus in a well-established in vivo model of post-exposure prophylaxis.	38	4.61	2007	VACCINE
PROSNIAK M[15]	The study employed recombinant DNA technology to express three human rabies virus-neutralizing monoclonal antibodies (huMAbs) in a rhabdovirus vector. Mice and hamsters treated once with this rhuMAb cocktail post-infection were protected. The postexposure prophylaxis (PEP) efficacy of the rhuMAb cocktail matched that of HRIG, indicating that rhuMAbs warrant serious consideration for future human PEP.	35	4.05	2003	J INFECT DIS
HANLON CA[16]	Rabies virus-neutralizing human monoclonal antibodies (Mabs) were evaluated in vitro and in a Syrian hamster model as a potential future alternative. However, a European bat lyssavirus was not neutralized by either Mabs or RIG. In hamsters, one Mab resulted in protection that was comparable to human RIG. These results suggest that Mabs may provide a promising alternative to RIG.	32	4.23	2001	VACCINE
DE KRUIF J[17]	This review sets out the criteria used to guide development of a cocktail of human monoclonal antibodies as a replacement for RIG. Using this process as a model, the general requirements for development of safe and efficacious monoclonal antibody alternatives to currently used polyclonal serum products are discussed.	32	3.88	2007	ANNU REV MED
BOTH L[18]	This article highlights advances in passive immunoprophylaxis for rabies, notably the transition from polyclonal human or equine immunoglobulins to monoclonal antibody therapies. The first rabies-specific monoclonal antibodies are in clinical trials, making passive immunization a potential standard in global rabies health practices.	30	5.94	2012	LANCET INFECT DIS
GOGTAY NJ[18]	This phase 2/3 randomized, single-blind, noninferiority study involved 200 participants with suspected rabies exposures. The PEP regimen with SII RMAb was safe and showed noninferiority to HRIG PEP in RVNA production. This new monoclonal offers a safe, potent alternative for PEP management of suspected rabid animal bites.	27	12.46	2018	CLIN INFECT DIS

subsequent research.[20] However, in low- and middle-income countries where this disease exists, majorly one of the significant challenges in mAb products is a refusal to receive mAb products due to expense, they remain at high risk of RABV infection.[20,21]

This study is the first bibliometric analysis on rabies mAb to highlight research and publication trends in the last three decades, which may be helpful for the academia, government organizations, scholars, policymakers, and funders, to critically evaluate the funding applications and future research trends. In addition to articles, reviews were also involved in analysis. Highly cited reviews reflect consolidated consensus, while emerging reviews highlight novel research frontiers, which play a necessary role in thematic mapping.

This bibliometric analysis found year-wise publication trend is roughly maintained stable with slight fluctuations in the last three decades and the cumulative publications followed a liner distribution. It may be because of the research popularity in rabies mAb was consistent, regardless of different country or funding provision.

Before 2010, the literature on anti-rabies mAb mainly focused on preparation methods and laboratory tests. Bakker et al. used phage antibody display technology to prepare mAb against RABV GP neutralizing epitope, which showed good neutralizing activity against RABV street strain.[22] Niezgoda et al. of the *CDC* have improved the laboratory testing system of anti-rabies mAb, identified its target by preparing escaped mutant strains of RABV mAb, and carried out mAb protection tests using mice as animal models to simulate rabies exposure, in vitro and in vivo tests were conducted to identify neutralization response spectra of mAb against different strains of RABV.[11] These works basically established the laboratory testing system for anti-RABV mAb. This framework provided essential data prior to clinical trials. Following this, global preclinical investigations on anti-RABV mAb largely adhered to comparable laboratory validation processes. During this period, the volume of publications was scant and confined to specific researchers and institutions. Notably, INIDA and CHINA did not exhibit any indications of bibliometric trade-offs at that time.

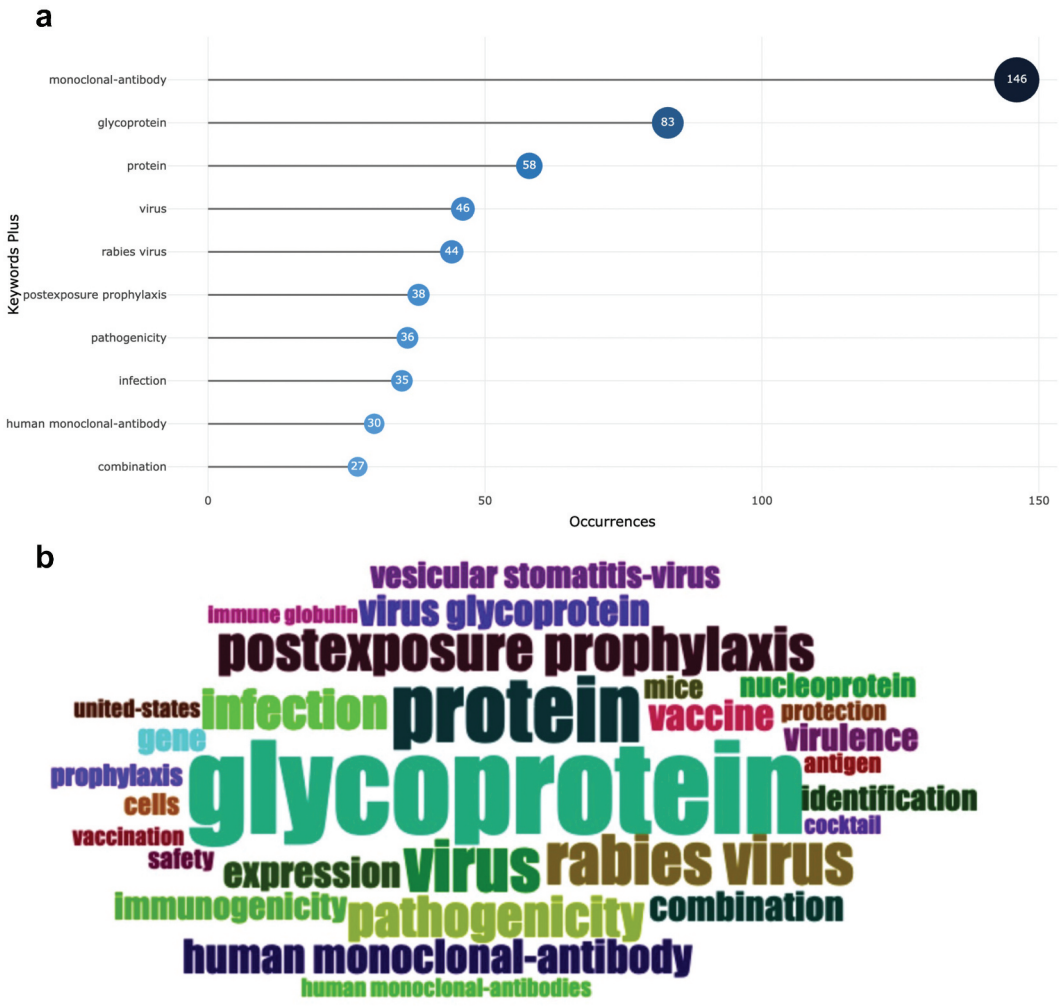
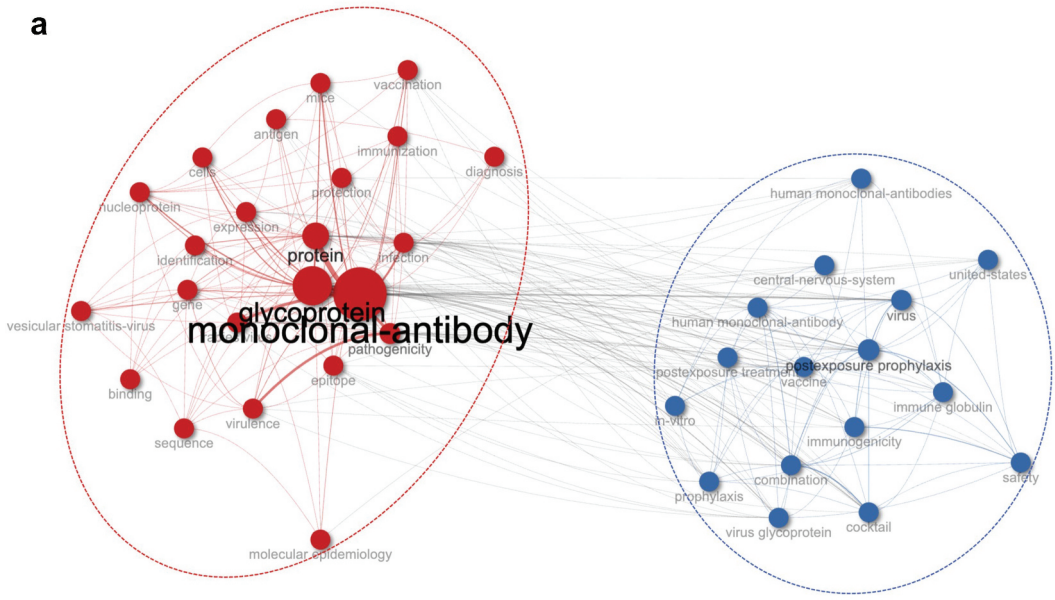


Figure 7. (a) The top 10 high-frequency keywords. (b) The word cloud of top 30 high-frequency keywords.

Between 2011 and 2020, global publications concerning anti-rabies mAb grew markedly. At the same time, the literatures indicate that most of the anti-rabies mAb have progressed to clinical research stages.[23–25] It also highlights a diversification among researchers and institutions. Notably, researchers in INDIA and CHINA have reported a substantial rise in the development of mAb targeting the RABV. The Serum Institute of India developed SII RMAb (market name Rabishield), a human mAb against the RABV, utilizing transgenic mice.[7] It received marketing authorization in India in 2017. RabiMabs (trade name TwinrabTM), a combination of two murine mAb against RABV prepared by Zydus Lifesciences Ltd in India using hybridoma cell technology, was approved for marketing in India in 2019.[26] In CHINA, the North China Pharmaceutical Group New Drug Research and Development Co., Ltd.,[27] Synermore Biologics (Suzhou) Co., Ltd,[28,29] and other institutions have reported the development of a number of anti-rabies mAb preparations. These agents are undergoing preclinical studies and different phase clinical studies. Several mAb preparations developed in CHINA were also studied in the neutralization response spectrum of Chinese street rabies virus strains at the Chinese Center for Disease Control and Prevention.[30,31] As the focus of anti-rabies mAb research and clinical trials shifts to developing nations, primarily INIDA and CHINA, the diversity of research organizations and researchers has increased. However, these efforts remain largely centralized within a limited number of specialized institutions and biomedical companies.

Since 2021, the world's most important anti-RABV mAb preparations research and development force has mainly gathered in China. Professional institutions and biomedical enterprises in China have successfully developed a variety of humanized mAb preparations against RABV. Among them, the single anti-RABV mAb preparation NM57 (Ormutivimab)[27] developed by North China Pharmaceutical Group New Drug Research and Development Co., Ltd. has been approved for listing in January 2022. Additionally, the SYN023 combination preparation (Zamerovimab/Mazorelvimab), developed by Synermore Biologics (Suzhou) Co., Ltd., has successfully completed phase III clinical studies and obtained the Drug Registration Approval on June 2024.[29,32] According to literature, the Yunnan Provincial Center for Disease Control and Prevention stands out as the primary institution conducting clinical research on



b

Keywords	Year	Strength	Begin	End	2013 - 2023
Immunogenicity	2018	3.32	**2018**	2021	
Vaccine	2019	2.65	**2019**	2020	
Noninferiority	2021	3.11	**2021**	2023	

Figure 8. (a) The co-occurrence of all keywords. (b) The top three keywords with citation Bursts.

anti-rabies mAb preparations in China, with Liu Xiaoqiang recognized as the leading researcher in this area. Except for the combination preparation clinical study initiated by Synermore Biologics (Suzhou) Co., Ltd. in the United States,[32,33] other mAb therapies developed in China have not yet pursued clinical trials outside the country.

Countries at the periphery of the global scientific network, depicted as isolated nodes in visualizations, encounter challenges in collaborating with other nations. From the network visualization, we could demonstrate that global collaboration plays an important role in research and a significant degree of global collaborative consensus in addressing pressing scientific issues. The USA, with most productive and most cited publications, played a central role in global collaboration and took the leading position in research area. CHINA was acknowledged as an emerging region in the realm of rabies research.[21] This shift highlights CHINA's rapid advance and a significant leap forward in this field. This disparity further emphasizes the significance of not only the quantity but also the quality and impact of publications.

Among the organizations focused on the rabies vaccine, *PASTEUR NETWORK* (a global healthy alliance) produced most publications, followed by *CDC*. This may be due to the focus and priority of the institutes on specific research problems.

It is worth mentioning that the journal *Vaccine* published the largest number of papers on rabies monoclonal antibody. *JOUNAL of VIROLOGY* is placed in 1st position among the most attractive journals. While our analysis comprehensively incorporates publications across all journal tiers, Bradford's Law highlights a concentration of influential studies in high-impact core journals. This skewness underscores the role of core journals in shaping dominant research paradigms, whereas peripheral journals foster niche explorations and methodological innovation

Of the top-10 most cited studies, 3 were published in *VACCINE* (2022 IF:4.5, JCR Q2) and top-2 were published in *JOUNAL of VIROLOGY* (2022 IF:4, JCR Q2). The article published by Xiang in 1993 was the most cited article with 53 citations. The year of publication and the nature of study both play a significant role in getting more citations. The prominence of these journals in rabies mAb research underscores their pivotal role in consolidating high-impact discoveries. These journals serve as conduits for translating structural insights into clinical innovations while elevating the global profile of rabies therapeutics.

The co-authorship visualization network mapping showed that cooperation exists among most of the authors. However, the international collaboration among the groups/labs working on rabies vaccine is not as connected and robust as it should be.

Future trends

In the coming decades, it is anticipated that research on anti-rabies monoclonal antibody will continue to evolve. Future studies are likely to focus on novel combinations of fully humanized mAbs to enhance neutralizing breadth and potency against diverse rabies virus strains. Two or more mAbs cocktail recognize nonoverlapping, noncompeting epitopes, cross-protect against viral escape mutations. Fully humanized mAbs also minimize potential risks associated with immunogenicity. While Phase III trials for mAbs like Ormutivimab and Zamerovimab/Mazorelvimab have demonstrated non-inferiority to HRIG, broader demographic inclusion remains essential. Future trials may involve pediatric populations, immunocompromised individuals, and patients exposed to atypical lyssaviruses. Post-marketing studies are expected to gradually increase, particularly in regions such as China and India, where the adoption of mAbs is rapidly growing. These studies will provide crucial data regarding long-term safety, real-world efficacy, and rare adverse events. Multi-center collaborations, such as those initiated by the Pasteur Network, could standardize data collection and harmonize protocols globally. Furthermore, the synergistic effects between mAbs and next-generation rabies vaccines represent an unexplored frontier. The future related research, such as the combination of mAbs with mRNA vaccines and novel adjuvant vaccines, may transform existing PEP strategies. Beyond PEP, mAbs could potentially serve as therapeutics for symptomatic rabies, a condition currently considered untreatable. Preliminary studies utilizing intrathecal mAb delivery to bypass the blood–brain barrier warrant further investigation. Additionally, advancements in nanobody technology, with their smaller size and enhanced tissue penetration, could revolutionize RABV neutralization in neural tissues. The future of anti-rabies mAb research hinges on interdisciplinary innovation, equitable access, and robust global partnerships.

Strengths and limitations

As the pioneering bibliometric analysis of anti-rabies monoclonal antibodies summarized and sorted out by experts across multiple fields, this study provides a foundational framework for understanding the current global status and future directions of research in this field.

However, there are some limitations in this study. First, due to the rigorous journal curation process, comprehensive journal coverage, and alignment with bibliometric standards, only publications indexed in the WoS database were included. However, its reliance on WoS highlights the need for future work to adopt more equitable data sourcing practices. Our analysis identified four developing countries (India: 5.3%, China: 13.4%, Brazil: 4.2%, South Africa: 3.1%) among the top ten productive nations, collectively contributing 26.0% of publications. While this reflects notable engagement, systemic biases persist. Inherent biases of WOS including language preferences, open access costs and limited digital library access might reduce visibility of local research in developing country and limit its ability to fully capture the global rabies mAb landscape. Complementary use of regional databases and equitable citation practices are critical to advancing inclusive scholarship in this field. Second, the document search was refined by considering the publication time, type, and language of the literature, which led to the exclusion of certain literature from this analysis.

Conclusion

The Systematic bibliometric analysis of the literature on anti-rabies mAb will help to reveal the internal relationship of the whole research and development network, and promote the improvement and perfection of related research and development work to a considerable extent.

Disclosure statement

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Author contributions

CL and SL: conceived and designed the experiments. CL, XJL and RY: performed the experiments and analyzed the data. CL, QJC and ZGZ: wrote the paper. CL, XJL, WWY and CLW: critical review. All authors read and approved the final manuscript.

Consent for publication

Not applicable since the manuscript is entirely original; the tables and figures presented are original for this article and have neither been published nor are currently under consideration for publication by any other journal.

Data availability statement

All original contributions are included in the manuscript.

References

1. Whitehouse ER, Mandra A, Bonwitt J, Beasley EA, Taliano J, Rao AK. Human rabies despite post-exposure prophylaxis: a systematic review of fatal breakthrough infections after zoonotic exposures. Lancet Infect Dis. 2023;23(5):e167–e74. doi: 10.1016/S1473-3099(22)00641-7.
2. Fooks AR, Cliquet F, Finke S, Freuling C, Hemachudha T, Mani RS, Müller T, Nadin-Davis S, Picard-Meyer E, Wilde H,

et al. Rabies. Nat Rev Dis Primers. 2017;3(1):17091. doi: 10.1038/nrdp.2017.91.
3. Wang L, Zhang J, Meng S, Ge L, You Y, Xu Q, Wang H, Yang J, Wang S, Wu H. Safety and immunogenicity of human rabies vaccine for the Chinese population after PEP: a systematic review and meta-analysis. Vaccine. 2022;40(32):4371–4379. doi: 10.1016/j.vaccine.2022.06.035.
4. World Health O. Rabies vaccines: WHO position paper, April 2018 – recommendations. Vaccine. 2018;36(37):5500–5503. doi: 10.1016/j.vaccine.2018.06.061.
5. Tarantola A, Tejiokem MC, Briggs DJ. Evaluating new rabies post-exposure prophylaxis (PEP) regimens or vaccines. Vaccine. 2019;37(Suppl 1):A88–a93. doi: 10.1016/j.vaccine.2018.10.103.
6. Fan L, Zhang L, Li J, Zhu F. Advances in the progress of monoclonal antibodies for rabies. Hum Vaccines & Immunotherapeutics. 2022;18(1). doi: 10.1080/21645515.2022.2026713.
7. Kang G, Lakhkar A, Bhamare C, Dharmadhikari A, Narwadkar J, Kanujia A, Kapse D, Gunale B, Poonawalla CS, Kulkarni PS. Active safety surveillance of rabies monoclonal antibody and rabies vaccine in patients with category III potential rabies exposure. Lancet Reg Health Southeast Asia. 2023;14:100207. doi: 10.1016/j.lansea.2023.100207.
8. Manna A, Kundu AK, Sharma Sarkar B, Maji B, Dutta T, Mahajan M. Real-world safety of TwinRab, the World's first novel cocktail of rabies monoclonal antibodies, in a clinical setting. Cureus. 2024;16(1):e52163. doi: 10.7759/cureus.52163.
9. Liu X, Li Y, Li J, Zhou J, Guo J, Pu Y, Jiang Y, Zhou Y, Jiang Z, Shu Q, et al. Comparing recombinant human rabies monoclonal antibody (ormutivimab) with human rabies immunoglobulin (HRIG) for postexposure prophylaxis: a phase III, randomized, double-blind, non-inferiority trial. Int J Infect Dis. 2023;134:53–62. doi: 10.1016/j.ijid.2023.05.017.
10. Quiambao BP, Payumo RA, Roa C, Borja-Tabora CF, Emmeline Montellano M, Reyes MRL, Zoleta-De Jesus L, Capeding MR, Solimen DP, Barez MY, et al. A phase 2b, randomized, double blinded comparison of the safety and efficacy of the monoclonal antibody mixture SYN023 and human rabies immune globulin in patients exposed to rabies. Vaccine. 2024;42(22):126018. doi: 10.1016/j.vaccine.2024.05.066.
11. Bakker AB, Marissen WE, Kramer RA, Rice AB, Weldon WC, Niezgoda M, Hanlon CA, Thijsse S, Backus HHJ, de Kruif J, et al. Novel human monoclonal antibody combination effectively neutralizing natural rabies virus variants and individual in vitro escape mutants. J Virol. 2005;79(14):9062–9068. doi: 10.1128/JVI.79.14.9062-9068.2005.
12. Marissen WE, Kramer RA, Rice A, Weldon WC, Niezgoda M, Faber M, Slootstra JW, Meloen RH, Clijsters-van der Horst M, Visser TJ, et al. Novel rabies virus-neutralizing epitope recognized by human monoclonal antibody: fine mapping and escape mutant analysis. J Virol. 2005;79(8):4672–4678. doi: 10.1128/JVI.79.8.4672-4678.2005.
13. Goudsmit J, Marissen WE, Weldon WC, Niezgoda M, Hanlon CA, Rice AB, Kruif J, Dietzschold B, Bakker A, Rupprecht C. Comparison of an anti-rabies human monoclonal antibody combination with human polyclonal anti-rabies immune globulin. J Infect Dis. 2006;193(6):796–801. doi: 10.1086/500470.
14. Sloan SE, Hanlon C, Weldon W, Niezgoda M, Blanton J, Self J, Rowley KJ, Mandell RB, Babcock GJ, Thomas WD, et al. Identification and characterization of a human monoclonal antibody that potently neutralizes a broad panel of rabies virus isolates. Vaccine. 2007;25(15):2800–2810. doi: 10.1016/j.vaccine.2006.12.031.
15. Prosniak M, Faber M, Hanlon CA, Rupprecht CE, Hooper DC, Dietzschold B. Development of a cocktail of recombinant-expressed human rabies virus–neutralizing monoclonal antibodies for postexposure prophylaxis of rabies. J Infect Dis. 2003;188(1):53–56. doi: 10.1086/375247.
16. Hanlon CA, DeMattos CA, DeMattos CC, Niezgoda M, Hooper DC, Koprowski H, Notkins A, Rupprecht CE. Experimental utility of rabies virus-neutralizing human monoclonal antibodies in post-exposure prophylaxis. Vaccine. 2001;19(28–29):3834–3842. doi: 10.1016/S0264-410X(01)00135-9.
17. de Kruif J, Bakker AB, Marissen WE, Kramer RA, Throsby M, Rupprecht CE, Goudsmit J. A human monoclonal antibody cocktail as a novel component of rabies postexposure prophylaxis. Annu Rev Med. 2007;58(1):359–368. doi: 10.1146/annurev.med.58.061705.145053.
18. Both L, Banyard AC, van Dolleweerd C, Horton DL, Ma JK, Fooks AR. Passive immunity in the prevention of rabies. Lancet Infect Dis. 2012;12(5):397–407. doi: 10.1016/S1473-3099(11)70340-1.
19. Kostense S, Moore S, Companjen A, Bakker AB, Marissen WE, von Eyben R, Weverling GJ, Hanlon C, Goudsmit J. Validation of the rapid fluorescent focus inhibition test for rabies virus-neutralizing antibodies in clinical samples. Antimicrob Agents Chemother. 2012;56(7):3524–3530. doi: 10.1128/AAC.06179-11.
20. Fan L, Zhang L, Li J, Zhu F. Advances in the progress of monoclonal antibodies for rabies. Hum Vaccin Immunother. 2022;18(1):2026713. doi: 10.1080/21645515.2022.2026713.
21. Sparrow E, Torvaldsen S, Newall AT, Wood JG, Sheikh M, Kieny MP, Abela-Ridder B. Recent advances in the development of monoclonal antibodies for rabies post exposure prophylaxis: a review of the current status of the clinical development pipeline. Vaccine. 2019;37(Suppl 1):A132–a9. doi: 10.1016/j.vaccine.2018.11.004.
22. Kramer RA, Marissen WE, Goudsmit J, Visser TJ, Clijsters-Van der Horst M, Bakker AQ, de Jong M, Jongeneelen M, Thijsse S, Backus H, et al. The human antibody repertoire specific for rabies virus glycoprotein as selected from immune libraries. Eur J Immunol. 2005;35(7):2131–2145. doi: 10.1002/eji.200526134.
23. Ding Y, Wu M, Zhang H, Zhu X, Hu Y, Li X, Liu J, Tsao E, Liu M, Li C. Safety, pharmacokinetics and pharmacodynamics of SYN023 alone or in combination with a rabies vaccine: an open, parallel, single dose, phase 1 bridging study in healthy Chinese subjects. Antiviral Res. 2020;184:104956. doi: 10.1016/j.antiviral.2020.104956.
24. Gogtay NJ, Munshi R, Ashwath Narayana DH, Mahendra BJ, Kshirsagar V, Gunale B, Moore S, Cheslock P, Thaker S, Deshpande S, et al. Comparison of a novel human rabies monoclonal antibody to human rabies immunoglobulin for postexposure prophylaxis: a phase 2/3, randomized, Single-Blind, Noninferiority, controlled study. Clin Infect Dis. 2018;66(3):387–395. doi: 10.1093/cid/cix791.
25. Gogtay N, Thatte U, Kshirsagar N, Leav B, Molrine D, Cheslock P, Kapre SV, Kulkarni PS. Safety and pharmacokinetics of a human monoclonal antibody to rabies virus: a randomized, dose-escalation phase 1 study in adults. Vaccine. 2012;30(50):7315–7320. doi: 10.1016/j.vaccine.2012.09.027.
26. Kansagra K, Parmar D, Mendiratta SK, Patel J, Joshi S, Sharma N, Parihar A, Bhoge S, Patel H, Kalita P, et al. A phase 3, randomized, open-label, noninferiority trial evaluating anti-rabies monoclonal antibody cocktail (TwinrabTM) against human rabies immunoglobulin (HRIG). Clin Infect Dis. 2021;73(9):e2722–e8. doi: 10.1093/cid/ciaa779.
27. Li L, Li Y, Bai Y, Li G, Zhang J, Yang L, Zhao W, Zhao W, Luo F, Zhao Q, et al. Neutralizing antibody activity, safety and immunogenicity of human anti-rabies virus monoclonal antibody (ormutivimab) in Chinese healthy adults: a phase IIb randomized, double-blind, parallel-controlled study. Vaccine. 2022;40(42):6153–6162. doi: 10.1016/j.vaccine.2022.09.022.
28. Chao TY, Ren S, Shen E, Moore S, Zhang SF, Chen L, Rupprecht CE, Tsao E. SYN023, a novel humanized monoclonal antibody cocktail, for post-exposure prophylaxis of rabies. PLOS Neglected Trop Dis. 2017;11(12):e0006133. doi: 10.1371/journal.pntd.0006133.

29. Chao TY, Zhang SF, Chen L, Tsao E, Rupprecht CE. In vivo efficacy of SYN023, an anti-rabies monoclonal antibody cocktail, in post-exposure prophylaxis animal models. Trop Med And Infect Disease. 2020;5(1):31. doi: 10.3390/tropicalmed5010031.
30. Wang Y, Rowley KJ, Booth BJ, Sloan SE, Ambrosino DM, Babcock GJ. G glycoprotein amino acid residues required for human monoclonal antibody RAB1 neutralization are conserved in rabies virus street isolates. Antiviral Res. 2011;91(2):187–194. doi: 10.1016/j.antiviral.2011.06.002.
31. Yu PC, Tao XY, Wang LH, Tang Q, Fan LY, Zhang SX, Liu S-Q, Lu X-X, Wu G-Z, Zhu W-Y. Establishment of a Chinese street rabies virus library and its application for detecting neutralizing activity. Infect Dis Poverty. 2018;7(1):117. doi: 10.1186/s40249-018-0500-x.
32. McClain JB, Chuang A, Reid C, Moore SM, Tsao E. Rabies virus neutralizing activity, pharmacokinetics, and safety of the monoclonal antibody mixture SYN023 in combination with rabies vaccination: results of a phase 2, randomized, blinded, controlled trial. Vaccine. 2021;39(40):5822–5830. doi: 10.1016/j.vaccine.2021.08.066.
33. McClain JB, Chuang A, Moore SM, Tsao E. Safety, pharmacokinetics, and neutralizing activity of SYN023, a mixture of two novel antirabies monoclonal antibodies intended for use in postrabies exposure prophylaxis. Clin Pharmacol Drug Dev. 2021;10(7):807–817. doi: 10.1002/cpdd.917.