

Advancements in rheumatoid arthritis immunotherapy: a comprehensive bibliometric analysis of research trends and hotspots (2003-2023)

Y. Tian¹, M. Jin², H. Li², D. Li², Y. Pei³

¹Microbiology and Immunology Department, Cangzhou Medical College, Cangzhou;

²National Institute for Viral Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing;

³School of Basic Medicine, North China University of Science and Technology, Tangshan, People's Republic of China.

Yi Tian, MM*

Miao Jin, PhD*

Huiying Li, PhD

Dandi Li, PhD

Yinhui Pei, PhD

*These authors share first authorship.

Please address correspondence to:

Yi Tian

School Of Basic Medicine,
Cangzhou Medical College

39 Jiuhe West Road, Yunhe District,
061001 Cangzhou City, Hebei, China.

E-mail: ty_19841112@163.com

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ABSTRACT

Objective. To analyse research trends and developments in rheumatoid arthritis (RA) immunotherapy through a comprehensive bibliometric analysis of literature from 2003 to 2023.

Methods. Publications related to RA immunotherapy were retrieved from Web of Science Core Collection database using specified search terms. Bibliometric analysis was performed with VOSviewer, CiteSpace, Pajek, and R packages to examine publication patterns, international collaborations, research hotspots, and emerging trends. Analysis covered publication outputs, country contributions, institutional networks, and keyword evolution patterns.

Results. Analysis based on a total of 940 publications showcased that the associated researches featured exponential growth ($R^2=0.885$) over the study period. The United States led with 285 publications (30.3%), followed by China (187, 19.9%) and Germany (156, 16.6%). International collaboration intensity increased, with average collaborating countries per paper rising from 1.8 to 2.7. Research focus evolved through three phases: fundamental immunology (2003-2010), therapeutic development (2011-2017), and precision medicine (2018-2023). Current hotspots encompassed immunomodulation mechanisms (38% of keywords), immune-related adverse events management, as well as cancer immunity interactions. Emerging trends highlighted nanotechnology applications and microbiome research, with respective growth rates of 218% and 245% in recent years.

Conclusion. This analysis revealed significant evolution in RA immunotherapy research, characterised by increasing international collaboration and meth-

odological sophistication. The involved fields displayed a clear transition from basic immunological research to precision medicine approaches. Emerging hotspots in nanotechnology and microbiome studies suggested promising therapeutic innovations. These findings were seen to provide valuable guidance for future research fields and resource allocation in RA immunotherapy.

Introduction

Rheumatoid arthritis (RA) is a systemic autoimmune disorder characterised by persistent joint inflammation and autoantibody production (1). Current treatments, including conventional DMARDs and biologics, often show insufficient efficacy or adverse effects (13). Immunotherapy represents a promising approach for achieving complete disease remission by reestablishing immune tolerance (3). Notwithstanding several bibliometric analyses have demonstrated RA research broadly (6, 7), no comprehensive analysis has focused specifically on immunotherapy developments.

The present study aims to analyse the intellectual landscape and development trajectory of RA immunotherapy research from 2003-2023, subsequently provides insights into research trends, collaboration patterns, as well as emerging therapeutic directions.

Materials and methods

Data collection

Publications from January 1, 2003, to September 30, 2023, were retrieved from the Web of Science Core Collection using search terms: TS=(“rheumatoid arthritis”) AND TS=(immunotherapy). Only research articles and reviews were included, excluding letters, newsletters, and book reviews.

Competing interests: none declared.

Bibliometric analysis

The analysis was conducted using VOS viewer 1.6.18 for the visualisation of collaboration networks, CiteSpace 6.2.R5 for temporal evolution analysis, Pajek 64 5.16 for network analysis, and R packages (circlize, chorddiag, ComplexHeatmap) for data visualisation. Microsoft Excel was used for the publication trend analysis.

Statistical analysis

Network parameters were calculated via built-in algorithms in VOSviewer. Collaboration intensity was measured through co-authorship analysis. Growth patterns were analysed by exponential regression models. Statistical significance was set at $p < 0.05$.

Results

A total of 940 publications were analysed during 2003–2023. The annual publication output soared from 16 papers in 2003 to 97 in 2022, featuring an exponential growth pattern ($R^2 = 0.885$). Publication growth experienced three distinct phases: 2003–2008 (15.3 papers/year), 2009–2016 (37.8 papers/year), and 2017–2023 (82.4 papers/year).

International collaboration analysis revealed extensive cooperation among 45 countries. The United States led with 285 publications (30.3%), followed by China (187, 19.9%) and Germany (156, 16.6%). The average number of collaborating countries per paper increased from 1.8 (2003–2010) to 2.7 (2018–2023). Citation analysis revealed international collaborative papers received 35% more citations than single-country publications.

Research focus evolved through three main phases identified through keyword analysis. Phase I (2003–2010) emphasised basic immunological mechanisms, with dominant keywords including T cells and cytokines (2, 4). During this period, T cells appeared 158 times and cytokines appeared 145 times in the literature. Phase II (2011–2017) focused on therapeutic approaches, particularly biologics and TNF inhibitors (5, 14), with these terms appearing 178 and 165 times respectively. Phase III (2018–2023) showed emergence of precision medicine terms including biomarkers

and personalised therapy, with respective frequencies of 85 and 76.

Current research hotspots identified through clustering analysis include immunomodulation (38% of keywords), immune-related adverse events management, and cancer immunity interactions. Emerging trends analysis revealed significant growth in nanotechnology applications (8, 9) (218% increase) and microbiome research (245% increase) since 2018.

Gene analysis organised 156 genes into three functional clusters: T cell-related (72 genes, 46.2%), inflammatory mediators (48 genes, 30.8%), and regulatory elements (36 genes, 23.1%). Network analysis identified 42 hub genes with high degree centrality (>0.75). Disease association patterns showed increasing focus on comorbidities, with studied disease associations growing from 45 (2003–2010) to 156 (2018–2023).

Discussion

This bibliometric analysis revealed significant evolution in RA immunotherapy research during 2003–2023. The exponential growth in publications reflected increasing recognition of the potential of immunotherapy in RA treatment (5). The dominance of US institutions, coupled with rising contributions from Asian countries, particularly China, indicates a globalising research landscape (6, 7).

The transition from basic immunological studies to precision medicine approaches represented a fundamental shift in research focus. Early emphasis on T cell mechanisms and cytokine networks (2, 4) has evolved into more sophisticated therapeutic strategies, particularly evident in the rising interest in nanotechnology-based delivery systems (15). This evolution suggested growing understanding of disease complexity and need for personalised treatment approaches.

International collaboration patterns showed a meaningful impact on research quality, with collaborative papers receiving significantly higher citations. This trend particularly benefited emerging research nations, supporting the value of cross-border scientific partnerships. The increasing focus on comor-

bidities and disease associations mirrored growing recognition of the systemic nature of RA.

Emerging research directions in microbiome studies and nanotechnology applications represented promising therapeutic frontiers. Microbiome research revealed crucial connections between gut flora and immune function (10–12), while nanomedicine approaches offer potential solutions for targeted drug delivery (8, 9). These developments suggested new possibilities for therapeutic intervention.

Study limitations included potential database bias against non-English publications and emerging research areas. Additionally, citation analysis may not fully reflect clinical impact, particularly for recent publications.

Conclusion

This analysis demonstrated clear evolution in RA immunotherapy research, characterised by increasing methodological sophistication and international collaboration. Emerging trends in nanotechnology and microbiome research indicated promising therapeutic innovations. These findings provided valuable guidance for future research directions and resource allocation in the development of RA immunotherapy.

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