Review

Research trends and hotspots on gut microbiota in rheumatoid arthritis: a bibliometric analysis from 2004 to 2024

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ABSTRACT

Objective. *Rheumatoid arthritis (RA) is an autoimmune condition linked to alterations in the gut microbiota. This study aims to conduct a comprehensive analysis of the literature on gut microbiota and RA over the past 21 years through bibliometric methods, thereby identifying emerging trends and hotspots, and providing insights for the precision treatment of RA.*

Methods. *The authors analysed articles on gut microbiota in RA published from 2004 to 2024 based on the Web of Science Core Collection database. Bibliometric methods employed tools such as CiteSpace, VOSviewer, and COOC to conduct visual analyses of countries, institutions, references, and keywords.*

Results. *1,267 articles from 80 countries led by China and the United States were included. A notable increase in annual publications reflects the growing interest in this field. Simultaneously, contributions and cooperation of institutions in the field are discussed. Furthermore, co-citation and keyword analysis revealed four research hotspots: 1. specific gut microbiota like Prevotella copri modulating immune responses in RA; 2. dietary interventions regulating gut microbiota as therapeutic approaches for RA; 3. high-throughput sequencing technologies enabling microbiome analysis for diagnostic RA; and 4. probiotics and plant-derived bioactive compounds serving as promising adjunctive therapies for RA management.*

Conclusion. *The relationship between RA and gut microbiota has been extensively studied. The hotspot of future research may be to further study the pathological mechanism of gut microbiota in RA and how to improve the symptoms of RA patients through dietary therapy and adjustment of the homeostasis of gut microbiota.*

Introduction

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disease characterised by persistent synovial inflammation that progressively damages joint structures and surrounding tissues. As one of the leading causes of disability and workforce loss worldwide, RA imposes substantial individual and societal burdens (1, 2). Beyond its articular manifestations, RA can lead to significant extra-articular complications, including interstitial lung disease, pulmonary fibrosis, and accelerated cardiovascular disease (3, 4).

Despite extensive research, the precise aetiology of RA remains unclear. Evidence indicates RA results from complex interactions between genetic predisposition and environmental triggers. Known environmental risk factors include smoking, air pollutants, gut microbiota alterations, exposure to infectious agents, dietary factors, and socioeconomic determinants. (5, 6). Among these, emerging evidence particularly highlights the critical role of gut microbiota dysbiosis in RA pathogenesis and progression (7, 8). A next-generation sequencing study found that newly diagnosed RA patients exhibit elevated levels of Prevotella copri., which is a specific gut microbiota species associated with pro-inflammatory response and disease progression (9). It is increasingly being recognised that gut microbiota dysbiosis plays a pivotal role in the pathogenesis of RA through diverse mechanisms, including altered metabolite production and immune system modulation. Consequently, we aimed to analyse the published literature and thus investigate the direct relationship between RA and gut microbiota in order to obtain a clearer and more comprehensive understanding of the microbiota-gut-joint axis and to inform

novel therapeutic strategies against this disabling autoimmune disease. Notably, bibliometric analysis is an effective method to achieve this goal.

In contrast to the traditional literature review, bibliometric analysis assesses published research and predicts future trends with the support of visual analytical tools (10). One such tool, VOSviewer, is a widely recognised software tool for visualising relationships in the scientific literature and analysing citation patterns, author collaborations, and keyword co-occurrences. In addition, tools such as Citespace, COOC, ArcMap and Pajek are often used to visualise the literature (11-13). This type of research is based on existing literature covering different countries, institutions, authors, journals and keywords. It utilises mathematical and statistical tools to quantify and predict the current state of scientific research to objectively evaluate the knowledge framework and identify research hotspots. Thus, bibliometric analysis is crucial for elucidating attributes and emerging trends in the discipline. Recently, the number of relevant research publications in this field has been rapidly increasing, but bibliometric analyses of the interrelationships between RA and the gut microbiota are still limited.

In this study, we conducted a systematic and innovative bibliometric analysis of global research on gut microbiota and RA from 2004 to 2024. Our approach moves beyond a mere summary of existing literature by offering a multifaceted evaluation, including a detailed examination of publication trends, collaborative networks, and emerging research directions. This originality allows us to assist researchers in rapidly identifying key hotspots and frontiers within the field. Moreover, we aim to bridge the findings of bibliometric analysis with their actual clinical implications. To achieve this, we delve into and emphasise the biological and clinical significance of key studies, focusing on academic developments in gut microbiota and RA, the advancement of microbiota-based therapies, and precision medicine approaches for RA. This comprehensive perspective provides not only an analytical framework but also a broad outlook and roadmap for future research in this interdisciplinary domain. Through this integrated approach, our work seeks to contribute meaningful insights, aligning bibliometric findings with clinical applications to support the advancement of research and therapeutic strategies in RA and gut microbiota.

Material and methods

Data retrieval strategy, data extraction, and cleaning

The research object of this paper is the correlation study of RA and gut microbiota. The Web of Science is an outstanding resource for bibliometric analysis, owing to its broad disciplinary scope, thorough citation indexing, robust analytical metrics and includes more than 12,000 highest-impact, top-quality scientific journals, which assist researchers in pinpointing research hotspots and trends within their respective domains (14). Thus, we selected the Web of Science Core Collection SCI-Expanded (SCI-E) database as the data source of the research object, and selected the advanced search, the search formula: TS = (gut OR intestine OR gastro-intestine OR gastrointestine OR gastrointestinal) AND TS = (microbiota OR microbiome OR flora OR microflora OR bacteria) AND TS = ("Rheumatoid Arthritis" OR RA). The study focused on literature published from 2004-01-01 to 2024-12-31, resulting in the retrieval of 1,347 papers. After excluding conference abstracts, and letters, we primarily retained original research articles and review papers. Without prior consultation, we simultaneously examined the titles, abstracts, and keywords of the retrieved literature to filter out irrelevant studies, ultimately narrowing our selection to 1,267 relevant articles. To ensure the reproducibility and reliability of the analyses, three independent reviewers were involved in the screening of the articles, and Cohen's kappa statistic was calculated to assess inter-reviewer reliability. The average Cohen's kappa among the reviewers was 0.783 ($p<0.001$), indicating substantial agreement. Following the initial evaluations, a group discussion was conducted to address any discrepancies in their assessments, ensuring a consensus on the final selection. The final dataset exported included 'full records and citations' in 'plain text' format. Figure 1 illustrates the specific data retrieval techniques and the inclusion process employed in this research.

Scientometric analysis methods

We employed Excel and various visual analysis tools, including Microsoft Excel 365, VOSviewer, CiteSpace, Pajek, ArcMap and COOC software, for comprehensive trend analysis. Microsoft Excel 365 is used to visualise the annual number of documents published and show the trend of posting. Due to its advanced visualisation capabilities, VOSviewer was selected to collect comprehensive data on countries, institutions, authors, citations and keywords, and to create a visual representation of the network. The size of each node represents the number of documents. The thickness of the link line between two nodes is an approximate indication of how well they collaborate and co-occur. In general, the thicker the link lines, the stronger the degree of collaboration and co-occurrence between them. Pajek software is used to adjust the visualisation graphics made by VOSviewer. Owing to its versatility, CiteSpace is used to analyse reference bursts, visualise keyword timelines, and identify keyword bursts in order to effectively represent the data. After extracting their geographical origins, we used ArcMap to build a map based on the number of posts in different countries, so as to intuitively reflect the number of publications in different countries. COOC is used to visualise the number of collaborations among different institutions.

Results

Analysis of global publication trends

A total of 1,267 routine articles on RA and gut microbiota were included in this study. Figure 2 illustrates the annual and cumulative publication counts related to RA and gut microbiota. In the first 10 years, the cumulative number of publications increased gradually, rising from 3 in 2004 to 63 in 2013. Overall, the annual number of published papers remained relatively low during this pe-

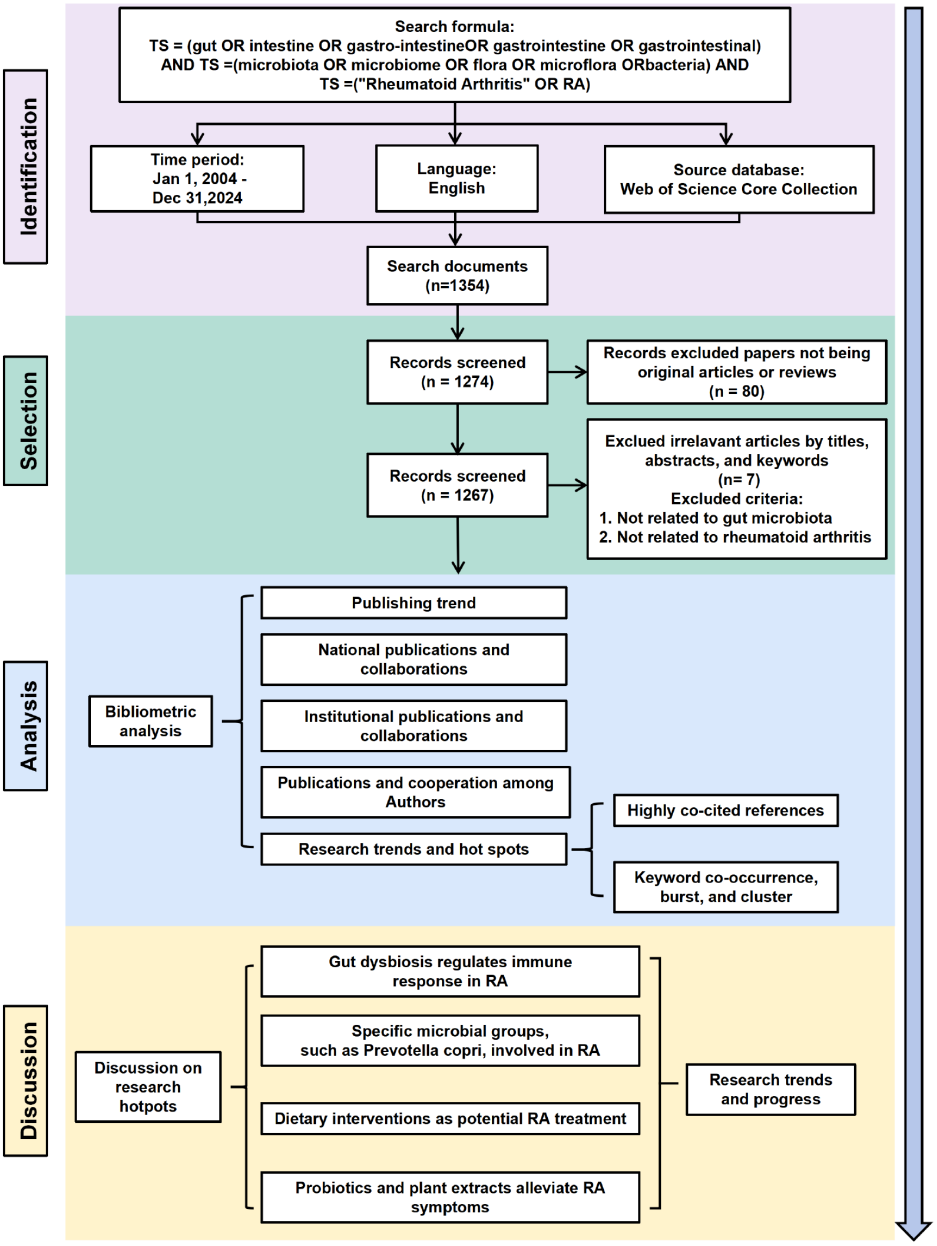

Fig. 1. Detailed flowchart steps of the search strategy in screening publications.

riod. The number of publications has surged over the past 11 years, reaching a total of 1,267 by 2024, with the highest number published in that year (n=184). Although the number of articles published in 2023 on RA and gut microbiota has decreased compared to the previous year, the overall trend remains upward, with the cumulative total steadily increasing. An exponential growth function was employed to assess the relationship between cumulative publications and the publication year, which aligned closely with the trend of the cumulative number of publications (R2 =0.9832). Notably, the cumulative publication volume curve and the cumulative publication trend curve exhibited a high degree of overlap during the period from 2004 to 2021. Based on the prediction curve of cumulative literature, research in this area was expected to continue increasing.

Analysis of national publications and collaborations

The study analysed the number of published studies related to RA and gut microbiota across different countries (Fig. 3A), achieved network visualisation (Fig. 3B), and overlay visualisation of national collaborations using VOSviewer software (Fig. 3C). The results from Figure 3A indicates that China, the United States, Italy, the England, Germany, and Japan are at the forefront in terms of publication volume, with China leading with 403 publications, followed by the United States (346), Italy (98), England (89), Germany (64), and Japan (58). These six countries have proven to be the top powerhouses in RA and gut microbiota research, while the remaining countries have fewer than 50 publications. Figure 3B further illustrates the degree of collaboration between these countries. Figure 3C shows that China has recently engaged in a significant number of research collaborations (The closer the node colour is to yellow, the more

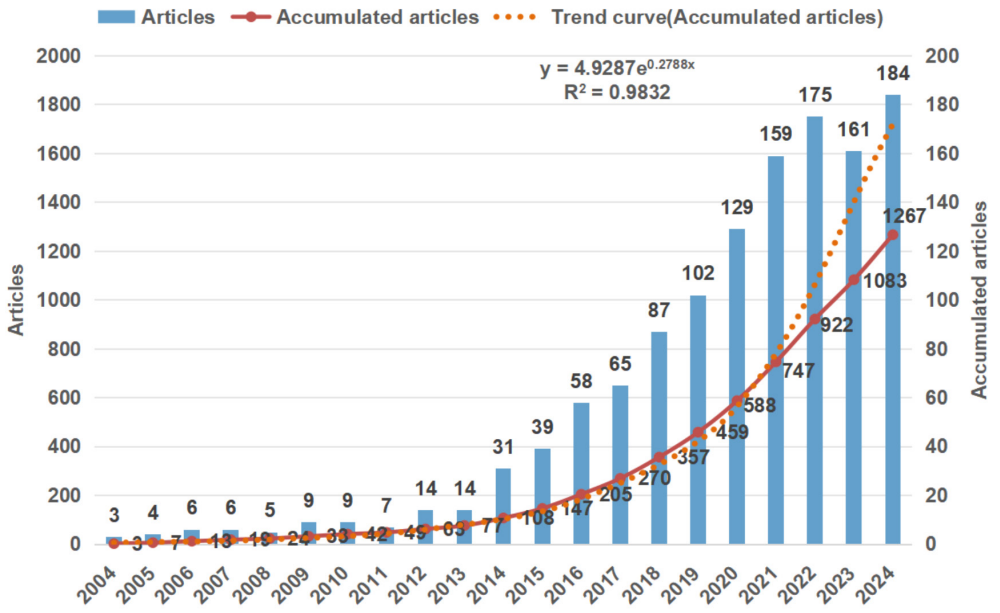

Fig. 2. Number of publications per year and cumulative number.

indicative it is of active collaboration in recent times). Figure 3D presents the geographical distribution of global publications related to national and regional contributions to gut microbiota and RA research. Additionally, Figure 3E illustrates the annual publication volume and the proportional contribution of the top five countries in publication output. Notably, in recent years, China has experienced a rapid increase in the number of publications, positioning it as the leading country in annual publication volume for three consecutive years in 2022, 2023, and 2024.

Analysis of institutional publications and collaborations

Figure 4A depicts the institutions that have published more than 10 articles. From this figure, it is evident that the majority of publications come from Chinese Academy of Sciences, Harvard University, University of California System, and Harvard Medical School. Figure 4B illustrates the number of collaborations between these institutions, with the numbers in the squares representing the total collaborations between each pair of institutions. Notably, the analysis revealed that the Chinese Academy of Sciences and the University of the Chinese Academy of Sciences collaborated the most, with a total of 12 collaborations. Additionally, there were significant collaborations between BGI Shenzhen and the University of Copenhagen, as well as between Catholic University of Korea and Seoul National University.

The presence of excessive items within a network can lead to cluttered and difficult-to-interpret visualisations. Con-versely, the appropriate selection of thresholds facilitates the generation of more coherent and insightful visual representations, thereby highlighting the primary trends and connections within the field. Through iterative adjustments, we established a minimum threshold of five publications per institution, thereby identifying 99 institutions that contributed to collaborative research as delineated by VOSviewer. The resulting institutional co-authorship network, comprising these 126 institutions and organised into 9 clusters, is depicted in Figure 4C. In recent years, Chinese institutions have increasingly influenced the field of gut microbiota and RA research, as evidenced by the overlay map in Figure 4D, which showed the historical trend of article publications.

Research trends and hot spots analysis

- Analysis of highly co-cited references

VOSviewer was employed to visualise co-cited references, which revealed a total of 70,015 citations. To ensure that the network includes only highly co-cited references while enhancing the clarity and readability of the network visualisation, we set a minimum threshold of 30. As a result, the number of documents included in the analysis was reduced to 133. As shown in Figure 5, the highly co-cited references in the network diagram are classified into four distinct clusters, each represented by a specific colour: red, green, blue, and yellow. An analysis of the number of cited articles revealed that the 10 most cited papers were cited more than 80 times each, with the most cited article being published in 2015 under the title "The oral and gut microbiomes are perturbed in RA and partly normalised after treatment". The second most cited paper was authored by Giovannucci, entitled "Expansion of intestinal Prevotella copri correlates with enhanced susceptibility to arthritis" (15).

- Analysis of keyword co-occurrence, burst, and cluster

Figure 6A displays keywords with frequencies greater than 10. A total of 222 high-frequency keywords were extracted from 1,267 studies and were categorised into following four clusters. Cluster 1 (Red cluster) primarily emphasises the relationship between gut microbiota and inflammatory processes in RA, highlighting terms such as 'gut microbiota', 'inflammatory response', and 'microbiome modulation'. Cluster 2 (Green cluster) focuses on concepts of autoimmunity relevant to RA pathogenesis, including 'auto-

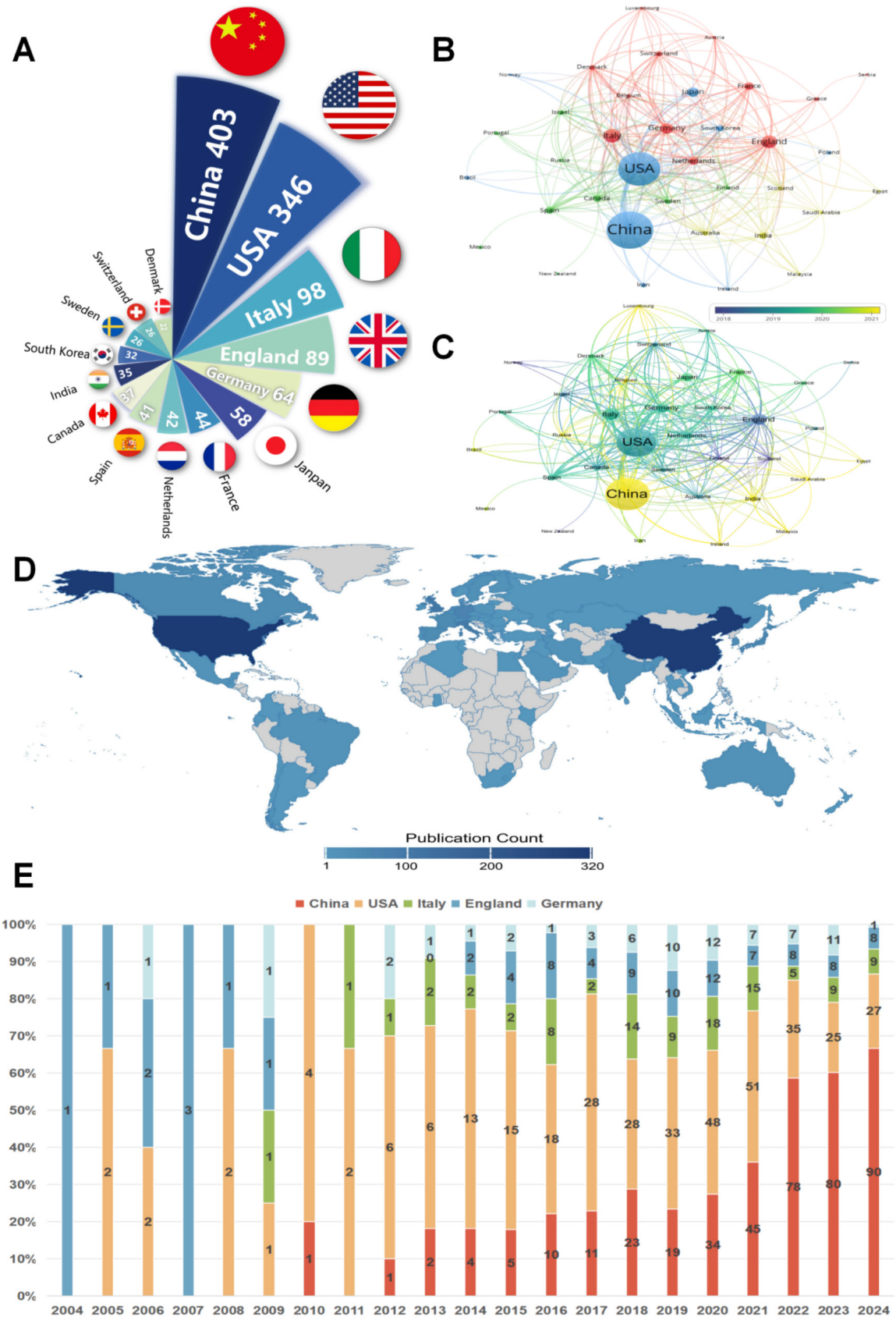

Fig. 3. Each country's contribution to gut microbiota and RA.
A: Number of publications by country; **B**: Network visualisation map of countries; **C**: Overlay visualisation map of countries; **D**: Geographic distribution of global publications on gut microbiota and RA. **E**: Bar graph of the top five productive countries.

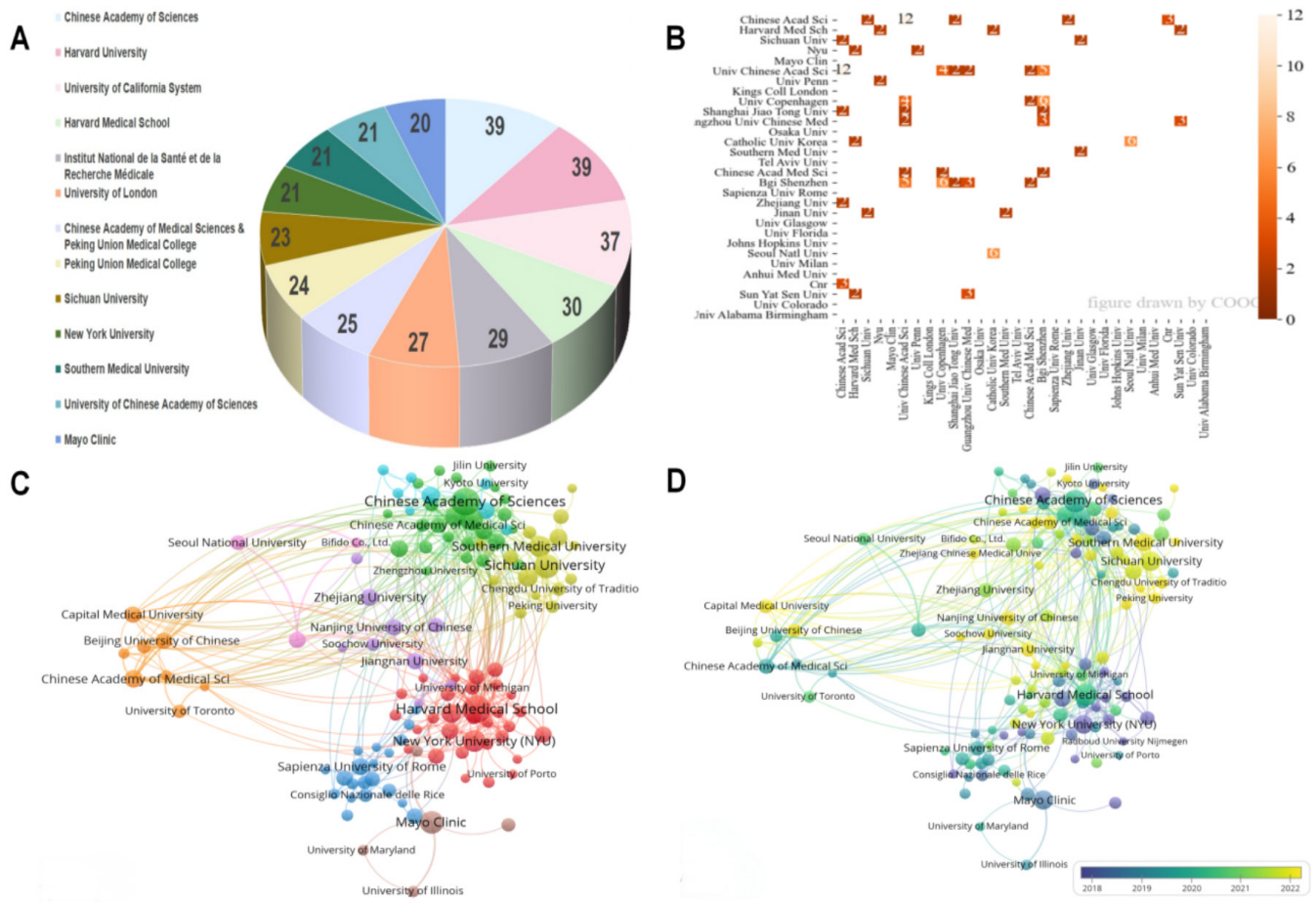

Fig. 4. Each institution's contribution to gut microbiota and RA.
A: Number of publications by institution; **B**: The collaboration between institutions. The number on the square indicates times of cooperation; **C**: Network visualisation map of institutions; **D**: Overlay visualisation map of institutions.

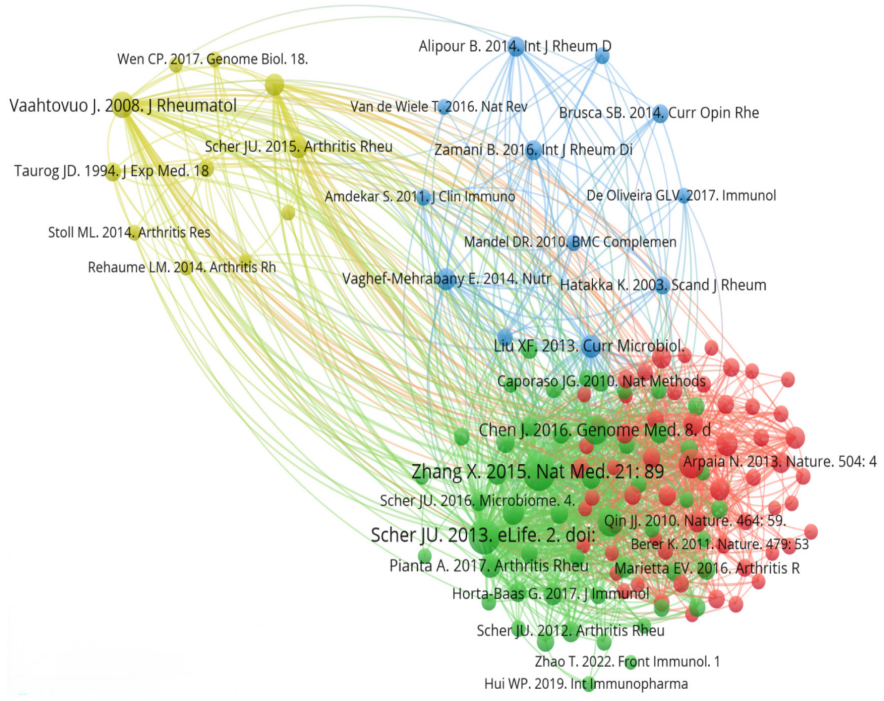

Fig. 5. Cluster mapping of highly co-cited literature.

immunity', 'immune response', and related inflammatory conditions. Cluster 3 (Blue cluster) delves into microbiome research methods, featuring terms like 'dysbiosis', 'microbiome stability', and 'health outcomes'. Finally, Cluster 4 (Yellow cluster) investigates the influence of diet and nutrition on gut health and RA outcomes, underscoring keywords such as 'dietary intervention', 'probiotics', and 'nutritional therapy'. The top 25 keywords with the strongest citation bursts are illustrated in Figure 6B. Figure 6C illustrates the connections among the top six keyword clusters. Notably, as illustrated in Figure 6D, 'multiple sclerosis', 'Crohn's disease', and 'responses' have emerged as persistent hotspots throughout the timeline from 2004 to the present, with topics such as 'gutmicrobiome', 'autoimmunity', gaining traction since 2010, and 'porphyromonas gingivalis' gaining traction since 2015.

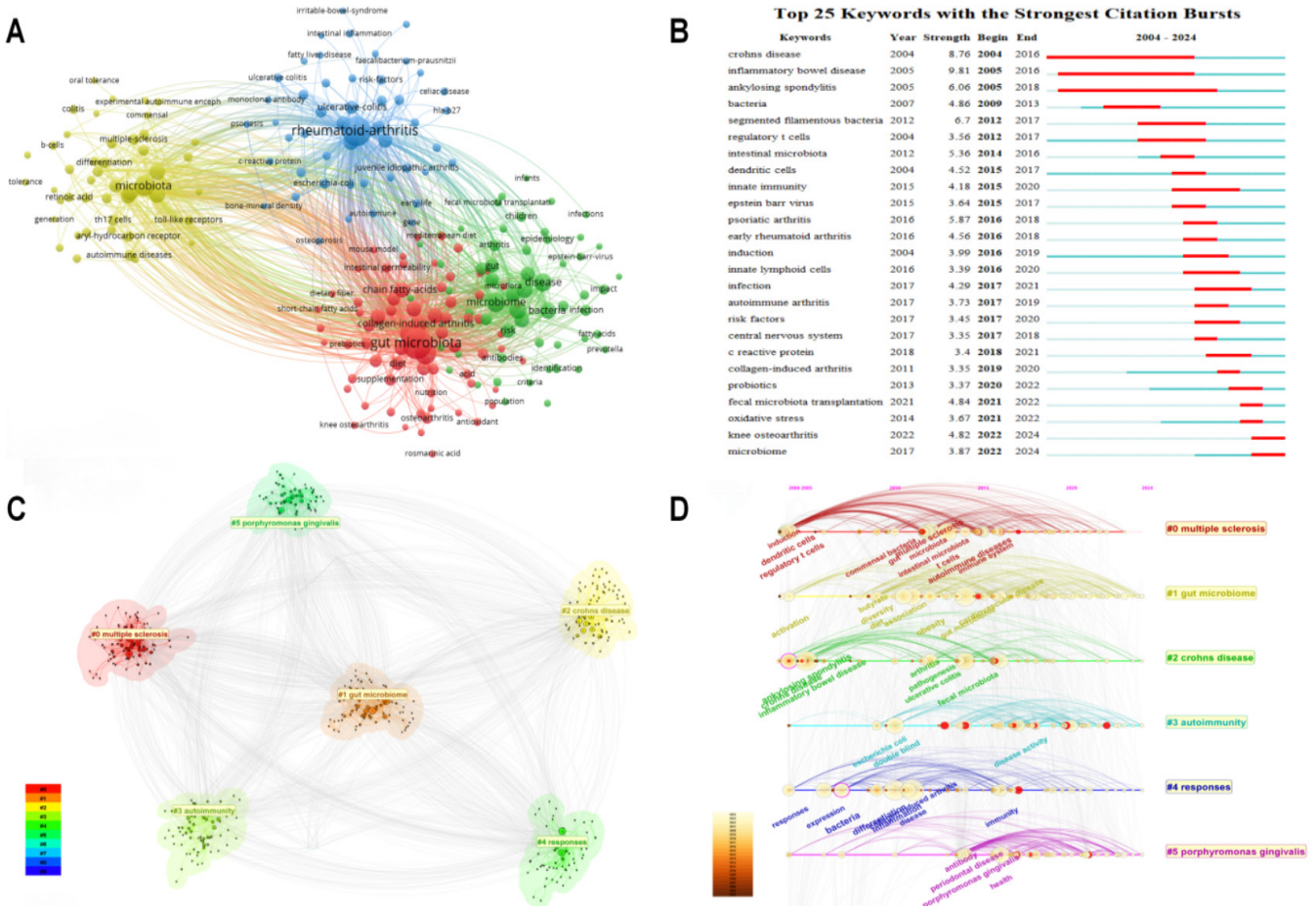

Fig. 6. A: Network visualisation map; **B**: The top 25 terms with the most significant gut microbiota and RA citation bursts; **C**: Keyword clustering; **D**: A timeline and keyword clustering display for the gut microbiota and RA.

Discussion

Global publication trends and research status

This study employed bibliometric analysis to investigate the evolution of research pertaining to the relationship between gut microbiota and RA from 2004 to 2024. The results of the study show a clear upward trend in the number of articles published during this period, indicating a growing interest in this area. This trend highlights that our understanding of the role of the gut microbiome in the pathogenesis of RA has come a long way, and researchers are increasingly shifting the focus of their studies on RA from an emphasis on autoimmunity alone to more complex models that consider host-microbe interactions. This shift highlights the complexity of RA and the need for an integrated approach to better elucidate its underlying mechanisms.

At the same time, the surge in research has accelerated therapeutic innovation, leading to the development of new microbiome-based preventive and precision treatments (16). Recent investigations have illuminated the close association between alterations in gut microbiome composition and the pathogenesis of RA (17). Dysbiosis, characterised by reduced microbial diversity and an imbalance between beneficial bacteria (*e.g.* Lactobacillus) and pathogenic species (*e.g.* certain Clostridia), has been shown to exacerbate inflammatory responses, thereby contributing to joint damage in RA patients (18, 19). In addition, specific gut microbial metabolites, such as short-chain fatty acids (SCFAs), have demonstrated protective effects in modulating inflammation and may influence the progression of RA (20). Furthermore, dietary patterns – especially the increasing prevalence of Western-style diets high in fats and sugars – have been linked to disruptions in gut microbiota, potentially exacerbating RA symptoms. This correlation underscores the importance of dietary modifications as a critical component in the prevention and management of RA (21). Overall, elucidating the intricate relationship between gut microbiota and RA enhances our understanding of the disease's underlying mechanisms and holds promise for advancing future research focused on RA treatment and personalised medicine strategies centered on the microbiome (22).

National publishing trends and cooperation

Figure 3A revealed that among the 15 countries researching the relationship between gut microbiota and RA, China and the United States are predominant, with each contributing over 300 publications to the body of research. Among them, China led in the number of publications concerning the relationship between gut microbiota and RA. This was largely attributed to the growing incidence of RA in China, influenced

by rapid urbanisation and changes in dietary habits, has intensified the focus on this disease within the scientific community (23). As the country grapples with the public health implications of RA, governmental and institutional support for healthcare research has surged, fostering increased funding and resources directed towards microbiome studies (24, 25). Consequently, investment in healthcare research in China rose. Figure 3B clearly demonstrates that the number of publications on the connection between gut microbiota and RA in China has steadily increased in recent years, establishing it as the country with the highest number of annual publications in 2022, 2023, and 2024. In addition, enhanced international collaboration is likely to facilitate the sharing of research information and new treatment strategies, driving innovation to optimise treatment options based on individual microbiome profiles. These advances are expected to improve patient outcomes through personalised interventions to address the underlying microbial imbalances that lead to RA pathology (26).

Research trends and hotspots analysis

- Tracing the research trends and hotspots from co-cited literature

Co-citation refers to researchers citing the same literature, thereby forming a knowledge foundation of co-cited documents and a research frontier of citing documents. This analysis aimed to identify the shared research basis between gut microbiota and RA in order to explore emerging trends and hotspots. We employed VOSviewer to conduct a comprehensive analysis of highly co-cited literature, categorising the papers into four interconnected clusters that collectively form a continuous research framework spanning from fundamental microbial mechanisms to clinical interventions.

- Microbial metabolites and immune regulation: foundational mechanisms

Our analysis of research hotspots began with the basic mechanisms by which the gut microbiota influences immune regulation (red clusters). It explained how gut microbiota and their metabolites, such as short-chain fatty acids (SCFAs), influence the development and function of regulatory T cells (Tregs). For instance, in their study entitled "Genome Sequence of Segmented Filamentous Bacteria Present in the Human Intestine", Jonsson *et al*. describe the metagenomic analysis of a unique segmented filamentous bacterium (SFB) isolated from a human ileostomy sample. They found that SFB closely interacts with the intestinal lining, promoting the differentiation of CD4 T helper cells into pro-inflammatory Th17 cells. These Th17 cells produce critical cytokines, including IL-17 and IL-22, which may amplify local inflammatory responses. This complex immune modulation implies that SFB could play a role in the development of autoimmune diseases like RA by influencing inflammation and immune dynamics (27).

Complementing this finding, Cao *et al*. demonstrated that butyrate-conjugated prodrug micelles (Neg-ButM) effectively promoted regulatory T cell differentiation while reducing myeloid cell activation in RA mouse models, highlighting the therapeutic potential of microbiota-derived SCFAs in autoimmune conditions (28). These studies deepen our understanding of how gut microbiota influence the development of RA and highlight the potential for developing more effective prevention and treatment strategies for this autoimmune disease.

- Microbial dysbiosis in RA pathogenesis: identifying key microbial signatures

Building upon these fundamental mechanisms, the second cluster (green) investigates specific microbial signatures associated with RA development and progression. Li*n et al*. demonstrated that individuals with pre-clinical RA present with significant gut microbiota dysbiosis, characterised by an elevated abundance of potentially pathogenic bacteria such as Prevotella, concomitant with a reduced prevalence of putatively beneficial strains including Lactobacillus and Ruminococcus. This microbial imbalance is hypothesised to contribute to immune dysfunction, exacerbate systemic inflammation, and potentially expedite the progression from pre-clinical stages to clinically manifest RA (29). This dysbiotic state provides a critical link between the immune dysregulation mechanisms identified in the first cluster and the clinical manifestation of RA. Notably, many studies within this cluster focused on the immune relevance of the specific gut microbiota Prevotella copri in RA patients. Iljazovic *et al*. demonstrated the role of the gut microbe Prevotella intestinalis in augmenting mucosal inflammation in a murine model, correlating alterations in the gut microbiome with enhanced inflammatory responses pertinent to conditions such as RA. Their findings elucidated that colonisation by P. intestinalis induced a diminution in short-chain fatty acids, notably acetate, culminating in reduced intestinal IL-18 levels. This alteration in the microbial milieu may correspond to observations in RA patients, wherein an overabundance of Prevotella copri has been correlated with elevated inflammatory cytokines, indicating a potential mechanism by which gut dysbiosis contributes to RA pathogenesis (30).

Further studies found that P. copri colonisation along with a high-fibre diet promoted the digestion of complex fibres, which led to the overproduction of organic acids, including fumarates, succinate, and short-chain fatty acids. As a result, these organic acids promote a pro-inflammatory response in macrophages, thereby exacerbating the course of RA. By modifying the dietary approach according to the specific gut microbiota (*e.g*. by reducing a high-fibre diet and thereby decreasing the inflammatory effects of copri Prevotella), it is possible to reduce inflammation and improve the prognosis of patients with RA, ultimately leading to more effective management and prevention of disease progression (31).

- Technical applications for microbiome assessment: diagnostic capabilities

The analytical techniques presented in the third cluster (yellow) provide the necessary diagnostic capabilities to link the identification of dysbiosis of specific microbial flora with targeted thera-

peutic interventions. High-throughput sequencing technologies, particularly 16S rRNA sequencing as employed by Ruiz-Limón *et al*. in their study entitled "Collinsella is associated with cumulative inflammatory burden in an established rheumatoid arthritis cohort", enable precise characterisation of gut microbiota profiles in RA patients. Through comparative analysis of fecal samples from 110 RA patients and 110 healthy controls, the researchers identified a significant increase in the relative abundance of the genus Collinsella in patients exhibiting moderate to high disease activity. Moreover, the study elucidated a diminished diversity in bacterial communities among RA patients, notably in those with higher inflammatory burdens. These findings underscore the significance of gut dysbiosis in RA and indicate that specific bacterial taxa may be associated with the disease's inflammatory processes (32). These advanced sequencing methods create a critical link between the specific patterns of dysbiosis identified in the second cluster and the potential intervention strategies outlined in the fourth cluster by providing specific microbiota profiles that can serve as diagnostic markers and therapeutic targets. The ability to accurately identify and monitor the composition of the gut microbiota enables clinicians to assess treatment efficacy and disease progression in RA, thereby informing personalised management strategies for RA patients (33).

- Therapeutic interventions targeting the gut-joint axis: clinical applications

The fourth cluster (blue) completes the integrated framework by investigating targeted interventions that address the microbial dysbiosis and immune dysregulation identified in the preceding clusters. Bungau *et al*. conducted a systematic review on the effects of Lactobacillus casei and Lactobacillus acidophilus in RA patients, documenting significant reductions in inflammatory markers, including serum high-sensitivity C-reactive protein (hs-CRP), as well as improvements in joint swelling and tenderness. Their findings suggested that patients administered these probiotics exhibited enhanced overall health and functionality, underscoring their potential as efficacious adjunct therapies in the treatment of RA (34). In another randomised trial, Jian *et al*. investigated the effects of daily supplementation with carrot-derived rhamnogalacturonan-I (cRG-I) on gut microbiota composition in healthy adults. Although this intervention did not elicit significant changes in overall gut microbiota composition, it induced a significant increase in the relative abundance of Bifidobacterium species, which are associated with beneficial effects on gut health (35). These studies highlight the potential of probiotics, specific plant extracts (*e.g*. carrot-derived rhamnogalacturonan-I), and gut health interventions as complementary strategies for managing RA. By reducing inflammatory markers and improving patient-reported outcomes, these probiotic treatments and the supplementation of specific plant extracts can offer a valuable complement to standard RA therapies, enhance overall quality of life, and may reduce the risk of complications associated with chronic inflammation (36). What is more, the usual disease-modifying anti-rheumatic drugs (DMARDs) and non-steroidal anti-inflammatory drugs (NSAIDs) and glucocorticosteroids (GCs), among others, are associated with a number of side effects in the treatment of RA (37), and a randomised controlled trial found no side effects were reported following intake of the synbiotic in RA patients (38). Thus, probiotics could represent an alternative and complementary therapy to the standard medications we already use to control rheumatologic activity, thus controlling the side effects that occur during RA treatment and ensuring the safety and efficacy of RA treatment (39, 40).

The collective research hotspots across these four interconnected clusters established a comprehensive framework for understanding and addressing RA through the gut-joint axis. The progression from fundamental mechanisms of microbial metabolites and immune regulation (red cluster) to dysbiosis of specific microflora in RA (green cluster), enabled by advanced diagnostic technologies (yellow cluster), ultimately informs targeted therapeutic interventions (blue cluster) that can restore microbial balance, modulate immune function, and potentially alter RA progression. This integrated approach offers significant clinical implications for RA management, potentially reducing the risk of complications associated with chronic inflammation while enhancing patients' quality of life.

Exploring research trends and hotspots through keyword co-occurrence and burst analysis

Cluster analysis of 222 keywords occurring more than 10 times identified four main clusters:

Cluster 1 (Red cluster) primarily emphasises the relationship between gut microbiota and inflammatory processes in RA, highlighting how specific microbial profiles may influence the pathophysiological mechanisms underlying RA through their impact on immune activation and inflammation.

Cluster 2 (Green cluster) focuses on the concepts of autoimmunity with direct relevance to RA pathogenesis. While terms like 'inflammatory bowel disease' appeared in this cluster, their inclusion is justified by the established common immunological pathways they share with RA, particularly regarding how gut dysbiosis can trigger similar autoimmune responses across these conditions. This cluster elucidates how dysregulation of the gut microbiome may contribute to the development and exacerbation of autoimmune phenomena, including RA.

Cluster 3 (Blue cluster) delves into methods of microbiome research and their clinical implications. This cluster underscores the significance of understanding microbiome diversity and stability in relation to systemic inflammation and disease trajectories, illustrating the potential of microbiome-targeted therapeutic strategies for RA management.

Cluster 4 (Yellow cluster) investigates the influence of diet and nutrition on gut health and RA outcomes. This cluster represents evidence demonstrating that dietary modifications can measurably impact microbial composition and metabolic profiles in RA patients, thereby influencing inflammation markers and clinical symptoms specific to RA.

Analysis of the keyword timeline graph and the top 25 trending terms reveals the increasing prominence of terms related to inflammatory mechanisms directly associated with RA from 2004 to 2024. Terms such as 'ankylosing spondylitis' and 'psoriatic arthritis' represent a growing understanding of the common immune mechanisms between these diseases and RA, particularly how similar gut microbial patterns influence their pathogenesis. Similarly, immune cell types such as 'regulatory T cells', 'TH17 cells', and 'innate lymphocytes', whose role in RA pathology is well established, were included. The prevalence of 'Porphyromonas gingivalis' and 'periodontal disease' in the analysis reflects their established mechanistic relationship with RA, as these oral microbiota factors can directly trigger and exacerbate inflammatory responses in RA patients through molecular mimicry and the process of citrullination (41).

Limitations

This bibliometric study was subject to several limitations. Firstly, our analysis relied exclusively on the Web of Science Core Collection. While WoS is a comprehensive resource that facilitates effective data analysis, focusing on a single database may introduce coverage bias, potentially omitting relevant studies indexed in other databases. Secondly, the dynamic nature of recent publications may result in high-quality articles having insufficient citation frequency, potentially underrepresenting emerging insights in the field. Lastly, variations in naming conventions for authors and institutions may have caused fragmentation in our data retrieval. Despite these limitations, our findings provide a valuable insight of the current research landscape regarding gut microbiota and RA.

Conclusion

Gut microbiota has important research value and application prospect in RA. The rapid growth in the number of published papers in the past 21 years indicates that the study of gut microbiota in RA has been increasingly emphasised by scholars around the world. Among them, China and the United States are in the leading position, but the cooperation and communication among countries and institutions still need to be strengthened. Through analysis of highly cited papers, citation bursts, and keyword analysis, we identified the primary research areas connecting gut microbiota and RA, including: 1. the critical influence of gut dysbiosis on the modulation of immune responses pertinent to RA, with particular emphasis on the role of specific microbial taxa, such as Prevotella copri; 2. the profound interplay between dietary patterns and gut microbiota composition, indicating that dietary intervention may be a viable approach for RA treatment and management; 3. analytical techniques such as high-throughput sequencing technology provide the necessary diagnostic capabilities for RA; 4. the potential of probiotics and bioactive compounds derived from plants as adjunctive therapies to mitigate RA symptoms and improve patient outcomes. Notably, probiotics and bioactive compounds have also been shown to improve the intestinal microenvironment and enhance the efficacy of immune checkpoint inhibitors. It is worth noting that compared to traditional therapeutic drugs for RA, probiotics are effective in controlling the side effects that occur during RA treatment, thus ensuring the safety and effectiveness of RA treatment. In addition to RA, the immunomodulatory role of probiotics and bioactive compounds in aging, tuberculosis, viral infections, and autoimmune diseases, as well as their potential in gut microbiota and anti-inflammatory therapies, are important for future research. Further exploration of the detailed mechanisms of probiotics in RA and their biodistribution in tissues is essential to optimise their clinical application. This comprehensive bibliometric analysis not only illuminates current research landscapes but also charts potential trajectories for advancing our understanding of the gut-articular axis. By embracing interdisciplinary approaches that integrate immunology, microbiology, nutrition science, and precision medicine, future research can transform theoretical insights into tangible improvements in RA prevention, diagnosis, and personalised treatment strategies.

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