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Research article

Glycosylation in autoimmune diseases: A bibliometric and visualization study

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ABSTRACT

An increasing amount of research has shown that glycosylation plays a crucial role in autoimmune diseases (ADs), prompting our interest in conducting research on the knowledge framework and hot topics in this field based on bibliometric analysis. Studies on glycosylation in the field of ADs from 2003 to 2023 were collected by searching the Web of Science Core Collection database. Bibliometric analysis was conducted using VOSviewer, CiteSpace, and Bibliometrix software. This study included a total of 530 studies. According to the H, G, and M indices, the United States has made the most contributions worldwide, with China making significant contributions in recent years. Leiden University from the Netherlands ranks among the top institutions in terms of publication and citation rankings, with the institution's author Manfred Wuhrer contributing the most to this field. Frontiers in Immunology is the journal with the highest H-index. Research in this field has focused on antibody glycosylation, particularly the specific glycosylation of IgG and IgA, and its role in various ADs. The application of glycoengineering glycosylated proteins in the synthesis of targeted monoclonal antibodies, drug delivery, and regenerative medical materials may be a new trend in the treatment of ADs. Artificial intelligence is an emerging tool in glycobiology. This study summarizes the objective data on glycosylation in the field of AD publications in recent years, providing a reference for researchers in this field.

1. Introduction

Autoimmune diseases (ADs) are a group of diseases characterized by inadequate self-tolerance and production of autoantibodies, leading to tissue damage [1]. Autoantibody Fc regions activate immune cells through Fc fragment receptors (FcRs), promoting a series of autoimmune reactions [2]. The function of immune cells appears to be closely associated with the unique extracellular matrix (ECM) that surrounds them; the glycocalyx is an important component of the ECM [3]. The glycocalyx is primarily composed of glycoproteins and glycosaminoglycans and can regulate cell interactions and influence immune recognition and disease development [4].

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Glycosylation is a widespread protein modification that regulates glycoprotein peptide structure and function [5]. Glycans can be linked to protein residues by N-glycosylation (attachment to asparagine) or O-glycosylation (attachment to serine/threonine residues) [6]. Glycoproteins include commonly secreted proteins (including immunoglobulins), cell membrane proteins, and cell surface receptor proteins [7]. The unique glycan modifications of these proteins may significantly affect their ability to bind to the innate and adaptive immune systems [8]. Immunoglobulin G (IgG) is an excellent example. Intravenous immunoglobulin (IVIg) is widely used to treat ADs because of its anti-inflammatory properties, and IgG Fc glycosylation is crucial for regulating its inflammatory function [9].

Research on glycosylations and ADs has increased in recent years, and understanding the progress and hot topics in glycosylation and AD research is essential. Bibliometric methods are commonly used for quantitative analysis in specific fields, providing information on the major countries/regions, journals, authors, references, and keywords associated with research output in that field [10, 11]. Currently, no bibliometric study on glycosylations in ADs has been reported. This study aimed to visualize and analyze literature published between 2003 and 2023 in the field of glycosylation in ADs, providing insight into future research trends in this area.

2. Materials and methods

2.1. Data source

For this study, the Web of Science core database (WOSCC) was selected as the data source, and the literature was searched from January 1, 2003 to May 29, 2023. The search equation was #1 = (((TS = (Autoimmune Diseases)) OR TS = (rheumatic diseases)) OR TS = (rheumatology)) OR TS = (rheumatism), #2 ((TS = (Protein Glycosylation)) OR TS = (glycosyl)) OR TS = (glycosylation), #3 = #1 AND #2. A total of 581 articles were retrieved. The articles were restricted to "review articles" or "articles" in English, and 530 articles were ultimately obtained. The literature screening process is shown in Fig. 1.

2.2. Data source

The preliminary data were obtained through VOSviewer software (version 1.6.19) and manually screened by two individuals for any duplicate information. All nodes generated in the visualization represent different elements, with the size of the nodes reflecting the quantity of the element, the color of the node representing the category to which it belongs, and the line width representing the strength of the connection between the elements. VOSviewer was used to visualize elements such as countries/regions, institutions, authors, cited journals, and keywords. Tableau software (version 2023) was used to refine the global map of countries/regions, while Pajek software was used to conduct a cluster analysis of these elements. The overlay map of journals and cited journals, the visualization analysis of cited references, and the clustering diagram were synthesized using CiteSpace software (version 6.2.2). Furthermore, author output over a period, hot topics, and thematic maps were synthesized using the Bibliometrix package of R software [12].

The H-index combines the total number of publications and the total number of citations to quantify the quantity and quality of an

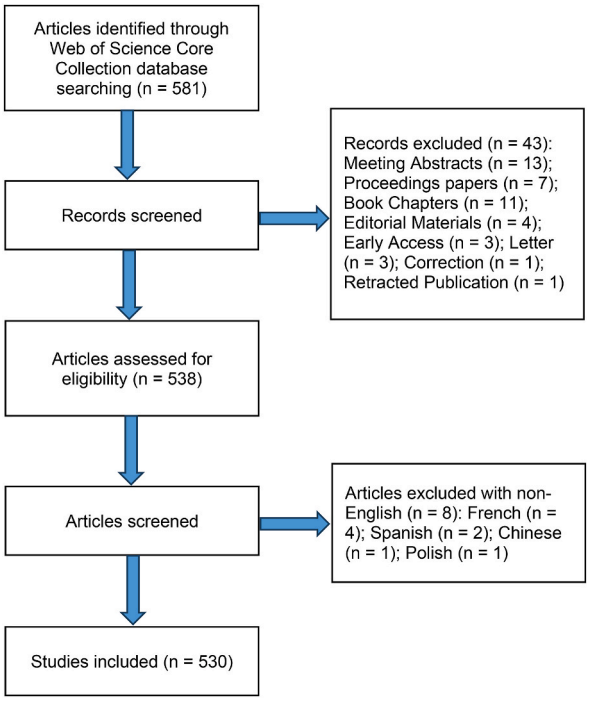

Fig. 1. Flow chart of the study inclusion and exclusion criteria.

author's publications [13]. However, the H-index is not sufficient for evaluating authors with a small number of highly cited articles in a specific field, which is why the G-index, another indicator of author impact, was introduced. The M-index is an author's H-index divided by the number of years since their first publication, thus eliminating bias caused by publication time [14]. These three indices are equally applicable to other elements, such as country and journal.

3. Results

3.1. Literature publication

The results of this study included 530 papers from 1011 organizations in 56 countries authored by a total of 3362 individuals published in 255 journals, citing 26757 references from 3317 journals. In addition, there were 146 review articles and 384 research articles, for a ratio of approximately 2:5, as shown in Fig. 2. The research field was in its early stage from 2003 to 2007. It entered a period of stable growth from 2008 to 2015, and from 2015 to the present, it has been in an era of rapid growth. The annual percentage growth rate is currently 2.84 %, suggesting that glycosylation may be a new hot topic in AD research.

3.2. Analysis of countries/regions and institutions

Glycosylation in the field of ADs has been studied globally, as shown in Fig. 3A and Supplementary Table 1. Among related research studies, the United States has the highest number of publications (n = 172), followed by China (n = 80), Germany (n = 66), and the Netherlands (n = 58). At least eight articles were published by each of the 20 countries, with the size of the nodes representing the number of publications and the links representing the frequency of communication between countries (Fig. 3B). The USA is the largest node in which research has been conducted for the longest period (Fig. 3C). China is the second largest node in the world and has published many articles more recently, indicating that Chinese scholars' attention to glycosylation in ADs has increased significantly in recent years. Multicountry publications (MCPs) refer to collections of articles written by authors from different countries or regions [15]. As shown in Fig. 3D. Germany has the highest MCP rate (43.1 %) and has the closest relationship with the United States, the Netherlands, and Sweden.

Of the 1012 organizations, Leiden University ranks first in terms of the number of published articles (n = 36), while the University of Amsterdam ranks third (n = 20), as shown in Supplementary Table 2. Both institutions are in the Netherlands. The University of Alabama at Birmingham in the USA ranks second (n = 20). In addition, 47 organizations published more than five articles, and the visualization and clustering of cooperation between organizations are shown in Fig. 4A and B. The most robust cooperation between institutions is between Leiden University and the University of Amsterdam.

3.3. Analysis of authors

The top 20 authors in the field of glycosylation in ADs from 2003 to 2023 are presented in Supplementary Table 3. Among high-productivity authors, Manfred Wuhrer from Leiden University ranked first in terms of the H-index, followed by Jan Novak and Bruce A. Julian. As depicted in Fig. 5A, M Demetriou started researching in this field the earliest, J Mestecky had the longest duration of

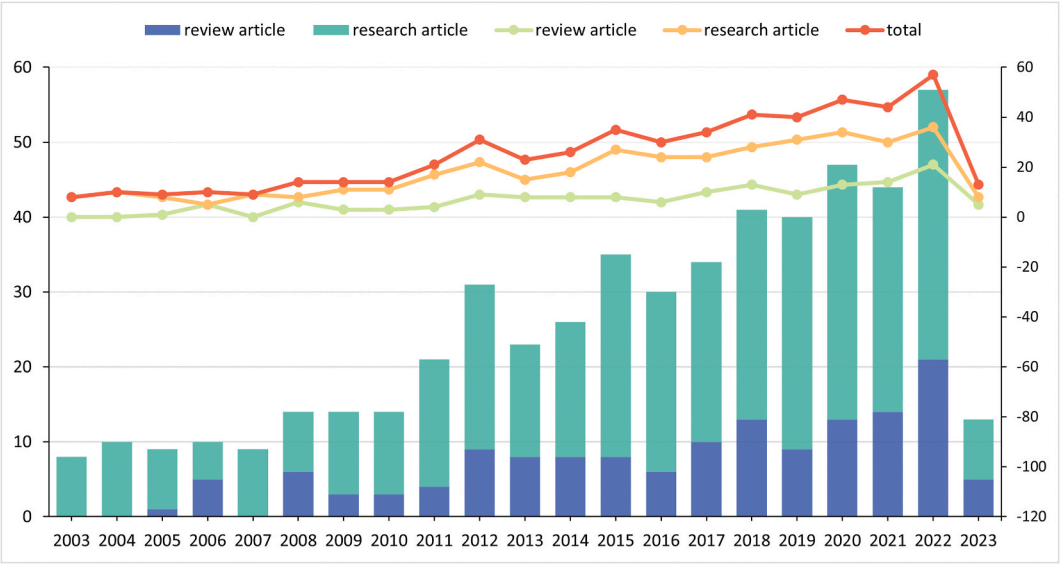

Fig. 2. Distribution of publications on glycosylation in ADs from 2003 to 2023.

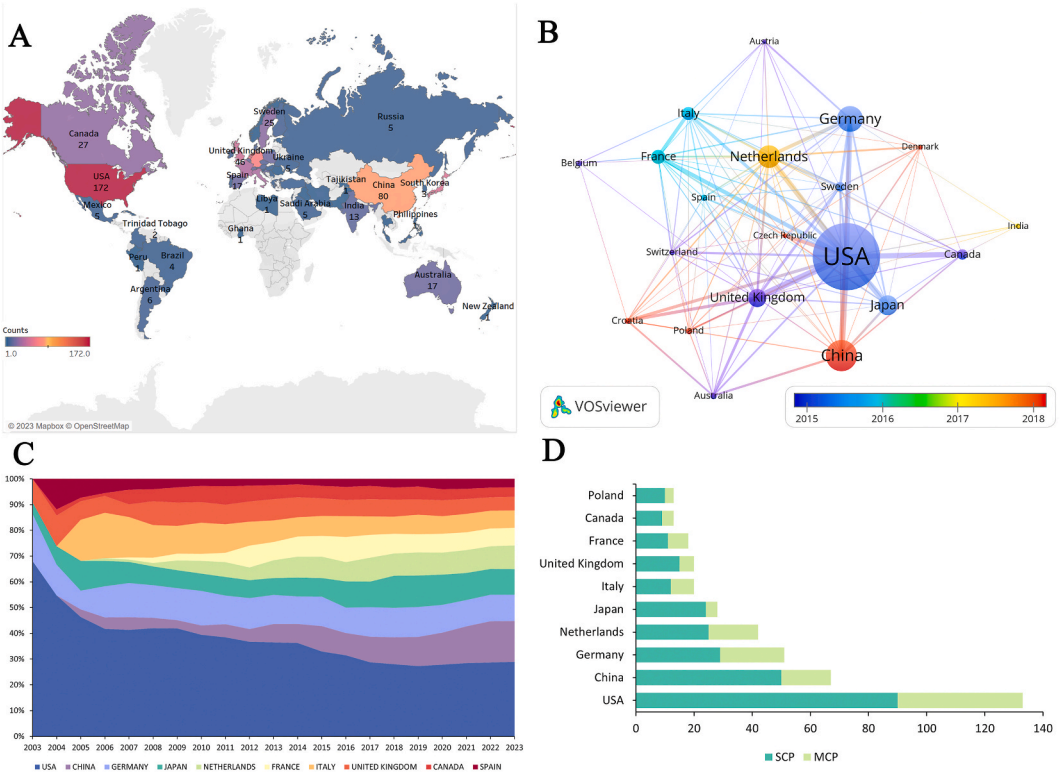

Fig. 3. Visualizations of country/region analysis. (A) Global distribution of all publications. (B) Collaboration network among the top 20 countries. (C) The top 10 countries/regions with the highest number of publications. (D) The 10 countries/regions with the highest number of articles according to the corresponding authors. MCP, multicountry publication. SCP, single-country publication.

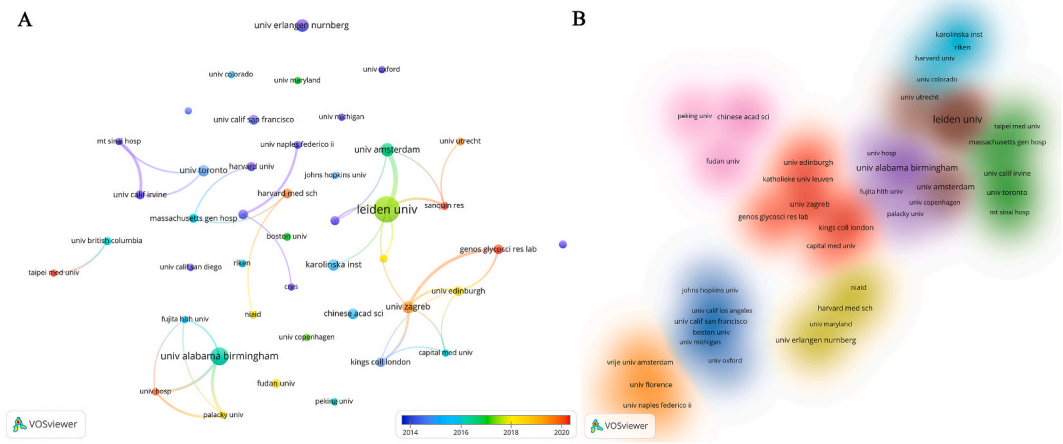

Fig. 4. Visualization of the institutional analysis of glycosylation in the field of ADs. (A) Cooperative networks across affiliations; (B) cluster analysis of cooperation among institutions.

research, and Manfred Wuhrer had the highest M-index. A visualization of the postcluster collaboration network among authors who have published at least four papers is shown in Fig. 5B. The largest node in the network is represented by Manfred Wuthrer, who collaborates closely with Rene E.M. Toes and Hans Ulrich Scherer, all of whom hail from Leiden University. Together, they form the largest cluster in the network. Additionally, there is a tight-knit collaboration between Bruce A. Julian, Jan Novak, and Colin Reily, all of whom are affiliated with the University of Alabama at Birmingham.

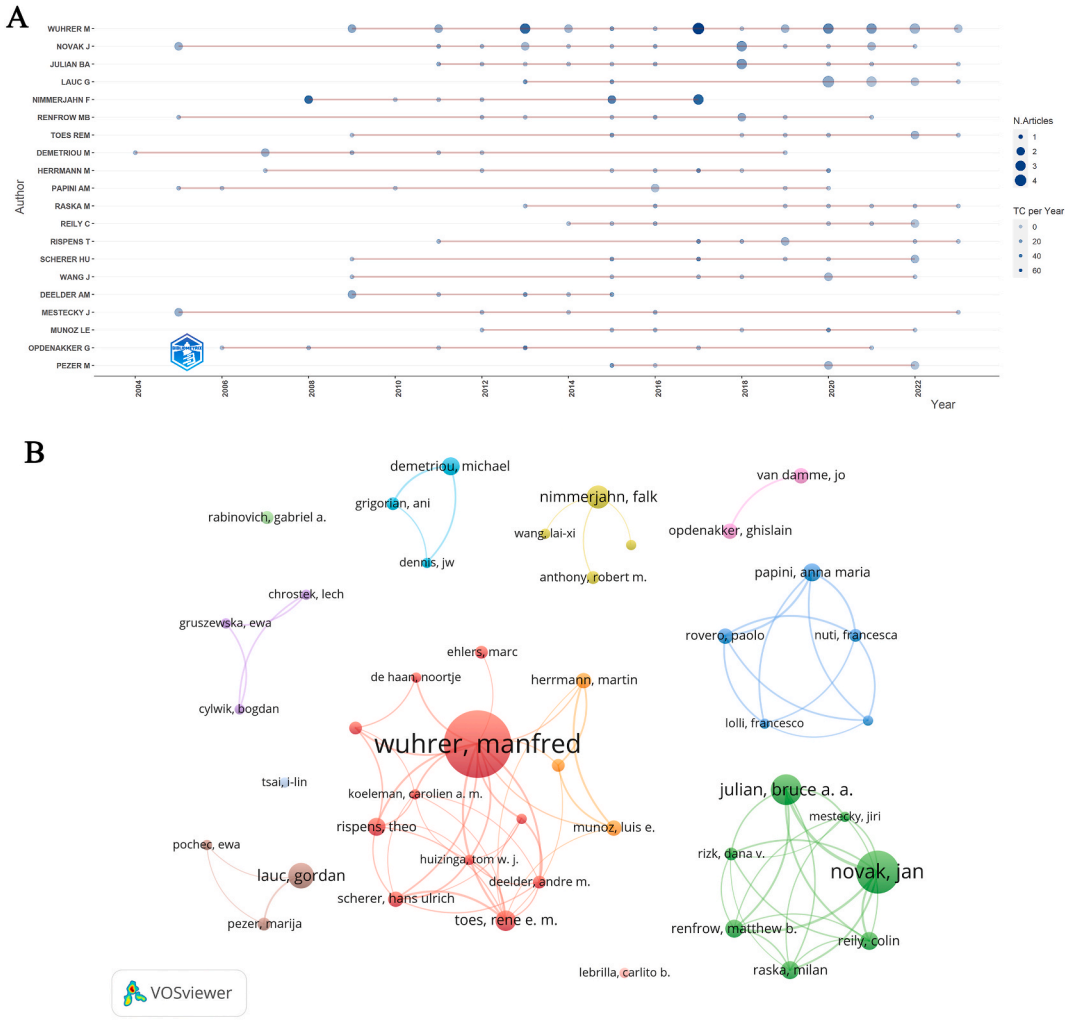

Fig. 5. (A) Author production over time and (B) collaborative network visualization of the authors.

3.4. Analysis of journals and cocited journals

Supplementary Table 4a reports the top 10 journals for publication. Based on the H-index, Frontiers in Immunology ranked first, followed by the Journal of Biological Chemistry and Proceedings of the National Academy of Sciences of the United States of America. Furthermore, PLoS One ranked second in the G-index rankings, indicating that the journal had a high number of published papers that were independently cited. All of the top 10 journals are from JCR1/2, and 7 of them have an impact factor greater than 5, among which the Proceedings of the National Academy of Sciences of the United States of America (12.779) and the Journal of Autoimmunity (14.511) have impact factors exceeding 10.

The frequency of journal citations reflects the influence of the journal in the research field. Among the top 10 cocited journals, 7 had an impact factor greater than 12, and 8 were from JCR1 (Supplementary Table 4b). Journals and cocited journals were mainly from the United States (7/10). The visualization of cocited journals revealed the clustering of journals that were cited at least 20 times (Fig. 6A). The red nodes represent comprehensive journals such as Science, Nature and Cell; the yellow nodes represent journals in the nephrology field; and the light blue nodes represent journals related to the hematology field. In addition, the Journal of Immunology is the highest-impact journal, cited a total of 1380 times. By overlaying the data on the journals and the cocited journals (Fig. 6B), it was found that papers published in Molecular Biology Immunology and Medicine Medical Clinical were typically cited in the field of Molecular Biology Genetics.

3.5. Analysis of references and cocited references

Local citation (LC) refers to the frequency of citation of a reference in a specific topic, while total citation (TC) refers to the frequency of citation of a reference worldwide. From among the literature reviewed in this study, the top 10 articles are shown in

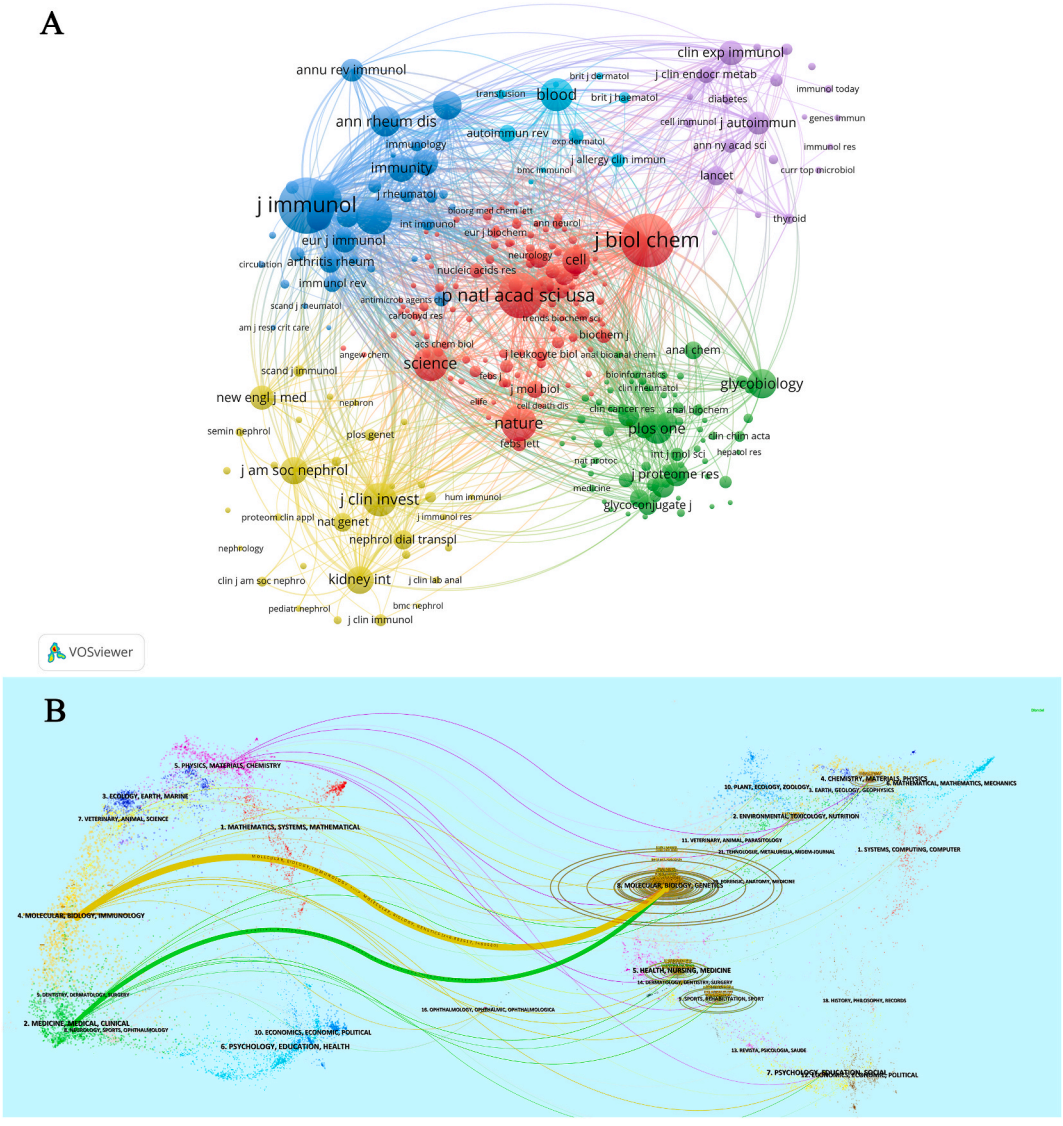

Fig. 6. Journal analyses of glycosylation in the field of ADs. (A) Visualization map of the co-citation of journals. (B) Dual-map overlay of journals.

Supplementary Table 5a. The article titled "Recapitulation of IVIG anti-inflammatory activity with a recombinant IgG Fc", published in Science, is ranked first in LCs. The reference with the highest TCs is titled "Therapeutic antibodies: successes, limitations and hopes for the future". Supplementary Table 5b also lists the top 10 cocited references, with "Anti-inflammatory activity of immunoglobulin G resulting from Fc sialylation" being the most frequently cited article. The second-ranked reference is "The impact of glycosylation on the biological function and structure of human immunoglobulins". The cocitation network is shown in Fig. 7A, and the clustering analysis results is shown in Fig. 7B. There were nine clusters in total, four of which were closely linked: #0 b cell, #7 immunosuppression, #2 Graves' disease and #5 glycoproteins.

3.6. Analysis of keywords and hot topics

Keywords can be used to analyze the research frontier of glycosylation in the AD field. Fig. 8A displays the 30 nodes that represent at least 25 frequently occurring keywords. Among them, "glycosylation," "rheumatoid arthritis," and "antibodies" were the three most common keywords, indicating that research on antibody glycosylation in rheumatoid arthritis is the most prominent theme. The keywords are divided into three clusters. The red cluster is the largest and is associated with the role of glycosylation in the immune system (including "glycosylation," "expression," "receptor," and "proteins"). The green cluster included 36 nodes and included keywords such as "rheumatoid arthritis," "IgG," "galactosylation," and "anti-inflammatory activity," which explore the relationship between glycosylation and rheumatoid arthritis, especially its anti-inflammatory effects. The blue cluster represents the characteristics of the

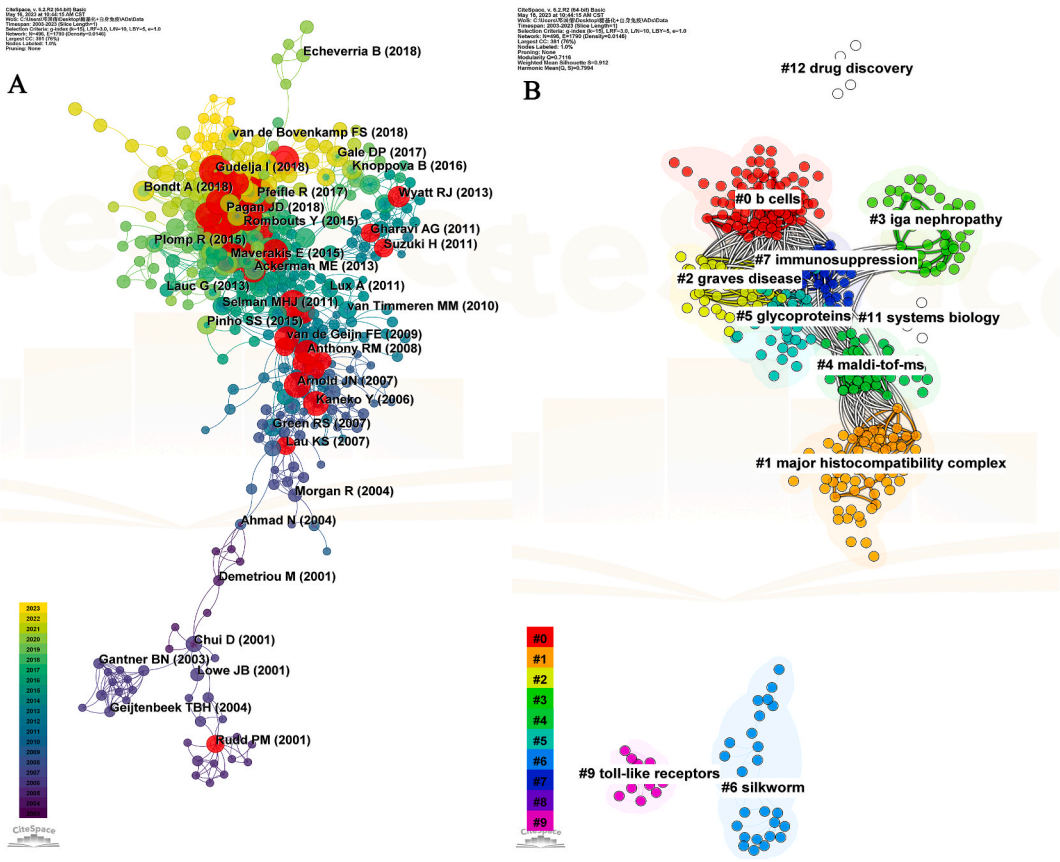

Fig. 7. Reference analyses of glycosylation in the field of ADs. (A) Cocited networks of references. (B) Cluster diagrams of references.

ADs. According to the node colors (Fig. 8B), the average time of occurrence of the high-frequency keywords appears after 2015.

To further analyze the timing of the appearance of keywords, trending topics were synthesized based on keywords, as shown in Fig. 8C. Before 2008, the keywords were relatively scattered, and research on glycosylation and ADs showed explosive growth after 2008. The contribution frequencies of keywords such as “neutrophil”, “glycopeptide”, “fc receptors”, and “apoptosis” were relatively average. Until 2016, the high-frequency keywords, included "mass spectrometry", "antibody", and "autoantibody". Mass spectrometry analysis is frequently used in the study of glycosylation in the field of ADs. The number of studies gradually increased after 2016, and a second peak of high-frequency keywords, "glycosylation," "inflammation," and "autoimmunity", appeared in 2018. The appearance of "posttranslational modifications" and "glycoengineering" in 2022 suggests that research in these areas will continue to be the focus in future years.

3.7. Analysis of topics

To better explore and summarize the development trends of glycosylation in the field of ADs, a thematic map was generated for visual analysis of the themes, as shown in Fig. 9. The thematic words were obtained based on the relationships between WOS-generated keywords plus, and their distinction was based on density and centrality, which are respectively represented by the vertical and horizontal axes, respectively. Density represents the cohesion between nodes, and a higher cohesion between nodes indicates a better development level in the field. Centrality represents the degree of correlation between different themes; the greater the number of relationships between different nodes is, the greater the centrality. Based on the differences in nodes and centrality, the map was divided into four quadrants.

The first quadrant (upper right corner) represents "motor themes" and contains keywords such as "rheumatoid arthritis," "anti-inflammatory activity," and "immunoglobulin G." These keywords also correlated with the green cluster in Fig. 9, indicating that IgG glycosylation is closely related to rheumatoid arthritis. The second quadrant (upper left corner) represents "highly developed and isolated themes" and contains two themes. One has a low centrality but high density and includes "immunoglobulin A nephropathy," "human serum IgA1," and "human mesangial cells." Glycosylation has been extensively studied in IgA nephropathy. The other includes "multiple sclerosis," "dendritic cells," and "experimental autoimmune encephalomyelitis." This theme has high centrality but low density, indicating that glycosylation has made significant progress in the study of multiple sclerosis.

In addition, there is a theme that involves both the second and third quadrants. The third quadrant represents "emerging or

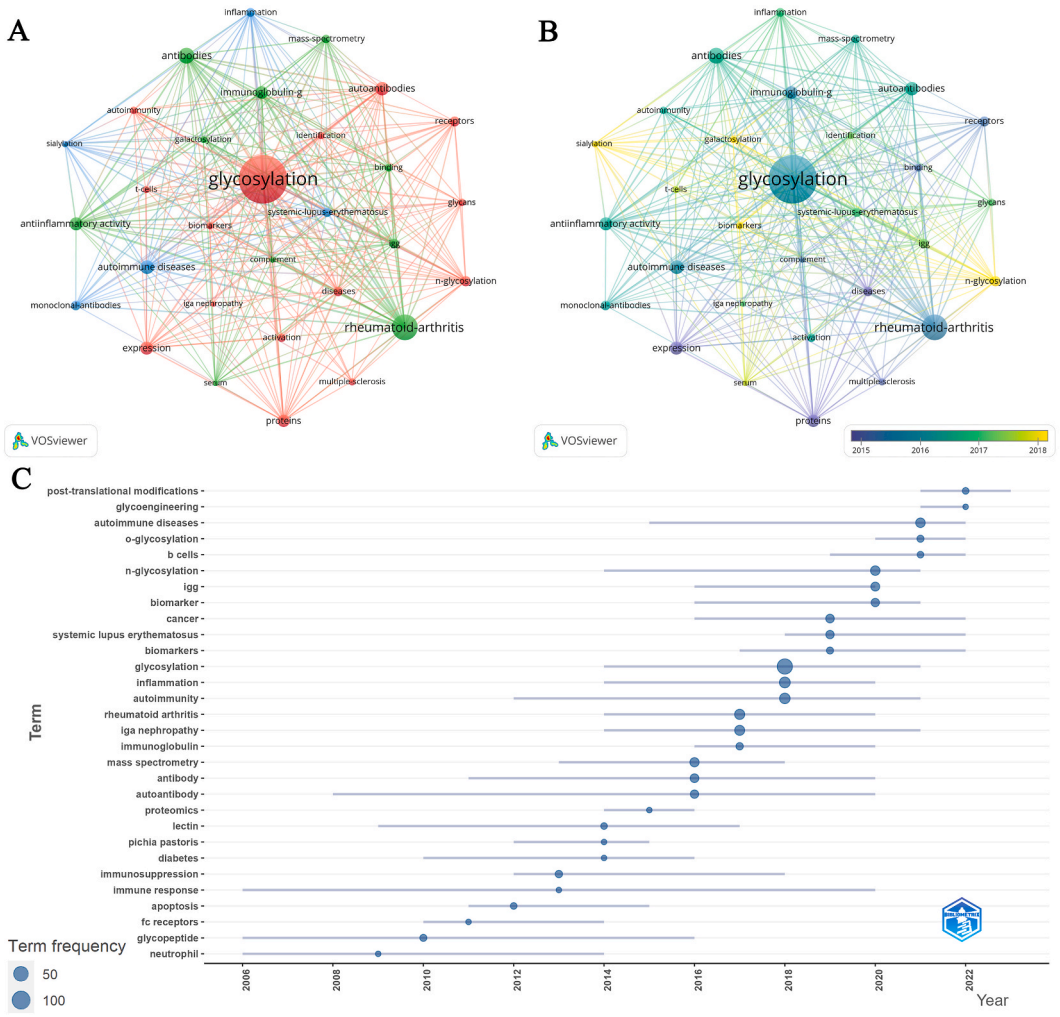

Fig. 8. Cluster analysis for keywords. (A) Visualization map of the keyword co-occurrence network; (B) timestamp visualization of the keyword co-occurrence network; (C) historical migration of research hotspots.

declining themes" and contains themes such as "galactose-deficient IgA1," "O-linked oligosaccharides," and "Oxford classification," focusing more on mechanistic research into the mechanism of glycosylation. Another theme in the third quadrant included ”O-glycosylation,” “immune complexes,” and “genome-wide association.” However, this theme is different from the previous theme because it also satisfies the conditions of the fourth quadrant, i.e., "basic and transversal themes." The fourth quadrant contains two themes, one related to autoimmune antibodies and the other related to the expression of glycosylation, mainly concerning the conceptual framework of the field.

4. Discussion

4.1. General information

This study included 530 research articles related to glycosylation in ADs from 2003 to 2023 in the WOSCC database, with more research articles than review articles. The first review article was published in 2005, and its main content was that a new technology, called proteomics, emerged in rheumatology research based on mass spectrometry and could be used to identify posttranslational modifications of proteins, laying the foundation for the study of glycosylation in rheumatology [16]. From 2003 to 2007, the field of study was in its early stages. With the advancement of technology, the expression of polysaccharide structures in cells and tissues is gradually being decoded, and the role of protein-polysaccharides in innate and adaptive immunity is receiving increased attention [17]. Research entered a stable growth period from 2008 to 2015, with two small peaks in 2012 and 2015.

In 2012, a highly cited review showed that IgG has dual effects on inflammation, which may be related to changes in the glycosylated portion of IgG, particularly in sialic acid residues, regulating its anti-inflammatory effect [18]. Subsequent studies have

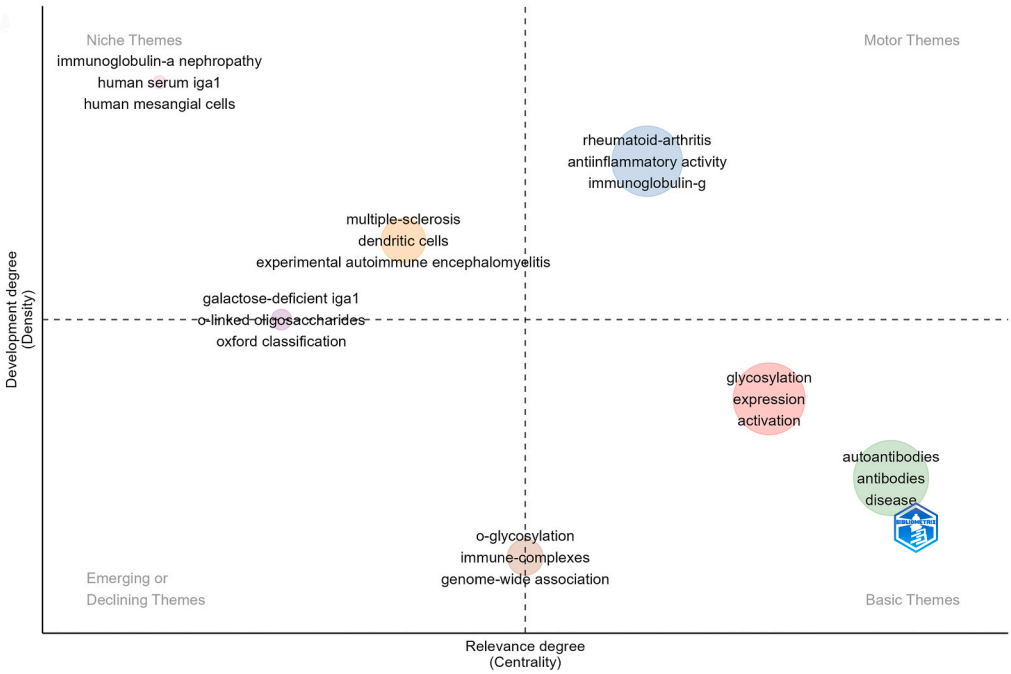

Fig. 9. The thematic map.

increasingly focused on the glycan interaction of antibodies, leading to a surge of highly influential publications since 2015. These publications investigated glycosylation sites on immunoglobulins associated with various ADs, such as rheumatoid arthritis, IgA nephropathy, systemic lupus erythematosus, and multiple sclerosis. This field has experienced rapid growth since 2016, reaching its peak in 2022. Overall, the annual growth rate of publications in this field is 2.84, indicating that the field is on the rise. Therefore, it can be predicted that research on glycosylations in ADs will be a future hot research topic.

This research field has drawn the attention of scholars worldwide, particularly in the United States, which ranks first in the H, G, and M indices. China ranks second in terms of total publications, and has contributed significantly to this field in recent years, but its total citation volume is low, which may be related to the delayed start of research in this field in China. Leiden University is the top ranked institution in terms of total publication output. According to the H-index, the highest contribution comes from Manfred Wuhrer at Leiden University, followed by scholars from the University of Alabama at Birmingham, including Jan Novak and Bruce A Julian. According to the G-index, one highly cited paper by Gordan Lauc had a significant impact in this field. This article describes the results of a genome-wide association study (GWAS) on human IgG N-glycans, in which 16 gene loci were found—some of which were related to IgG glycosylation, while others were closely related to ADs [19].

4.2. *Research bases*

4.2.1. *IgG glycosylation and ADs*

In highly cited journals and references, many studies have focused on the correlation between IgG glycosylation and ADs. FcγR and complement work synergistically to mediate inflammatory responses in ADs [20]. IgG specifically binds to Fcγ receptor III (FcγRIII) on natural killer (NK) cells to promote antibody-dependent cell-mediated cytotoxicity (ADCC) mediated by NK cells [21]. ADCC is a process that involves the recruitment of effector molecules and cells to target cells, promoting the destruction of cells via self-antigen reactivity [22]. In addition, immune complexes (ICs) that form by the binding of IgG to antigens activate the complement system, facilitating the clearance of IC to prevent tissue damage caused by IC deposition [23]. The glycosylation of the IgG Fc region, such as fucosylation, galactosylation and sialylation, is crucial for the binding of IgG to FcγR and the complement component C1q [24].

A highly cited article (TC = 181) showed that low fucosylation of IgG1 Fc resulted in increased binding with the FcγRIII family, while fucosylated IgG lacked ADCC activity [25]. IgG without fucose residues showed higher ADCC efficiency, while the exposure of fucose glycan residues in IgG complexes was associated with high disease activity in systemic lupus erythematosus [26]. Additionally, highly galactosylated IgG1 antibodies also promoted ADCC while increasing C1q binding and promoting downstream complement deposition [27]. Furthermore, studies on IgG sialylation have been controversial and have received increased amounts of attention. The most highly cocited reference according to LC first proposed that IVIg exhibits anti-inflammatory effects on ADs related to the sialylation of N-linked oligosaccharides in the IgG Fc fragment [28]. The use of enriched IgG-sialylated fragments in this study was achieved through the Sambucus nigra agglutinin (SNA) method. A highly cited article published in PLoS One indicated that when SNA enriches the IgG sialic acid fragment in IVIg, sialic acid is concentrated in the Fab region, and the use of IVIg with Fab-IgG sialylation

leads to a decrease in the efficacy of IVIg [29].

4.2.2. IgA glycosylation and ADs

IgA is an important immunoglobulin in serum that is second only to IgG, and binds to Fcα receptor I (FcαRI), which is expressed by myeloid cells (including monocytes, neutrophils, and macrophages) [30]. Excessive amounts of IgA-containing immune complexes can lead to dysregulation of immune modulation mediated by FcαRI, resulting in sustained inflammatory reactions [31]. IgA glycosylation is an important influencing factor in the deposition of ICs [32].

According to the clustering analysis of the literature, "#3 IgA nephropathy" was a relatively independent cluster (Fig. 7B), and was a keyword in many articles published approximately 2017 (Fig. 8C). IgA nephropathy (IgAN) is the most common primary glomerulonephritis and is characterized by IgA deposition in the glomeruli, promoting mesangial cell proliferation and inducing kidney damage [33]. In 1993, it was first discovered that the reduction in O-galactosylation of O-linked glycans on IgA1 may be a crucial factor in the deposition of ICs in IgA nephropathy [34].

4.3. The hot topic of glycosylation in ADs

4.3.1. Glycosylation and rheumatoid arthritis

Among the top 10 articles and cited articles according to LC ranking, a total of 6 articles studied the relationship between glycosylation and rheumatoid arthritis (RA) (shown in Supplement Table 5). According to the keyword analysis, glycosylation and RA were the two most common keywords (Supplemental Table 6). "Rheumatoid arthritis" belonged to the first main cluster according to keyword clustering analysis and started to appear frequently in the field of glycosylation in 2017 (Fig. 8). According to the reference list and keyword analysis, RA is closely related to glycosylation.

RA is a common inflammatory disease characterized by synovitis and destruction of cartilage and bone [35]. In 1985, for the first time, changes in IgG glycosylation were observed in RA patients, particularly due to a lack of galactosylation [36]. In 1995, an article showed that the absence of IgG Fc galactosylation induced the complement system and promoted RA inflammation [37]. Pregnancy is the only natural condition that could cause spontaneous improvement in RA incidence, and total IgG galactosylation increases during pregnancy but decreases significantly after delivery [38]. Furthermore, patients with RA have lower levels of serum IgG sialylation and increased fucosylation [39]. Anti-citrullinated protein antibodies (ACPAs) are specific antibodies for RA that promote joint destruction by enhancing inflammation and activating Fc receptors in specific cells [40]. The decrease in IgG1 galactosylation and increase in fucosylation of serum ACPA-IgG1 before the onset of RA may be related to the proinflammatory function of IgG [41]. In addition, compared with those in serum, ACPA-IgG1 in synovial fluid lacks sialic acid residues in comparison with serum samples [42]. The activation of synovial fibroblasts is a key pathological factor in RA. The N-glycoprotein terminus of synovial fibroblasts is sialylated, and this increase in sialylation is closely related to RA disease remission, while desialylation may lead to pro-inflammatory cell responses. Further research has shown that sialylation may prevent the interaction of polysaccharides on the surface of synovial fibroblasts with galectin-3 (Gal-3), reduce the generation of proinflammatory cytokines, and prevent the transformation of fibroblast synovial cells into an inflammatory phenotype [43].

4.3.2. Glycosylation and other autoimmune diseases

Through keyword and citation analysis, it is evident that glycosylation is closely related to systemic lupus erythematosus (SLE), multiple sclerosis (MS) and IgA nephropathy (IgAN), and the relationship between glycosylation and IgAN has been elucidated above. SLE is an AD that affects multiple organs throughout the body and is characterized by the deposition of ICs in tissues and organs leading to an inflammatory response [44]. A study from 1992 showed that the glycosylation of IgG in SLE patients was altered [45]. The research team led by Gordan Lauc made a significant contribution to the study of SLE, with their article ranking number 4 in the LC ranking. This article proposes that the IKZF1 gene locus is associated with multiple IgG N-glycans and that changes in IgG glycosylation may be one of the molecular mechanisms affecting SLE [46]. Additionally, the galactosylation and sialylation of IgG in the serum of SLE patients are decreased, which can regulate the proinflammatory function of IgG [47].

Furthermore, Lauc's research team reported a significant decrease in IgG core fucosylation in MS, and the decrease in core fucosylation of IgG led to an increase in proinflammatory cytokine levels, consistent with previous reports [48]. MS is a neurodegenerative form of AD characterized by the degradation of myelin and is composed of myelin phospholipids and proteins [49]. The degradation of myelin promotes the formation of self-antigens, such as myelin oligodendrocyte glycoprotein (MOG) [50]. By establishing an experimental autoimmune encephalomyelitis (EAE) mouse model of MS, researchers have shown that the pathogenicity of MOG is correlated with O-glycosylation and that the N-glycan structure of MOG (including LacNAc and Fucα1-3GlcNAc) could inhibit the aggregation of MOG O-glycosylation peptides [51].

4.3.3. Application potential of glycosylation in ADs

Recently, "glycoengineering" was the most frequently used keyword (Fig. 8C). IgG-type monoclonal antibodies (IVIgs) are widely used for the treatment of ADs [52], and there is increasing interest in developing alternatives to IVIg production by increasing the activity of IVIg active ingredients [53]. However, synthesized antibodies have unstable characteristics, which makes it difficult to synthesize antibodies artificially [54]. One significant challenge is that IgG glycosylation can increase the affinity between IgG Fc and FcR, which decreases their overall efficiency (such as the occurrence of core fucosylation). Therefore, glycoengineering based on reducing the glycan heterogeneity of monoclonal antibodies represents a promising strategy for the treatment of autoimmune disorders.

Precise gene editing technology offers the possibility of altering glycosylated protein mechanisms, particularly through CRISPR/Cas-mediated elimination or induction of glycosyltransferases or direct modulation of the expression of glycosylation-related genes [55,56]. For example, induction of IgG Fc glycosylation via soluble sugar transferases incorporating either oligomannose or sialic acid residues can convert self-reactive IgG into anti-inflammatory IgG [57]. Knocking out α-1,6-fucosyltransferase (FUT8) to synthesize low-fucosylation monoclonal antibodies can significantly improve ADCC activity [58]. In addition, artificial intelligence tools can assist in analyzing and processing experimental datasets, optimizing the production and engineering of therapeutic glycoproteins [59,60].

Interestingly, the use of sugar-modified nanoparticles for targeted therapy through receptor recognition on immune cells provides a promising new approach for selective drug delivery [61]. Furthermore, human embryonic stem cells (HESCs) are generated by isolating embryos from the body; these cells possess powerful immunoregulatory abilities and are included in the category of mesenchymal stem cell therapies for ADs [62]. HESCs also exhibit differential glycosylation features, which affect their pluripotency and differentiation [63]. In addition, human pluripotent stem cells (hPSCs) are key participants in regenerative medicine, and their therapeutic efficacy is also limited by drug delivery pathways [64]. Therefore, glycosylation also has tremendous potential value in drug delivery and regenerative medicine.

4.4. Strengths and limitations

This study is the first to evaluate the relevant literature characteristics and perform bibliometric analysis of glycation reactions in the field of autoimmune diseases from 2003 to 2023 based on the WOSCC. By including the reference data from the literature, a high citation probability was obtained, and high-quality literature published before 2003 was accurately screened; moreover, a more detailed description of this part of the literature was provided, increasing the comprehensiveness of this study. However, this study focused only on the literature published in English in the WOSCC, which may lead to the neglect of potential high-quality literature and an increased risk of publication bias. Due to the inherent limitations of commonly used software for bibliometric studies, it may not be possible to reduce the risk of bias, and artificial intelligence may be a better tool to address this limitation [65].

5. Conclusions

In recent years, research on glycosylated proteins in the field of ADs has shown a significant increase and has continued to increase overall. The United States is the country with the longest research time and greatest academic influence in this field, with China making significant contributions in recent years, and some institutions in the Netherlands ranking highly in publications and citations. Antibody glycosylation in immune reactions is the basis of research in this field and is related to various ADs. Glycosylation is a new trend in the treatment of ADs in areas such as the synthesis of targeted monoclonal antibodies, drug delivery, and regenerative medicine. Artificial intelligence is an emerging tool in glycobiology.

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Data availability statement

Data included in article/supp. material/referenced in article.

Author contributions statement

Guoqian Deng, Xinyi Chen, and Le Shao: Conceived and designed the experiments; Contributed reagents, materials, analysis tools, or data; Wrote the paper. **Qibiao Wu and Shenzhi Wang:** Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data and wrote the paper.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Not applicable.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e30026.

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