# Knowledge Domain and Emerging Trends of IgG Glycosylation: A Bibliometric Study Based on CiteSpace

**Jian Lv**
Department of Epidemiology and Health Statistics, School of Public Health, Shandong First Medical & Shandong Academy of Medical Sciences, Tai'an, China

**Xueyu Chen**
Department of Epidemiology and Health Statistics, School of Public Health, Shandong First Medical & Shandong Academy of Medical Sciences, Tai'an, China

**Yuejin Li**
Department of Epidemiology and Health Statistics, School of Public Health, Shandong First Medical & Shandong Academy of Medical Sciences, Tai'an, China

**Xia Feng**
Department of Epidemiology and Health Statistics, School of Public Health, Shandong First Medical & Shandong Academy of Medical Sciences, Tai'an, China

**Kai Zhu**
Shandong Center for Disease Control and Prevention, Founding

**Dong Li**
Department of Epidemiology and Health Statistics, School of Public Health, Shandong First Medical & Shandong Academy of Medical Sciences, Tai'an, China

**Long Ji** ( lji@sdfmu.edu.cn )
Shandong First Medical University - Tai'an Campus

**Research**

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# Abstract

**Background**: The purpose of this paper is to evaluate the international scientific output of Igg glycosylation research by a stoichiometric analysis of the related papers published in the field of IGG glycosylation from 2009 to 2020, to explore the hot spot of IGG glycosylation and the evolution path of IGG glycosylation.

**Methods:** Using the Web of Science core database (WoSCC) to collect the articles related to IgG glycosylation from 2009 to 2020 as the research object, using CiteSpace visualization software to analyze the co-occurrence of countries and institutions, core authors, and keywords. Cited authors and literature, Co-citation analysis of journals, obtaining cooperation maps of research countries / institutions and core authors, literature citation and clustering maps, co-occurrence maps of high-frequency subject headings, displaying related clusters, mutual influences between clusters and Keyword timeline view spectrum of the historical span of important keywords in clustering.

**Results:** We searched 482 articles related to IgG glycosylation published in 227 journals, and observed that in the past 10 years, the number of articles published has generally increased year by year; it has been cited 13262 times, with an average of 27.5 citations per article, showing an upward trend year by year. The core team in the field of IGG glycosylation is mainly from University and research institutes in USA, Australia, Netherlands, Croatia, England, Germany, Ireland, Scotland, China and Japan. A total of 2408 authors participated in the writing of literature on Igg glycosylation, Among them, Wuhrer, Manfred□ Lauc, Gordan□Irena Trbojevic Akmacic, Wei Wang and other scholars are the representatives of this research field and have important influence. There are 281 keywords under the theme of IgG glycosylation, of which there are 4 keywords with word frequency ≥100, and hot keywords that serve as bridges are pregnancy□complex□glycan□biosimilar□N-linked glycosylation□hilic-uplc□glycation and form 8 clusters. IgG glycosylation, as the "biomarker" of disease diagnosis and its mechanism has been a research hotspot in recent years.

**Conclusion:** The use of CiteSpace software for quantitative analysis of IgG glycosylation related literature can intuitively demonstrate its development history and current research hotspots and trends, and can provide researchers with reference to the topic selection and research direction. Value and meaning.


# 1. Background

In recent years, people have conducted in-depth research on the glycosylation of various proteins, and clearly understand the important role of protein glycosylation in the occurrence and development of various diseases in humans [1–6]. People's interest in the research of immunoglobulin G (Ig G) glycosylation has increased dramatically, and many magazines have published a large number of articles on IgG glycosylation. Many studies have shown that changes in Ig G glycosylation level and sugar chain structure are often accompanied by the occurrence and development of various chronic disease [6–8],Because Ig G glycosylation is highly heterogeneous and can be regarded as a disease phenotype, it may

be used as a dynamic disease biomarker from the perspective of predictive, preventive and personalized medicine Thing [9–14]. With the rapid increase in the number of articles published, it becomes very difficult to identify new developments and new trends in IgG glycosylation research. The author found that there is no researcher at home and abroad to analyze the development trend of IgG glycosylation in the process of analyzing and analyzing relevant documents of IgG glycosylation, and there is still a lack of a comprehensive literature visualization measurement widely used in the knowledge structure and development of specific research field's analysis.

CiteSpace "Citation space" is one of the information visualization software developed by Chaomei Chen, a famous Chinese-American scholar and professor at Drexel University in the United States. It was used to measure and analyze scientific literature data [15, 16]. It focuses on finding the key points in the evolution of a research field. It combines methods such as cluster analysis, social network analysis, and multi-dimensional scale analysis. It can achieve co-citation analysis, keyword co-occurrence analysis, and collaborative analysis of agency authors [17]. By drawing a knowledge map of the development of science and technology, it can intuitively display the panoramic view of information in the field of scientific knowledge, explore key literature, hot research and frontier directions in a scientific field. Compared with other visualization software, CiteSpace V has convenient data processing, Good visualization effect, easy interpretation, etc., can meet the requirements of large sample literature co-citation and keyword co-occurrence analysis [18, 19]. The software has been widely used to evaluate the productivity of different regions, countries, institutions, authors of various University subjects, compare the cooperation of authors in national institutions, and explore research hotspots and development trends in a specific subject area. [17]. From an objective and quantitative point of view, bibliometric analysis is a typical method of using citation relationships to generate effective materials for scientists, so it can reflect hot spots, evolutions and emerging trends in specific fields [20].

This article uses CiteSpace5.6.R5 to conduct a comprehensive visual analysis of the research literature of IgG glycosylation in 2009–2020 in the Web of Science database using document measurement methods and data mining algorithms. CiteSpace shows the history of knowledge development in a field and status quo. Measure and analyze the content of relevant research institutions and related research scholars in the field through the volume of statistics; draw and interpret the knowledge map of hot keywords in the field of IgG glycosylation research, establish an IgG glycosylation research cluster and discuss current research Hot spots and future development trends, with a view to providing a more comprehensive reference for further research on IgG glycosylation. The second part introduces the data sources and research methods. The third part visually analyzes the results of IgG glycosylation research articles and shows the latest development and emerging trends of IgG glycosylation. The fourth part draws the main conclusions of this study, and points out the future research direction and limitations.

# 2. Data Sources And Research Methods

### 2.1 Data sources and retrieval methods

The data required for this research is obtained from the Web of Science database, select Web of Science Core Collection [21], The search conditions are: TS=( Glycan OR Glycosylation) AND TS=(Ig G OR Immunoglobulin G), The time span is from 2009 to 2020, and the deadline is (April 20, 2020). After screening, 482 eligible documents were obtained, and each piece of data was downloaded as a full-text plain text format. (Table 1)

### 2.1.1 Data inclusion criteria

(1) The time span is from 2009 to 2020

(2) Articles retrieved in WoSCC database

(3) Articles about IgG glycosylation research, including Original research and Review

(4) Articles with basic information required for analysis.

### 2.1.2 Data exclusion criteria

(1) Meeting summary, meeting minutes, letters, corrected articles and repeated articles

(2) Unpublished articles do not have sufficient information for further analysis.

## 2.2 Research methods

Import full-record plain text information into CiteSpace V 5.6.R5 software for visual analysis. The time span was selected from 2009 to 2020. In order to obtain high-impact nodes from the data set, according to the analysis method in Professor Chen Chaomei's article Set the time slice to one, and divide it into 11 periods from 2009 to 2020. Analyze the node types to select Author, Country, Institution, Keyword, Reference, Cited Author, and Cited Journal. The source of the subject word is selected by default; the threshold selection system default: Top N per slice = 50, which means that the top 50 nodes with the highest number of citations in each year are selected to build the network of the year, and then the network of each year is synthesized. Draw a visual knowledge map of IgG glycosylation. In order to study the details of collaboration more clearly, we use Pruning Pathfinder Pruning sliced networks Pruning each merged network to improve the clarity of the composite network. This research uses four scientific measurement techniques: (1) Co-author analysis, including co-authors of authors, countries, and institutions; (2) Cod analysis to determine keywords and topic categories; (3) Co-author analysis, including cooperative journals, Co-authors and co-authored literature; (4) Cluster analysis based on co-cited literature and keyword analysis. (Figure 1)

## 2.3 Data analysis

Excel 2016 was used to make statistics and tables of published literature, and CiteSpace v (5.6.R5) was used to make visual analysis of data

# 3. Results

According to the above search strategy, 482 articles related to IgG glycosylation were published in 227 journals. The annual distribution of publications and the annual citations of the documents were shown in Figure 2. These 482 articles were cited 13,262 times, with an average of 27.5 citations. Since 2009, the number of papers published and cited on Igg glycosylation research has been on the rise. In 2009-2019, the publication time of the papers related to the research of Igg glycosylation can reflect the development speed and the hot period of this field to some extent, which indicates that people pay more and more attention to this research field. Figure2

On the superimposed result of the double images of the journal, the citation map is on the left and the citation map is on the right. The curve is a citation line, which completely shows the ins and outs of the citation. In the figure on the left, the more papers published in the journal, the longer the vertical axis of the ellipse; the more the number of authors, the longer the horizontal axis of the ellipse. (Figure3)

### 3.2 Country / Region and institution cooperation network analysis

The 482 articles included in the analysis were supported by 750 fund projects, and the National Natural Science Foundation of China Nation funded a maximum of 42 projects. Figure 3a below shows the academic cooperation between 53 countries / regions conducting IgG glycosylation research. Overall, the cooperation between countries in the field of IgG glycosylation research is relatively close. The top ten countries in frequency are USA (136), Netherlands (96), China (75), Germany (63), Croatia (60), England (53), Australia (28), Japan (27), Ireland (24), and Scotland (22). Centrality describes the importance of nodes. The size of Centrality was reflected in the purple circle on the outer edge of the node on the cooperative network map. The highest Centrality country in the map we made is USA (centrality = 0.48) followed by GERMANY (centrality = 0.35), AUSTRALIA (centrality = 0.27), ENGLAND (centrality = 0.23), CROATIA (centrality = 0.22) According to the meaning of centrality described above, that is, intermediary centrality $\geq$0.1 represents the node has a turning point in the network, indicating that these five countries the importance of is self-evident. (Figure 4a)

We use the CiteSpace software to draw an institutional cooperation network map (Figure 4b). 684 institutions worldwide have cooperated or independently completed the writing of articles, mainly distributed in North America, Europe, Australia and Asia. We can see that Leiden University (79, Centrality=0.35) in the Netherlands has the largest node, followed by the University of Zagreb (53, Centrality=0.12), Geno's Glycosci Res Lab (33, Centrality=0.01), University Edinburgh of the Republic of Croatia (21, Centrality=0.14), Capital Medical University (21, Centrality=0.04), Edith Cowan University (20, Centrality=0.01), Vrije University Amsterdam (17, Centrality=0.06), University Amsterdam (13, Centrality=0.00) , Shandong First Medical University & Shandong Academy of Medical Sciences (10, Centrality=0.09), Kings Coll London (9, Centrality=0.18). We can see in Figure 3b that Leiden University and the University of Zagreb are at the heart of the collaborative network, and Leiden University is number one in the world with 79 articles published. (Figure 4b Figure 4c)

Comprehensive Analysis showed that the relationship between the national institutions involved in the study of Igg glycosylation was very close, which indicated that the subject has been in the process of close cooperation. Globally, IgG glycosylation research is relatively concentrated, and scientific research institutions are located in Europe, Asia, North America and Australia. The nature of scientific research institutions is mainly university laboratories and research institutes, countries such as the Netherlands, Croatia, England, Germany, Ireland, Scotland, the China in Asia, Japan, and USA in the Americas and Australia in Australia in Europe focus on co-operation, while Leiden University in the Netherlands works more with other institutions.

### 3.3 Analysis of author and cited author

According to our 199 nodes, 531 Wire Author Cooperative Network Atlas, Figure 4. The top 10 contributors are Manfred Wurudd 74, Gordan LAUC 55, Andre M elder 22, Irena Trbojevicakmacic 21, Wei Wang 19, Pauline M Rudd 16, jerko Stambuk 16, Maurice H J Selman 15, Frano Vuckovic 14, Youxin Wang 14.

The authors of the Centrality ≥0.1 are Gordan LAUC 0.23, Manfred Wuhrer 0.19, Jasminka Kristic 0.13, Frano Vuckovic 0.11, Noortje De Haan 0.11, and Wei Wang 0.10. (Table2 Figure 4a)

The Core Author Group refers to the author group with numerous publications and wide influence in a certain subject area. Price's law measures the distribution of authors across disciplines. In Price's famous book little science, Big Science, he states: "Half of all papers on the same subject are written by a group of highly productive authors, a collection of authors equal in number to the square root of the total number of authors. " [22] The formula is m = 0.749(NMAX)1 / 2, where Nmax refers to the number of papers published by the most authors, and those who published more than M are considered to be the core authors in this field [23]. A total of 2,408 authors were involved in the writing of Igg glycosylation studies, with the most prolific contributors being Wuhrer, Manfred, (74 articles) , or Nmax 74, m27.7 can be calculated from Price's law, which indicates that the authors of more than 28 papers are the core authors in the field of IGG glycosylation, That's Wuhrer, Manfred, and LAUC, Gordan. According to the latest research from Wuhrer, Manfred of Leiden University in the Netherlands, variation in key transcription factors coupled with regulatory variation in glycogenes modifies IgG glycosylation and has influence on inflammatory diseases [24]. Croatia, LAUC, Gordan's group at the University of Zagreb, Selected N-glycans improve type 2 diabetes and CVD prediction established beyond risk marker. Plasma Protein N-glycan profiling may thus be useful for risk purification in the context of precisely targeted primary prevention of cardiovascular diseases [25].

The authors were cited in the top 10 for Kaneko Y 185, Arnold JN 157, Anthony RM 153, Jefferis R 149, Parekh RB 137, Shields RL 133, Wuhrer m 124, Nimmerjahn F 122, Pucic M 112, Selman MMHJ 102.

The authors are Nimmerjahn F 0.12, Shinkawa t 0.11; ROOK GAW 0.11, JN Arnold 0.1, Anthony RM 0.1, Parekh RB 0.1, and Ferrara C 0.1. Kaneko Y, Arnold JN and so on are the representatives of IGG glycosylation. (Table4)

### 3.4 Research Focus and cutting-edge cluster analysis

Key words are the most concentrated words that can show the main content of the paper. The frequency of key words is usually positively correlated with the research focus, this shows that by analyzing the frequency of keywords appearing in the literature of a certain field, we can find out the current research hotspot of this field, and we can understand the development and changes of this field according to the appearance of keywords in different periods [18]. In the co-occurrence graph, the frequency of the keywords indicates the extent of the research in this field. We can identify the research hotspots in this field by the terms of high Centrality or Bursts, according to the frequency of emergence words in different periods, we can understand the development of this field in the time line, and then judge the research frontiers and trends. Bursts refers to the significant increase in the frequency of keyword use in a short period of time, and measures the rate of change in the frequency of citation of literature containing keywords, the high Bursts vocabulary will become the hot spot in the future. Using key words that can reveal or express the core content of the literature in a field of frequency of keyword frequency analysis could be found in the center and frequency of emergence of vocabulary.

#### 3.4.1 IgG glycosylation research keywords general situation

We used the CiteSpace 5.6.R5 software to analyze the collinearity of keywords, and generated 211 nodes and a high frequency keyword co-occurrence graph of 906 connections (Figure 6). The node size represents the frequency of keywords, that is, the larger the cross shape, the higher the frequency of changing keywords. The connection between nodes indicates that the connected keywords appear together in the literature, and the thickness of the connection reflects the number of co-occurrences to reflect the degree of keyword relevance in the research [19]. From January 2009 to April 2020, there were 281 keywords in 482 articles under the theme of IgG glycosylation research. The basic vocabulary of this research field, so we have not analyzed it specifically. It could be seen in Figure 5 that rheumatoid arthritis has the highest number of occurrences, 121 times, which may be related to IgG glycosylation that has been used as an effective diagnostic biomarker for autoimmune diseases in recent years. Followed by Anti-inflammatory activity, appeared 104 times. Immunoglobulin G and Glycosylation are in the central area of the network map and the keywords distributed around it are mainly rheumatoid arthritis, Anti-inflammatory activity, igg, antibody, monoclonal antibody, mass spectrometry, glycol, galactosylation. The top 5 in Centrality are mass spectrometry 0.17, liquid chromatography 0.12, oligosaccharide 0.11, flame 0.10, identification 0.10; the top 5 in Bursts are biomarker 9.00, N-glycan 7.12, oligosaccharide 5.76, structural change 4.99, N-glycosylation 4. 64. It is worth noting that although the biomarker appears only 36 times, it is Centrality = 0.01, Bursts = 9.00, indicating that it has an important position in recent research. Table5 Table6

#### 3.4.2 Dynamic frontier evolution of IgG glycosylation keywords

From the change of keywords, we can find that IgG glycosylation involves a lot of content. To better analyze the research direction of IgG glycosylation, use the Timeline view function in CiteSpace software

to display the dynamic frontier map to see the IgG glycosylation Clustering and development of keywords in the process of research. Taking the publication year as the X-axis and the cluster number as the Y-axis to obtain the IgG glycosylation timeline evolution chart can clearly see the literature of these 7 clusters. The more important. The research on IgG glycosylation is mainly divided into 7 major themes, namely # 0pregnancy, # 1complex, # 2glycan, # 3, biosimilar, # 4N-linked glycosylation, # 5 hilic-uplc, # 6 glycation. Based on the results of keyword clustering, we can draw the development and structural changes of IgG glycosylation research hotspots in recent years. (Figure7)

### 3.4.3 Frontier topics in IgG glycosylation research

We use CiteSpace to select keywords with a large frequency of change. According to the frequency of changes, we can judge the development trend of IgG glycosylation research and Burst by keywords provides a reasonable basis for the research frontier prediction. In the figure, there is a flashing bar after each keyword. Each cell of the flashing bar represents a year. The blue line indicates the time interval. The red line indicates the flashing year of the keyword. The length represents the flashing duration of the keyword. In the figure, we can see that the hotspots of IgG glycosylation research in 2009-2020 have evolved significantly and could be divided into 3 stages. 2009-2014 was mainly based on n linked oligosaccharide, oligosaccharide, structural change, crystal structure, glycopeptide, human igg are the research hotspots, and then from 2014 to 2018, mainly based on hilic-uplc, igg fc, high throughput, pregnancy, chromatography, systemic lupus erythematosus as the research hotspots Since 2018, the research focus has been mainly on n-glycan, biomarker, mechanism, and diagnosis. (Figure8)

## 3.5 Analysis of Journal co-citation network

482 articles on IgG glycosylation screened in this study cited 14443 references published in 534 journals, with an average of 29.9 articles per article. Table3 shows the top ten most cited journals. According to the number of citations, the best journal is "Journal of Biological Chemistry", there are 328 cited records. Therefore, we can think that "Journal of Biological Chemistry" is our journal. The best reference source for the research topic of IgG glycosylation; in terms of impact factor (IF), there is no doubt that "Science" (IF = 41.037) and "Nature" (IF = 43.070) have the greatest impact on our research and the most significant Far-reaching. In the visual map, we can also see that there are multiple journal nodes surrounded by purple rings. These journals have a high Centrality. Centrality was used as an indicator to measure and discover the importance of nodes in the graph. Purple rings indicate the structure of nodes The characteristic, the thickness of which implies the degree of centrality, here the nodes with intermediary centrality ≥0.1 are highlighted with purple circles[15]。In the map, you can see "Molecular Immunology" (centrality = 0.17); "Current Opinion in Immunology" (centrality = 0.11); "Cell" (centrality = 0.11), these journals play an important role in connecting different journals, and are IgG An important turning point in glycosylation research. In the visual analysis, we found that some journals have burst. Figure 4 shows the main journal and citation Burst detection. Burst detection acts as an indicator of active nodes in the visualization process. We can see that the nodes of "Scientific Reports" (burst strength = 21.72, 2016) and "Frontiers in Immunology" (burst strength = 19.99, 2017) are red, which proves that Burst appears, indicating that the

articles published by the journal are in the near future Being cited heavily, the journal has attracted great attention from peers in a short period of time[18] (Figure9)

### 3.6 Co-citation analysis of References

In bibliometric, the research frontier represents the development status of a research field, and the citations of research frontier articles constitute the subject knowledge base of the research field. Co-citation analysis is one of the important methods of bibliometric. Since Small[26]introduced the concept of co-citation, and defined it as "two documents appear in the reference list of the third citing document together", we conducted a total of literature citations on a collection of literature spatial data sets. Consider the process of mining cited relationships could as co-cited analysis of the literature. It could also be said that when certain literatures are cited in large numbers by other authors in the field, the theoretical knowledge reflected in the literature is widely recognized by the scientific community[27] The citation frequency of the citation can be used to measure the academic influence of the article [28] Articles with high citation frequency show the core achievements in this field. At the same time, citations can also be used to find "classical articles" in the field through the co-citation network.[29] We made 446nodes and 2297lines of the literature total citation map through the software shown in Figure 6. We can see in Figure 6 that 10 articles cited more than 45 times are at the core of the literature co-cited network graph. Table 7 lists the 10 articles with the highest cited frequency. Puci M (2011) the article titled “High throughput isolation and glycosylation analysis of IgG-variability and heritability of the IgG glycome in three isolated human populations” published in MOL CELL PROTEOMICS was cited the most, namely 100 times. Pucic M conducts IgG glycosylation studies at Genos Ltd, Glycobiology Division in Croatia, Zagreb. Through the continuous efforts of researchers in the field of IgG glycosylation, the knowledge structure of research in this field has been formed and developed, which provides a more comprehensive knowledge network for the subsequent research of IgG glycosylation. Overall, the network of core co-citation relationships is complex, indicating that academic research results in the field of IgG glycosylation have a strong co-citation relationship. (Figure 10 Table8 Table9)

# 4. Discussion

This article uses CiteSpace software to perform a retrospective visual analysis of the literature on IgG glycosylation in the Web of Science database from 2009 to 2020. The combination of analysis and reference co-citation analysis and keyword co-occurrence analysis can basically reflect the research hotspots and development trends in the field of IgG glycosylation in the past decade. To the best of our knowledge, this article is the first article to use CiteSpace software to perform bibliometric analysis of IgG glycosylation. This study can deepen researchers' understanding and understanding of IgG glycosylation research from the following aspects. It can provide help for the further development of IgG glycosylation.

### 4.1 IgG glycosylation research status

In the third part, it could be seen that the amount of articles published in the field of IgG glycosylation is generally increasing year by year. Judging from the connection and color of each node in the visual knowledge graph, from 2009 to now, institutions in various countries have cooperated closely and formed a high-yield network diagram with the university laboratory as the core. In particular, Leiden University in the Netherlands and the University of Zagreb in the Republic of Croatia are the most eye-catching, indicating that countries with a dominant position in the field of proteomics also have certain advantages in the field of IgG glycosylation. The distribution of institutions and authors involved in IgG glycosylation research is relatively concentrated, mainly based on intra-team cooperation, and most articles belong to multiple authors. An Authors 'cooperative relationship network with Wuhrer, Manfred, Lauc, Gordan, Irena Trbojevic Akmacic, and Wei Wang as core nodes. They promote the development of the IgG glycosylation field with a higher volume of posts. The major influencers are NETHERLANDS, Wuider of Leiden University, Professor Manfred 's team, CROATIA, University of Zagreb 's Lauc, Professor Gordan 's team, CHINA, Capital Medical University Professor Wei Wang's team has made great contributions to the development of the IgG glycosylation field with high influence and published articles and a relatively high citation frequency. The line color between the author and the institution was mainly based on warm colors, which shows that the authors in the field of IgG glycosylation have cooperated more in recent years. Since 2014, with the further deepening of proteomics and glycemic research, IgG glycosylation has attracted more and more attention as a biomarker for early detection and diagnosis of various chronic diseases, and corresponding research results have continuously emerged. However, it could be seen that there are not many countries participating in IgG glycosylation research. This is because the extraction methods and testing equipment required for IgG glycosylation research are more expensive, and the research institutions need stronger scientific research capabilities. The inconsistency and imbalance in the development of scientific research capabilities of different institutions in different countries have a great relationship.

*The articles of IgG glycosylation research were mainly published in professional journals such as JOURNAL OF PROTEOME RESEARCH, Molecular and Cellular Endocrinology, ANALYTICAL CHEMISTRY, SCIENTIFIC REPORTS. In recent years, Glycobiology, Moll Cell Proteomics and other professional magazines also have a large number of reference sources in top magazines such as Science and Nature, which shows that the direction of IgG glycosylation research has been more and more widely valued.*

### 4.2. Research hot content analysis

Since all IgG contains polysaccharides and the specific interaction of IgG Fc domain with Fc receptors is in antibody-dependent cell-mediated cytotoxicity (ADCC)[30], complement-dependent cytotoxicity (CDC)[31], Anti-inflammatory activity[32-34], pharmacokinetic half-life [35] and immunology[36] all play an important role, so IgG glycosylation modification research has been subject to the development of tumor immunology, biosimilar, and antibody drugs Attention to the field. Protein glycosylation is involved in many human physiological and pathological processes, such as cancer[37-42], aging[1,43-45], congenital glycosylation disease[46], diabetes[47-49], neurological diseases[6,50,51], pregnancy-related diseases [52], autoimmune diseases [53,54], primary desiccation syndrome [55], thrombocytopenic purpura (ITP), chronic

inflammatory demyelination Multiple neuropathy (CIDP), myasthenia gravis, and some rare diseases. At the same time, glycosylation also plays an important role in the human immune system, and these roles help us to specifically recognize these reactions [56]. Because IgG is the most abundant glycoprotein in immunoglobulin and its N-glycan participates in many physiological case processes, it was often considered an effective biomarker for us to recognize a certain disease [9,11,57]. It can also be seen from the cutting-edge trends of this research that since 2018, IgG glycosylation as a diagnostic biomarker for chronic diseases has gradually become a major research hotspot in the field.

In addition, as antibody drugs have been developed as effective preparations for disease prevention, diagnosis and treatment for hundreds of years in recent years, the vast majority of antibody drugs approved abroad are IgG1 and are expected to become the fastest growing in the entire pharmaceutical industry One of the areas. Since all IgG contains polysaccharides and the Fc domain of IgG specifically interacts with Fc receptors, these glycans all bind to the Fc R-terminus and C1q [58,59], thus affecting the function of IgG, which has led to the development of therapeutic monoclonal antibodies that enhance the effectiveness of antibody-dependent cell-mediated cytotoxicity (ADCC) in glycosylation engineering of these Fc glycans [60,61]. This kind of glycosylation modification of the Fc region of the antibody controls the oligosaccharide composition of the antibody to enhance its efficacy. This process was called glycosylation engineering. One of the goals of the new generation of antibody drug development is mainly glycosylation engineering antibodies , Mainly including three directions: (1) lack of core fucose to improve antibody ADCC response function[62],

(2) increase bismuth acetyl glucosamine content to improve antibody ADCC effect[63], (3) Increase the sialic acid content to increase the anti-inflammatory activity of antibodies [64]. At the same time, in recent years, more and more IgG is used for the immunomodulation of acute and chronic autoimmune diseases through intravenous injection (IVIG) or subcutaneous injection (SCIG) [65,66], so some scholars believe that a small part of IgG The occurrence of Fab sialylation leads to the anti-inflammatory effects of intravenous immunoglobulin (IVIG). Fleur S. van de Bovenkamp et al. proved through a series of experiments that Fab glycosylation could enhance the affinity of antibodies for homologous antigens [61]. Therefore, IgG glycosylation occupies an important position in the field of antibody preparation research and development.

### 4.3. Limitations of this study

This study only includes the literature collected from the Web of Science database from 2009 to the present. Due to the year of the database, the number of articles included may be lacking, and it needs to be more detailed and comprehensive in related research in the future.

# 5. Conclusion

Through this study, we found that the amount of articles published in the field of IgG glycosylation is generally increasing year by year. Using CiteSpace software to carry out quantitative analysis of IgG

glycosylation-related literature can initially and intuitively show its development process and current research hotspots. Trends can provide researchers with reference topics and research directions. The results have certain important value and significance.

# Declarations

### *Ethics approval and consent to participate*

Not applicable

### *Consent for publication*

Not applicable

### *Availability of data and materials*

Not applicable

### *Competing interests*

The authors declare that they have no competing interests


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### *Authors' contributions*

Long Ji is responsible for providing article ideas and modifying the article, providing research funding..

Jian Lv is responsible for the selection, sorting and analysis of article data and the revision and writing of articles.

Xueyu Chen is responsible for the revision of the article map and the revision and writing of some articles

Yuejin Li is responsible for the selection of article data and assistance in map production.

Xia Feng is responsible for the selection of article data and assistance in map production .

Kai Zhu is responsible for the selection of article data and assistance in map production.

DongLi is responsible for the idea of the article and some modifications to the article, providing research funding.

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# Tables

Table 1
Summary of search details

| Setting | Contents |
|---|---|
| Index | Web of Science Core Collection |
| Search rule | TS=( Glycans OR Glycosylation) AND TS=(Ig G OR Immunoglobulin G) |
| Literature types | Article, proceeding papers, review |
| Time span | 01/2009–04/2020 |
| Total | 482 |

Table 2
The amount of articles published and the author list of the top ten intermediaries

| Rank | Freq | Burst | Degree | Centrality | Author | Freq | Centrality | Author |
|---|---|---|---|---|---|---|---|---|
| 1 | 74 | 6.32 | 17 | 0.19 | Manfred Wuhrer | 55 | 0.23 | Gordan Lauc |
| 2 | 55 | | 19 | 0.23 | Gordan Lauc | 74 | 0.19 | Manfred Wuhrer |
| 3 | 22 | 10.46 | 6 | 0.04 | Andre M Deelder | 13 | 0.13 | Jasminka Kristic |
| 4 | 21 | 3.71 | 14 | 0.04 | Irena Trbojevicakmacic | 14 | 0.11 | Frano Vuckovic |
| 5 | 19 | | 16 | 0.1 | Wei Wang | 9 | 0.11 | Noortje De Haan |
| 6 | 16 | 6.55 | 10 | 0.06 | Pauline M Rudd | 19 | 0.1 | Wei Wang |
| 7 | 16 | | 24 | 0.08 | Jerko Stambuk | 16 | 0.08 | Jerko Stambuk |
| 8 | 15 | 5.79 | 4 | 0.01 | Maurice H J Selman | 14 | 0.08 | Youxin Wang |
| 9 | 14 | | 29 | 0.11 | Frano Vuckovic | 12 | 0.07 | Igor Rudan |
| 10 | 14 | | 16 | 0.08 | Youxin Wang | 10 | 0.07 | Gestur Vidarsson |

Table 3
Top ten-distribution table of cited authors

| Rank | Freq | Centrality | Author | Year |
|---|---|---|---|---|
| 1 | 185 | 0.06 | Kaneko Y | 2009 |
| 2 | 157 | 0.1 | Arnold JN | 2009 |
| 3 | 153 | 0.1 | Anthony RM | 2009 |
| 4 | 149 | 0.07 | Jefferis R | 2009 |
| 5 | 137 | 0.1 | PAREKH RB | 2009 |
| 6 | 133 | 0.07 | Shields RL | 2009 |
| 7 | 124 | 0.06 | Wuhrer M | 2009 |
| 8 | 122 | 0.12 | Nimmerjahn F | 2009 |
| 9 | 112 | 0.04 | Pucic M | 2012 |
| 10 | 102 | 0.07 | Selman MHJ | 2011 |

Table 4
Centrality greater than 0.1 Co-cited authors

| Rank | Freq | Centrality | Author | Year |
|---|---|---|---|---|
| 1 | 122 | 0.12 | Nimmerjahn F | 2009 |
| 2 | 88 | 0.11 | Shinkawa T | 2009 |
| 3 | 20 | 0.11 | ROOK GAW | 2009 |
| 4 | 157 | 0.1 | Arnold JN | 2009 |
| 5 | 153 | 0.1 | Anthony RM | 2009 |
| 6 | 137 | 0.1 | PAREKH RB | 2009 |
| 7 | 100 | 0.1 | Ferrara C | 2009 |

Table 5
Top 10 keywords appearing frequently in IgG glycosylation research papers 2009–2020

| Rank | Frequency | Centrality | Key words |
|---|---|---|---|
| 1 | 283 | 0.05 | immunoglobulin g |
| 2 | 209 | 0.05 | glycosylation |
| 3 | 121 | 0.05 | rheumatoid arthriti |
| 4 | 104 | 0.04 | antiinflammatory activity |
| 5 | 92 | 0.06 | igg |
| 6 | 87 | 0.07 | antibody |
| 7 | 79 | 0.07 | monoclonal antibody |
| 8 | 75 | 0.17 | mass spectrometry |
| 9 | 67 | 0.04 | glycan |
| 10 | 60 | 0.08 | galactosylation |

Table 6
Top 10 hot keywords in IgG glycosylation research papers 2009–2020

| Rank | Frequency | Centrality | Bursts | Key words |
|---|---|---|---|---|
| 1 | 36 | 0.01 | 9.00 | biomarker |
| 2 | 22 | 0.01 | 7.12 | n-glycan |
| 3 | 51 | 0.11 | 5.76 | oligosaccharide |
| 4 | 18 | 0.02 | 4.99 | structural change |
| 5 | 23 | 0.01 | 4.64 | n glycosylation |
| 6 | 11 | 0.02 | 4.21 | crystal structure |
| 7 | 24 | 0.08 | 3.85 | pregnancy |
| 8 | 9 | 0 | 3.82 | mechanism |
| 9 | 11 | 0.01 | 3.55 | glycopeptide |
| 10 | 11 | 0.01 | 3.19 | fc gamma riii |

Table 7

Top 10 journals in terms of frequency and Impact Factor IF (JCR) in 2018

| Rank | Name of Journal | Counts | Centrality | Year | Half-life | Impact Factor |
|---|---|---|---|---|---|---|
| 1 | Journal of Biological Chemistry | 328 | 0.04 | 2009 | 7 | 4.106 |
| 2 | Glycobiology | 306 | 0.06 | 2009 | 7 | 4.194 |
| 3 | Science | 293 | 0.08 | 2009 | 7 | 41.037 |
| 4 | Proceedings of the National Academy of Sciences of the United States of America | 282 | 0.06 | 2009 | 7 | 9.580 |
| 5 | Journal of Proteome Research | 270 | 0.04 | 2009 | 7 | 3.780 |
| 6 | Nature | 259 | 0.07 | 2009 | 7 | 43.070 |
| 7 | Mol Cell Proteomi | 257 | 0.08 | 2011 | 6 | 4.828 |
| 8 | Plos One | 229 | 0.02 | 2011 | 6 | 2.776 |
| 9 | Glycoconjugate Journal | 227 | 0.04 | 2009 | 7 | 2.926 |
| 10 | Journal of Immunology | 212 | 0.09 | 2009 | 7 | 4.718 |

Table 8

Ten Important Articles of CiteSpace Software Analysis

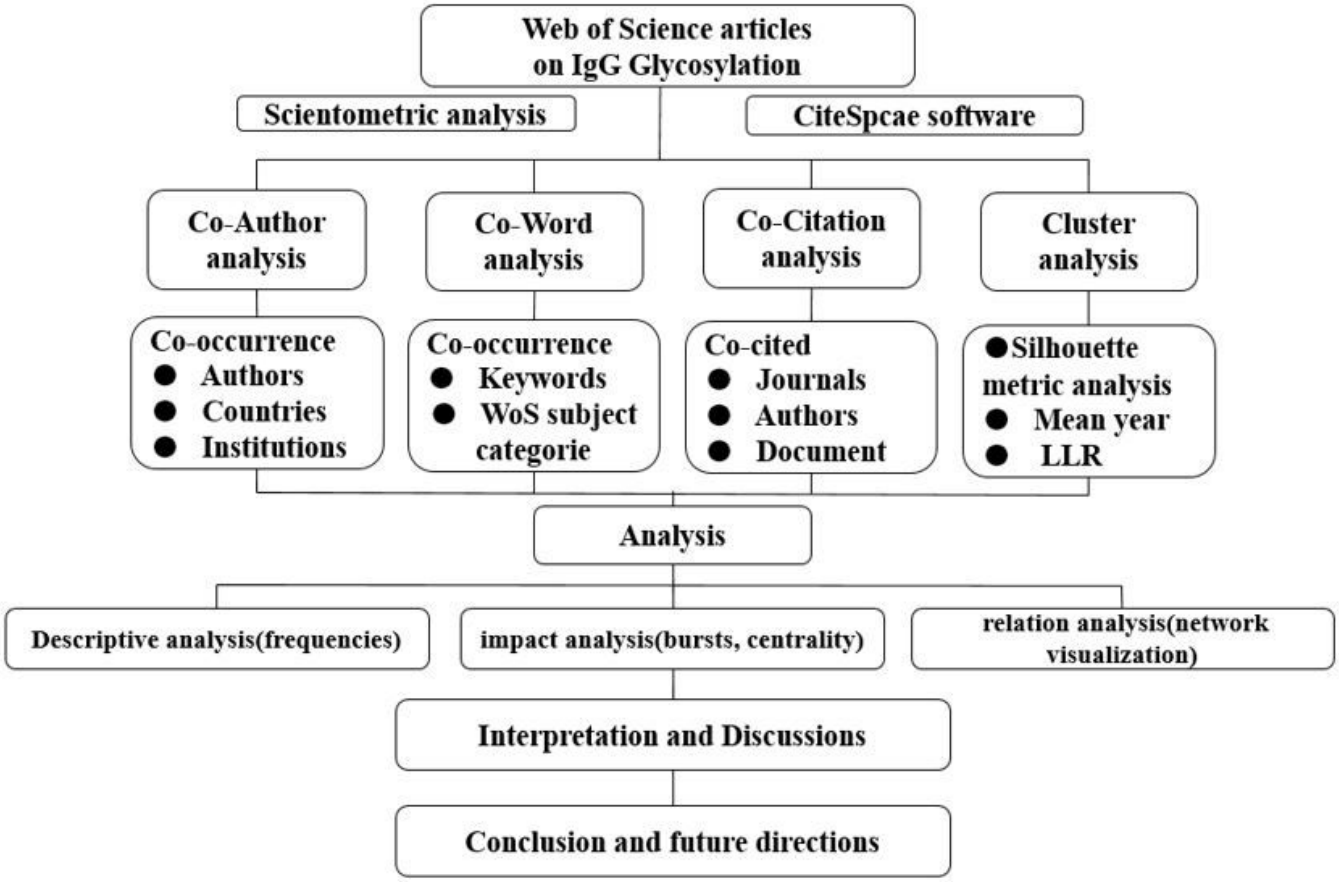
| Rank | Citation counts | Title | Author | Year | Source |
|---|---|---|---|---|---|
| 1 | 100 | High throughput isolation and glycosylation analysis of IgG-variability and heritability of the IgG glycome in three isolated human populations | Pucic M | 2011 | Mol Cell Proteomics |
| 2 | 72 | Anti-inflammatory activity of immunoglobulin G resulting from Fc sialylation. | Kaneko Y | 2006 | Science |
| 3 | 69 | Unique carbohydrate-carbohydrate interactions are required for high affinity binding between FcgammaRIII and antibodies lacking core fucose. | Ferrara C | 2011 | P Natl Acad Sci Usa |
| 4 | 63 | Loci associated with N-glycosylation of human immunoglobulin G show pleiotropy with autoimmune diseases and haematological cancers. | Lauc G | 2013 | Plos Genet |
| 5 | 63 | The impact of glycosylation on the biological function and structure of human immunoglobulins | Arnold JN | 2007 | Annu Rev Immunol |
| 6 | 58 | Anti-inflammatory activity of IgG1 mediated by Fc galactosylation and association of FcγRIIB and dectin-1 | Karsten CM | 2012 | Nat Med |
| 7 | 58 | Recapitulation of IVIG anti-inflammatory activity with a recombinant IgG Fc. | Anthony RM | 2008 | Science |
| 8 | 54 | Immunoglobulin G (IgG) Fab glycosylation analysis using a new mass spectrometric high-throughput profiling method reveals pregnancy-associated changes | Bondt A | 2014 | Mol Cell Proteomics |
| 9 | 50 | Immunoglobulin G galactosylation and sialylation are associated with pregnancy-induced improvement of rheumatoid arthritis and the postpartum flare: results from a large prospective cohort study | van de Geijn FE | 2009 | Arthritis Res Ther |
| 10 | 46 | Fc specific IgG glycosylation profiling by robust nano-reverse phase HPLC-MS using a sheath-flow ESI sprayer interface | Selman MHJ | 2012 | J Proteomics |

Table 9

The top 10 cited documents with a total citation centrality

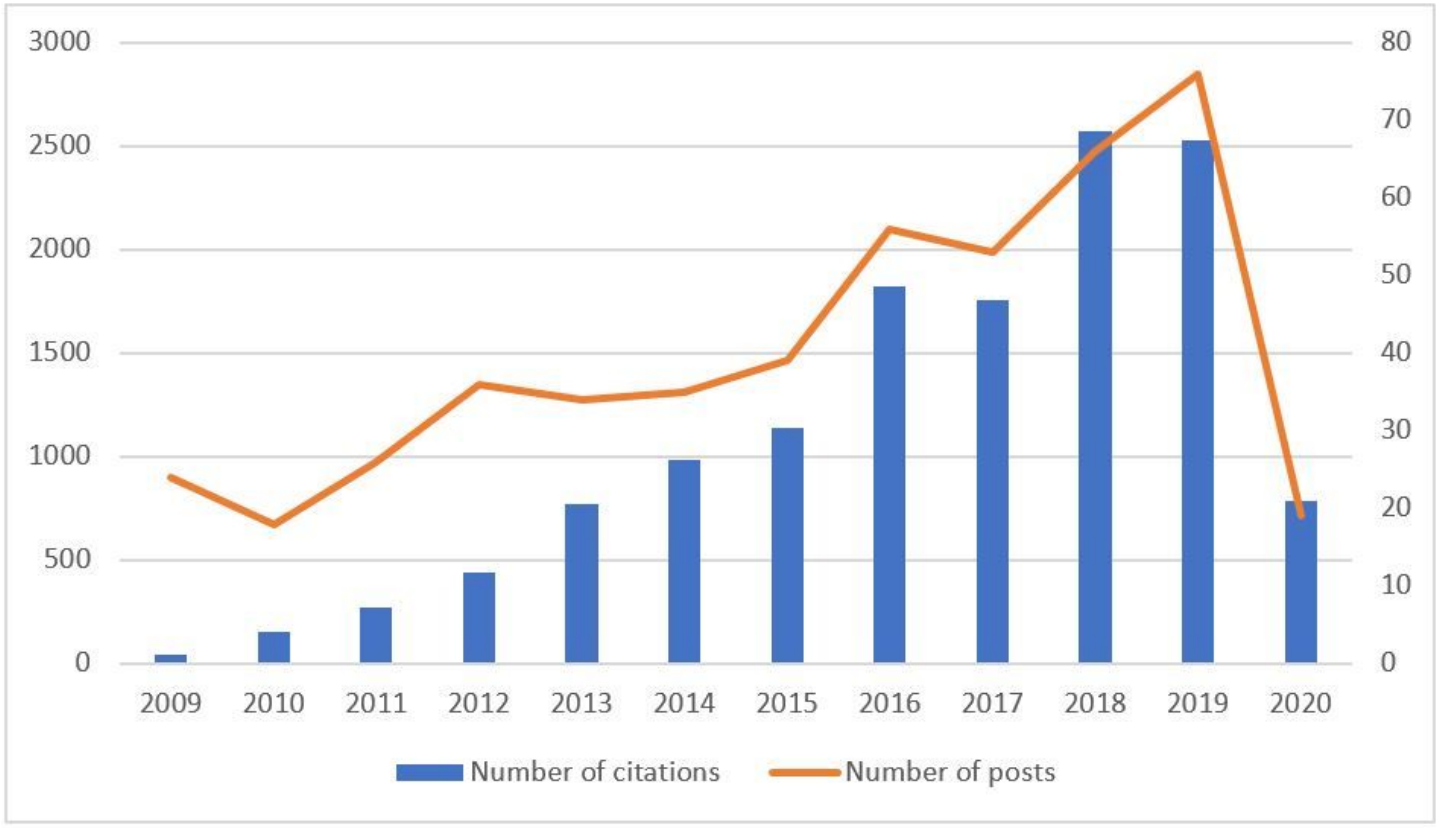
| Rank | Centrality | Title | Author | Year | Source |
|---|---|---|---|---|---|
| 1 | 0.14 | Analysis of immunoglobulin glycosylation by LC-ESI-MS of glycopeptides and oligosaccharides | Stadlmann J | 2008 | Proteomics |
| 2 | 0.13 | Fcgamma receptors as regulators of immune responses | Nimmerjahn F | 2008 | Nat Rev Immunol |
| 3 | 0.12 | High-throughput IgG Fc N-glycosylation profiling by mass spectrometry of glycopeptides | Bakovic MP | 2013 | J Proteome Res |
| 4 | 0.12 | IgG glycosylation analysis | Huhn C | 2009 | Proteomics |
| 5 | 0.11 | Glycosylation as a strategy to improve antibody-based therapeutics | Jefferis R | 2009 | Nat Rev Drug Discov |
| 6 | 0.11 | Ultra performance liquid chromatographic profiling of serum N-glycans for fast and efficient identification of cancer associated alterations in glycosylation | Bones J | 2010 | Anal Chem |
| 7 | 0.1 | Nonfucosylated therapeutic IgG1 antibody can evade the inhibitory effect of serum immunoglobulin G on antibody-dependent cellular cytotoxicity through its high binding to FcgammaRIIIa | Iida S | 2006 | Clin Cancer Res |
| 8 | 0.1 | Differential glycosylation of polyclonal IgG, IgG-Fc and IgG-Fab isolated from the sera of patients with ANCA-associated systemic vasculitis | Holland M | 2006 | Bba-gen Subjects |
| 9 | 0.09 | Unique carbohydrate-carbohydrate interactions are required for high affinity binding between FcgammaRIII and antibodies lacking core fucose | Ferrara C | 2011 | P Natl Acad Sci Usa |
| 10 | 0.09 | Increased levels of galactose-deficient anti-Gal immunoglobulin G in the sera of hepatitis C virus-infected individuals with fibrosis and cirrhosis | Mehta AS | 2008 | J Virol |

# Figures



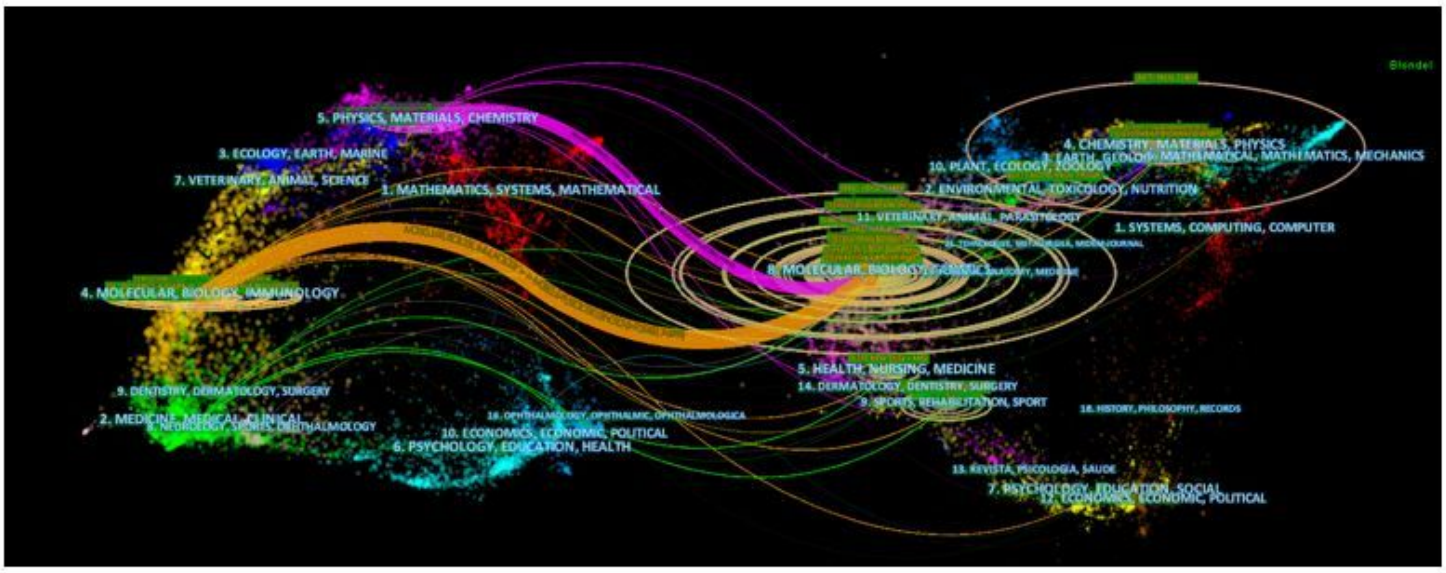

## Figure 1

Research methodology



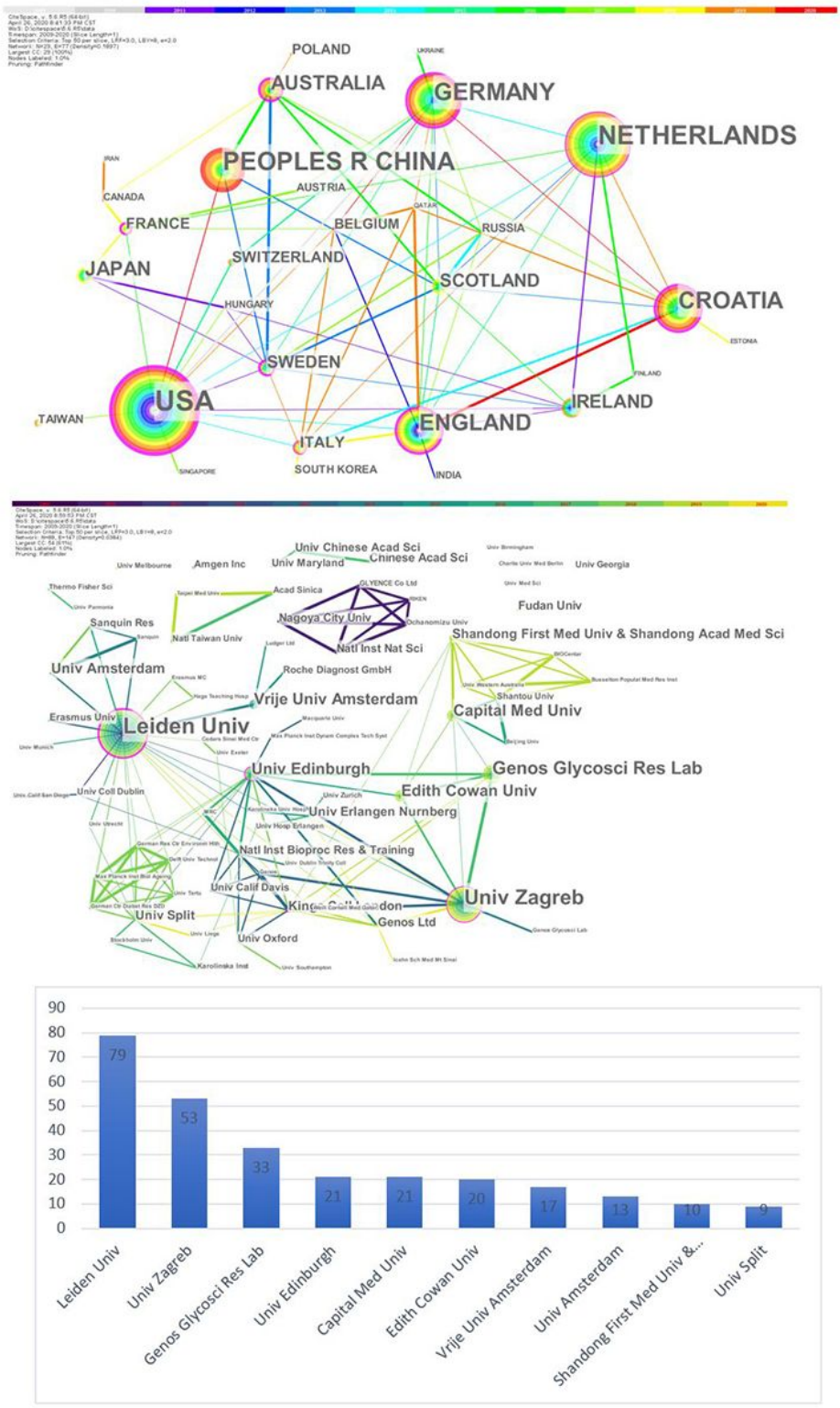

## Figure 2

The quantitative trend of IGG glycosylation



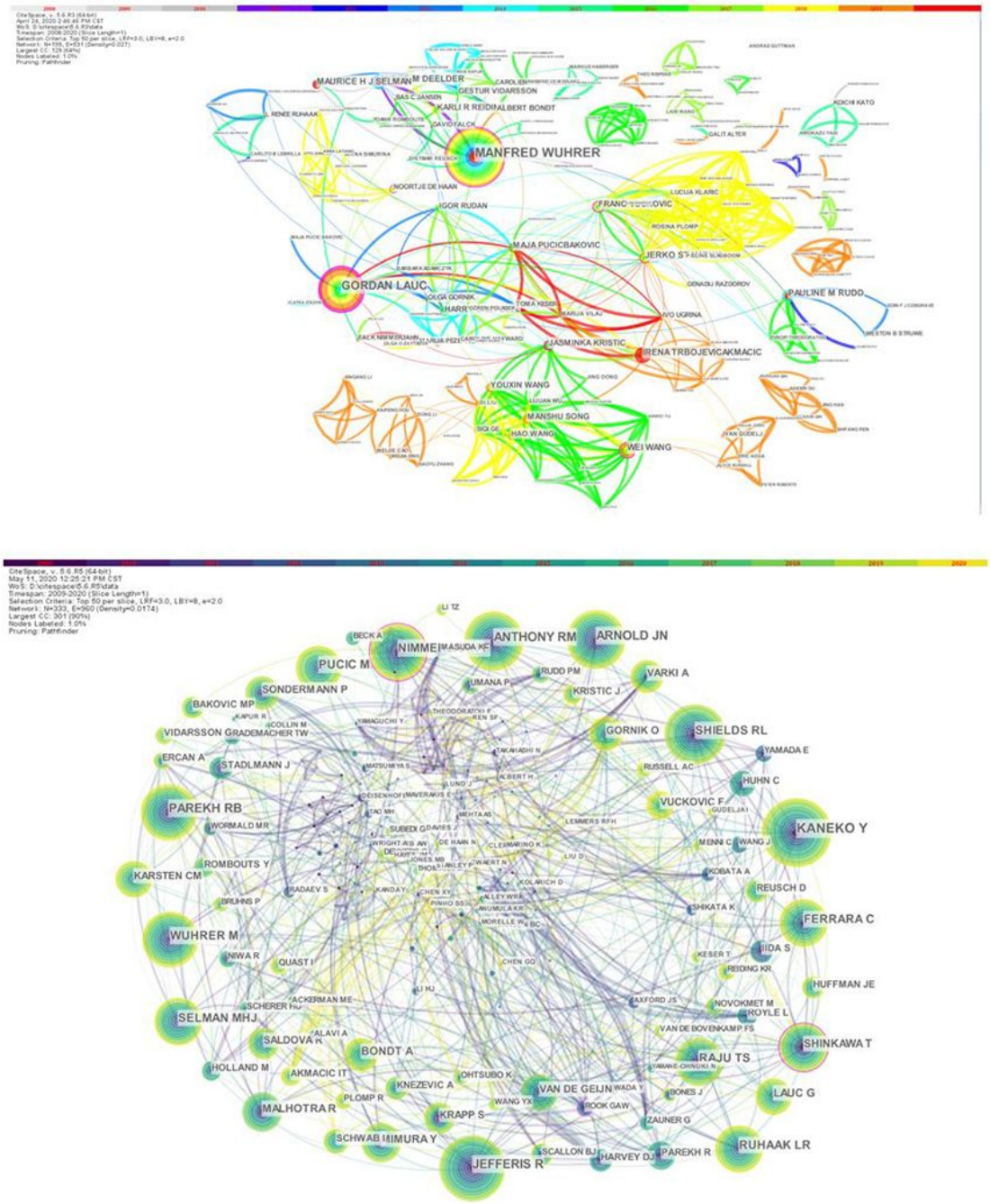

## Figure 3

Periodical double image overlay



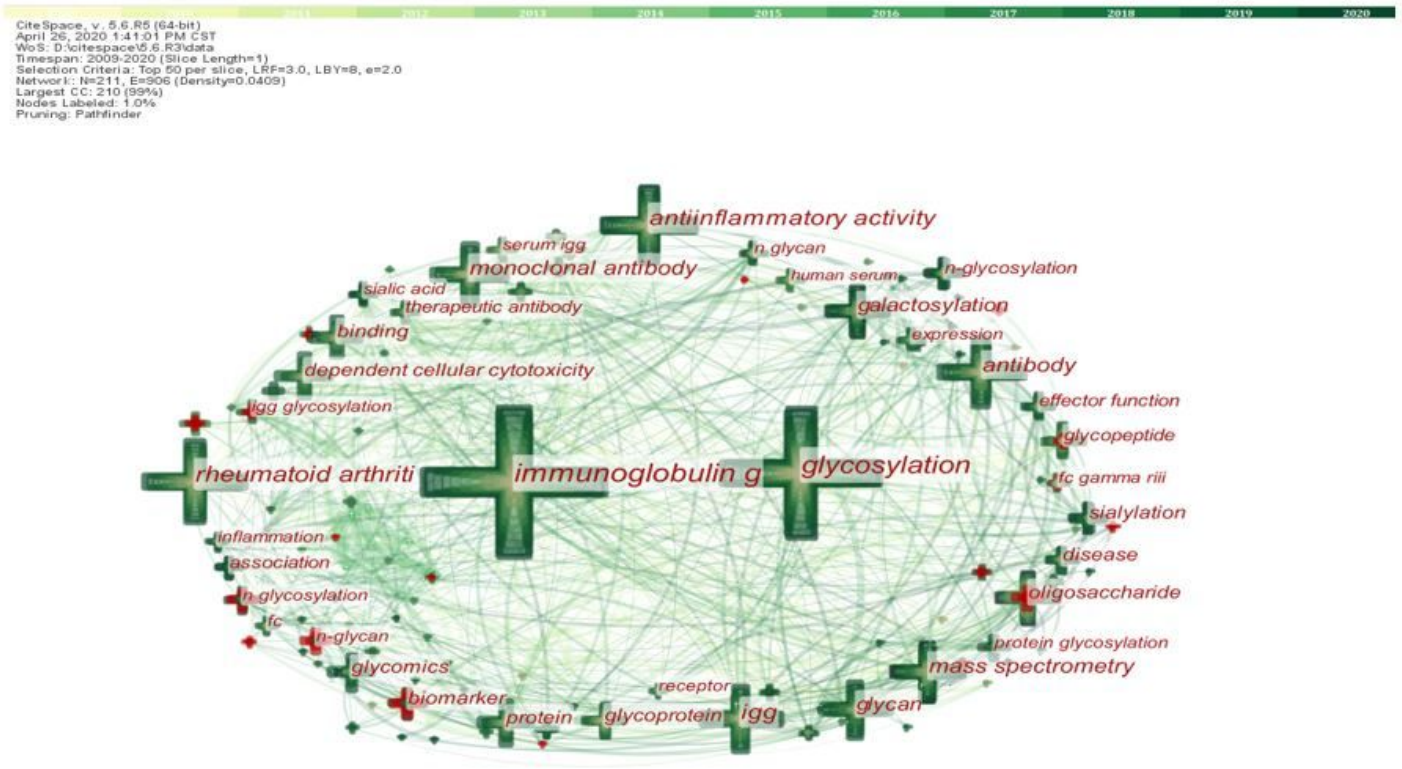

## Figure 4

a Atlas of cooperation between countries b Visual Atlas of Inter-Agency Cooperation c Top 10 institutions



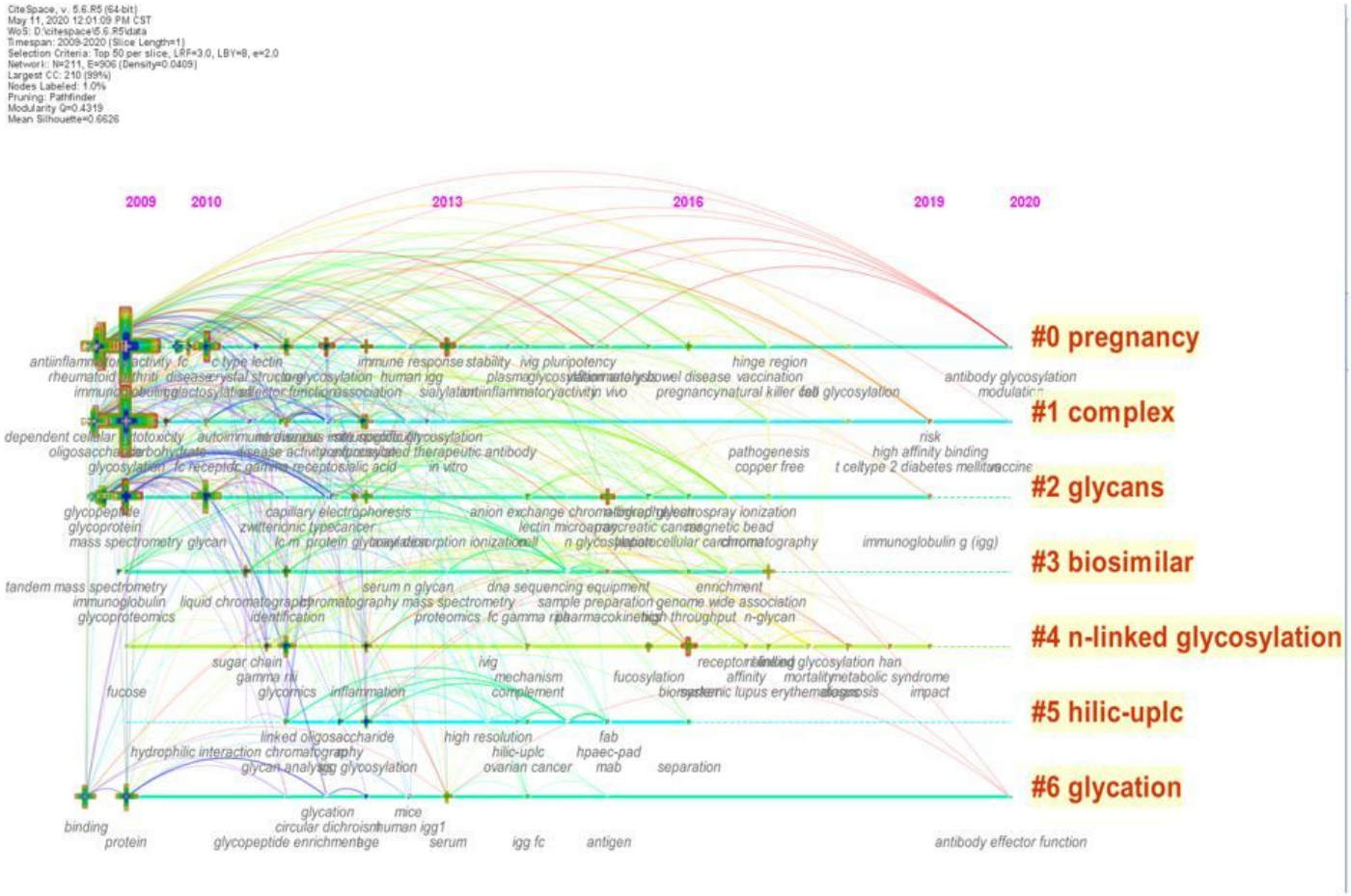

## Figure 5

a Co-author network map b Author co-citation Network Atlas




## Figure 6

2009-2020 IgG glycosylation high-frequency keyword co-occurrence map (more than 20 occurrences)




## Figure 7

Research frontier timeline evolution map

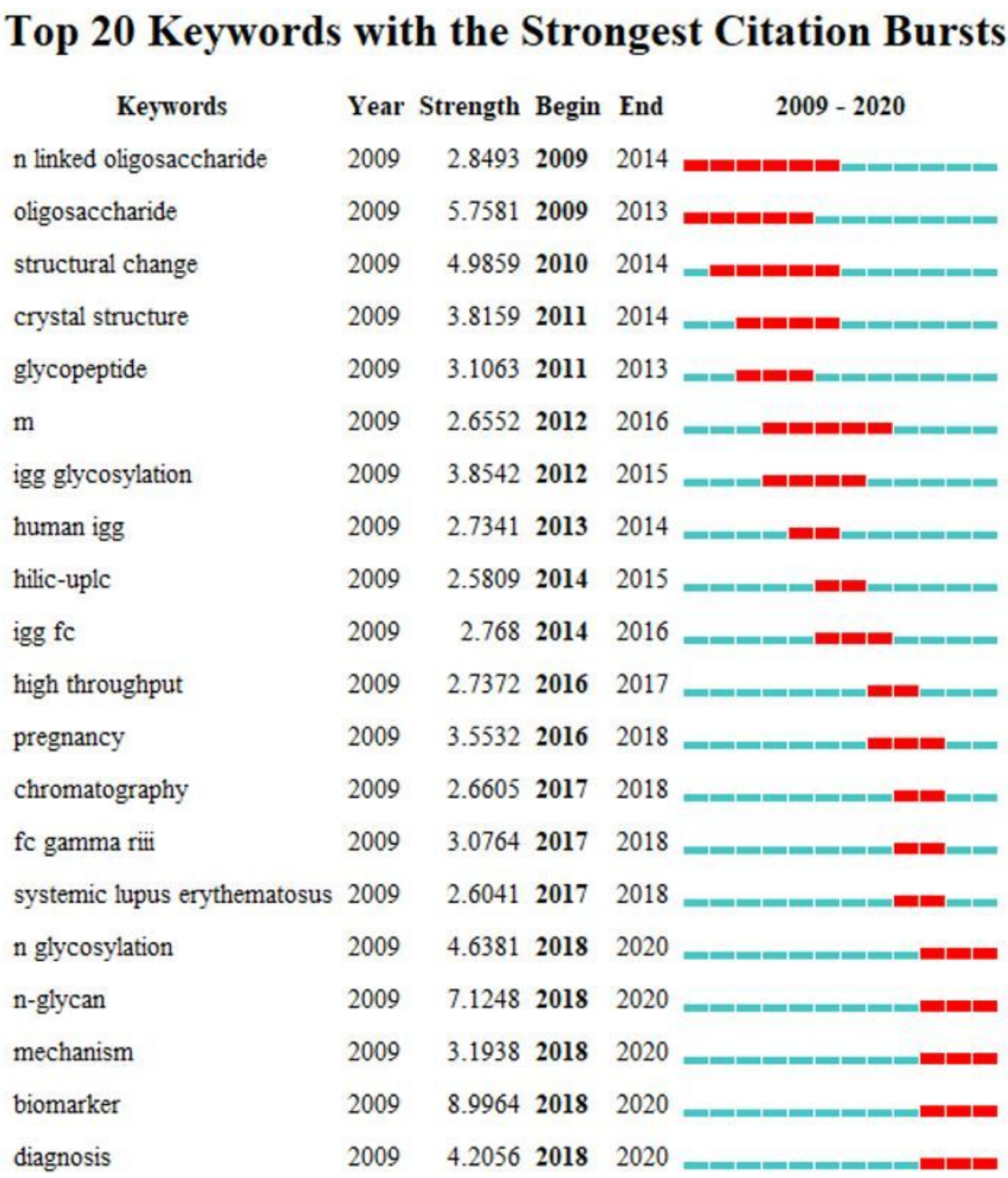
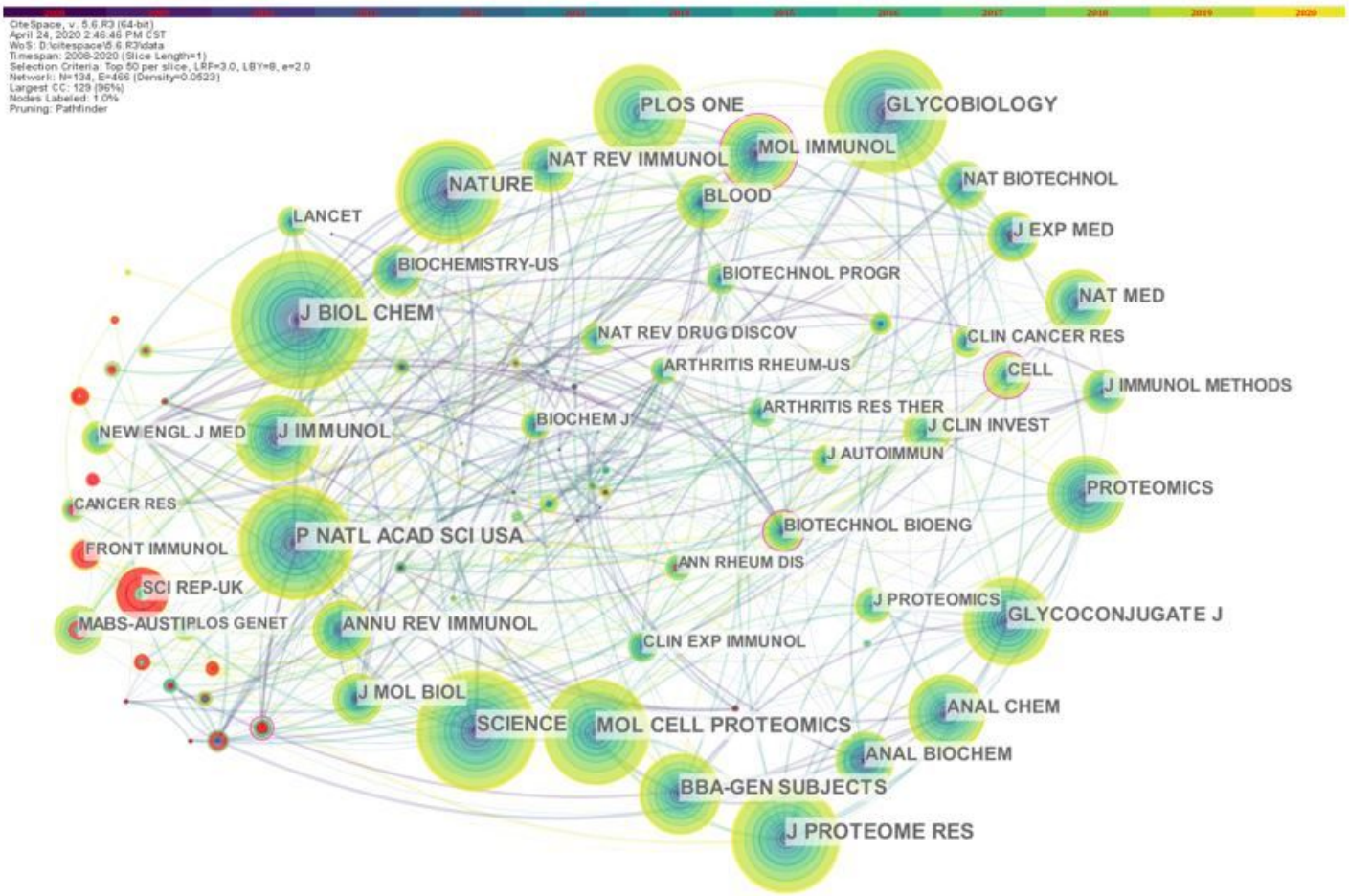


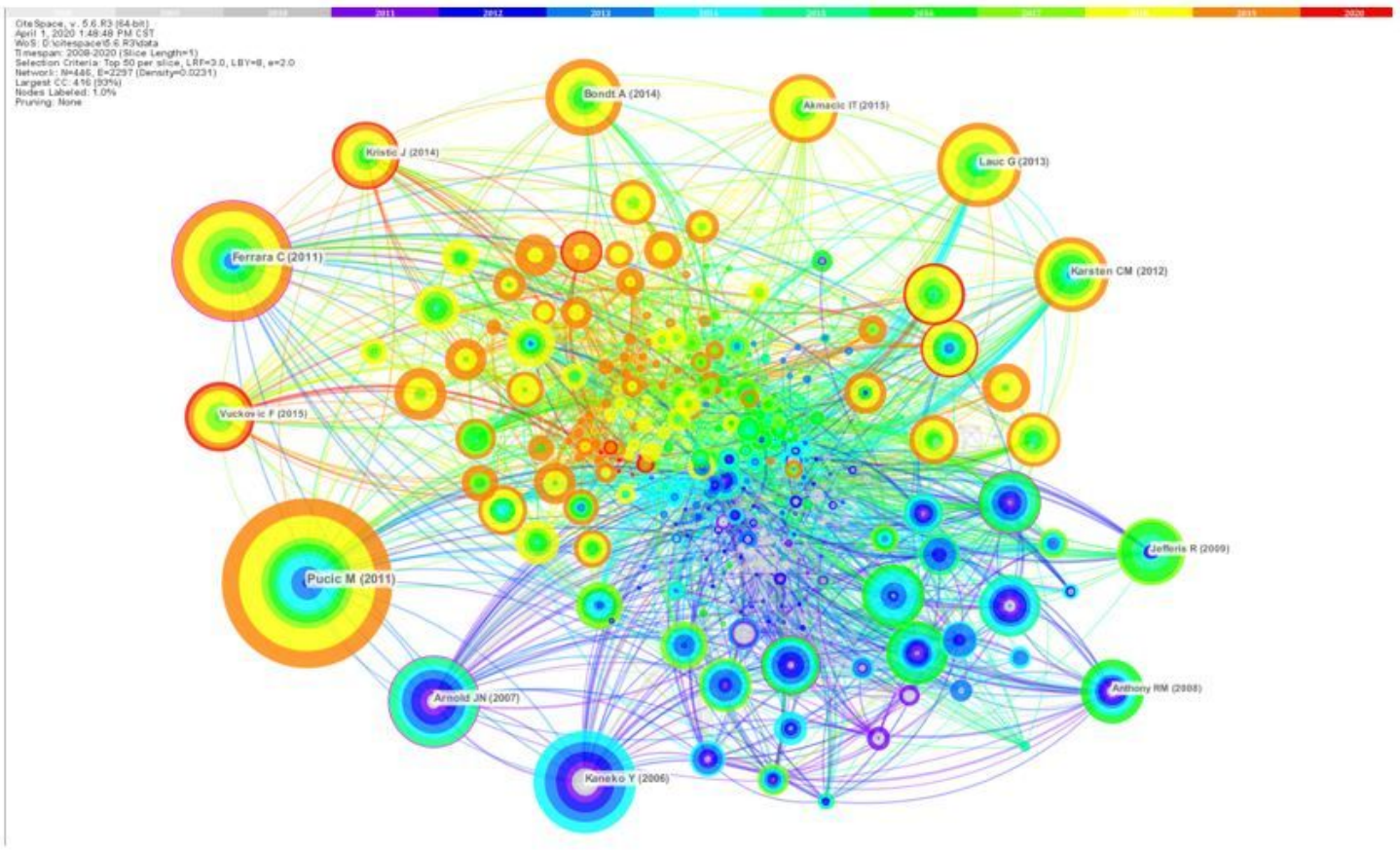

**Figure 8**

Evolution of keywords in research on IgG N-glycosylation




## Figure 9

The network organized by the cited journal Note: Red circles represent the citation burst




## Figure 10

Visual analysis of the literature co-citation network