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Research article

# Knowledge mapping of links between dendritic cells and allergic diseases: A bibliometric analysis (2004–2023)

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ABSTRACT

In this study, bibliometric analysis was carried out to comprehend the global research trends, hotspots, scientific frontiers, and output characteristics of the links between dendritic cells (DCs) and allergic diseases from 2004 to 2023. Publications and their recorded information were retrieved from the Web of Science Core Collection (WoSCC). VOSviewer and Citespace were used to visualize the hotspots and trends of research area. ChemBio 3D, Autodock tools, and Discovery Studio were used to visualize the molecular docking results of hotspots. A total of 4861 articles were retrieved. The number of publications (Np) was in a high and stable state. Years 2011 and 2017 were two peaks in Np. The largest contributor in terms of publications, scholars, and affiliations was the USA. The paper published in NATURE MEDICINE (IF: 82.9) and written by Trompette, A in 2006 had the highest global citation score (GCS). Keywords, such as "asthma," "t-cells," "inflammation," "expression," "atopic dermatitis," "food allergy," "gut microbiota," "murine model," and "cytokines related to immunity" appeared the most frequently. Most of the binding free energy of the key active components of *Saposhnikovia divaricata* docked with toll-like receptor proteins well. This bibliometric study aimed to help better comprehend the present state and make decisions from a macro viewpoint.

## 1. Introduction

Allergic diseases, which include allergic asthma (AS), allergic rhinitis (AR), allergic dermatitis (AD), food allergy, and drug allergy, are caused by improper type 2 T lymphocyte (T cell) responses and immunoglobulin E (IgE) antibody responses to innocuous environmental antigens [1]. The incidence of allergic diseases has increased remarkable over the past few decades, thus becoming a worldwide public health issue. In an epidemiological investigation involving 30 countries organized by the World Allergy Organization (WAO), 22 % of 1.2 billion population suffered from allergic diseases mediated by IgE [2]. Among the 1.2 billion population, 400,300 and 250 million people were attacked by AR, AS, and food allergy [3]. In addition, a large amount of clinical data showed that the risk of allergic disease attacking of filial generation could increase if the maternal generation were attacked by allergic diseases [4–7]. Allergic diseases have had a serious influence on public health.

Antigen-presenting cells (APCs) are important for immunological recognition, immune response, and immune regulation because they can recognize environmental signals and convey these information to naive $CD4^+$ T cells to start differentiating into regulatory or effector subsets [8]. Dendritic cells (DCs) are the most functional APCs with two-way immunoregulation. In addition to identifying and

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presenting antigens to naive T cells to stimulate antigen-specific adaptive immunity, they can encourage the growth of regulatory T (Treg) cells to stimulate immunological tolerance [9]. DCs participate in the initiation of allergic reactions and have a close relationship with the occurrence of allergic diseases [1,10].

Bibliometrics, first proposed by Pritchard in 1969, has been used for providing quantitative analysis of written publications, such as the most influential publications, major nations, core journals, and well-linked subject categories [11–13]. As a mature method in information science, bibliometric research can estimate the status and developing trends in a scientific file [14]. It can also help forecast development trends and assess the worth of research in a certain area [15]. Besides, bibliometrics can effectively offer evidence to guide experimentation strategies and funding decisions [16,17]. Over the years, the bibliometric methods have been widely used for AD [17], AS [18,19], microbiome [20], and allergic publications [21,22], but their usage on publications regarding links between DCs and allergic diseases has not been reported.

In our study, bibliometric analysis was performed to investigate the cooperation, literature influence, journals, researchers, references, and keywords in the field of DCs and allergic disorders between 2004 and 2023. Our study aimed to assess the current state of the relationship between DCs and allergic disorders.

## 2. Materials and methods

### 2.1. Data sources and search strategies

The data used in the study was obtained from the Science Citation IndexExpanded (SCI-E) and Web of Science Core Collection (WoSCC, https://www.webofscience.com/wos/woscc/basic-search). Due to the database being updated rapidly, the data search was completed in 1 day (March 12, 2024) to avoid various kinds of deviations. The search strategy was [(TS=(allergy) OR TS=(allergic disease) OR TS=(allergic diseases) OR TS=(atopy) OR TS=(atopic disease) OR TS=(atopic diseases) OR TS=(anaphylaxis) OR TS=(anaphylactic response) OR TS=(anaphylactic responses) OR TS=(anaphylactic reaction) OR TS=(anaphylactic reactions) OR TS=(hypersensitivity) OR TS=(hypersensitive response) OR TS=(hypersensitive responses) OR TS=(hypersensitive reaction) OR TS=(hypersensitive reactions)] AND [(TS=(dendritic cell)OR TS=(dendritic cells) OR TS=(dendrocyte) OR TS=(dendrocytes)]. The timespan of publication year was set to be from 2004 to 2023 to explore the global scientific trends. Only articles would be included in various publication types.

### 2.2. Data collection and cleaning

The retrieved results were downloaded in the plain "text" and "full records and references" format. The collected information included the number of publications (Np), citations, publication year, H-index, countries/regions, affiliations, journals, authors, references, and keywords. The majority of the raw data in this study were reliable, even though inaccurate analysis could not be completely prevented due to various citation formats, variations in cited references, and authors using the same abbreviated name. Eventually, the data were analyzed by VOSviewer (version 1.6.10.0) and CiteSpace (version 6.2.4).

### 2.3. Bibliometric analysis

The numbers of papers and citations are the general bibliometric indicators. Bibliometric analysis also includes H-index, impact factor (IF), co-citation analysis, co-occurrence analysis, cluster analysis of references, and keywords. It can be carried out through VOSviewer (version 1.6.10.0), CiteSpace (version 6.2.4), and the web tool Bioinformatics (http://www.bioinformatics.com.cn/?p=6).

Np is used for evaluating output, whereas the number of citations (Nc), excluding self-citations, is used to evaluate the impact [23]. These two are known as the essential viewpoints for evaluating the level of research [24]. The H-index and IF are the most well-known and widely used bibliometric indices for evaluating the productivity of individual researchers [25]. The IF of journals can be obtained from Journal Citation Reports (JCR) 2022. The H-index was introduced by Professor Hirsch in 2005 for the first time [25]. Researchers could have a H-index if they had written H articles, each of which had been referenced H times. As a result, the H-index may evaluate a researcher's quantitative (productivity) and qualitative (citation) study output in a single number. Additionally, it has the ability to forecast a researcher's future success and assess the overall scholarly influence of an author's output [26]. The H-index can now be used to define a nation's or region's publishing output as well as a company's or journal's output [24].

The network maps of co-citation and co-occurrence analysis were constructed and visualized by VOSviewer. The node's size represents the number of publications, the line's thickness shows the strength of the relationship, and the colours of the nodes represent the distinct clusters or periods. Cluster analysis of references and keywords can be constructed and visualized by CiteSpace. The visualization includes references, timeline or time zone views, and keywords citation bursts. These are frequently utilized to reveal developing trends and discover new trends of research [27]. A network of co-occurrence keywords was also constructed. Detecting new research trends in the topic is frequently performed using keyword and reference bursts.

### 2.4. Molecular docking

Molecular docking was used to investigate the interaction of the key targets with main active components further [28]. The structure files of important components were downloaded from Traditional Chinese Medicine Systems Pharmacology Database and Analysis Platform (TCMSP, https://old.tcmsp-e.com/tcmsp.php). ChemBio 3D was performed to minimize the energy of 3D structure.

The crystal structures of proteins were downloaded from the RCSB Protein Data Bank (http://www.pdb.org/) and modified using the Autodock tools version 1.5.6 and Pymol. The modified conformations of proteins include hydrogen addition, ligand and water removal, amino-acid optimization, and computation of charge. The native formats of proteins and components were converted into PDBQT formats. Autodock Vina version 1.1.2 was used for docking, and Discovery Studio version 3.5 was used to visualize the docking results.

## 3. Results

### 3.1. Overview of publications on the links between DCs and allergic diseases

In accordance with the retrieval approach used in this study, a total of 4861 articles published between 2004 and 2023 were retrieved. The average Nc for each article was 46.57, and the total Nc of all publications was 212,703. The H-index of all publications was 188. The flowchart for this study's literature search and screening is shown in Fig. 1.

### 3.2. Annual trend of publication quantity

The articles included in our research were divided into three types of basic research, clinical research and other types through searching one by one. Other types covered bibliometrics, diagnosis and treatment guidelines, bioinformatic and so on. The publication quantity and trend of different types of annual Np are obviously shown in Fig. 2. The publication quantity was in a relatively stable state in the period of 2004–2023, causing a Np higher than 100. The Np of basic research had a significant impact on the overall situation, because the Np of basic research was also higher than 100. Besides, the Np of total and basic research had almost the same change trend, while there was not much trend fluctuation of clinical and other types research. Two peaks from 2004 to 2023 were observed. As depicted in Fig. 2, the first peak appeared in 2011, and its Np was 342. The second peak appeared in 2017, and its Np was 290. In addition, the Np in 2022 was the lowest in the period of 2004–2023, and its Np was 149.

### 3.3. Contributions of countries/regions to global publications

A country's attachment to this field and its level of impact on it can be determined by examining the publications in various countries and regions. It may also be reflected in a cluster analysis of international collaboration between nations or regions. Besides, the closeness in countries' cooperation can be revealed in cluster analysis.

In Table 1, the top 10 high-output countries/regions on the basis of Np are listed. The USA published the most articles (1615/33.22

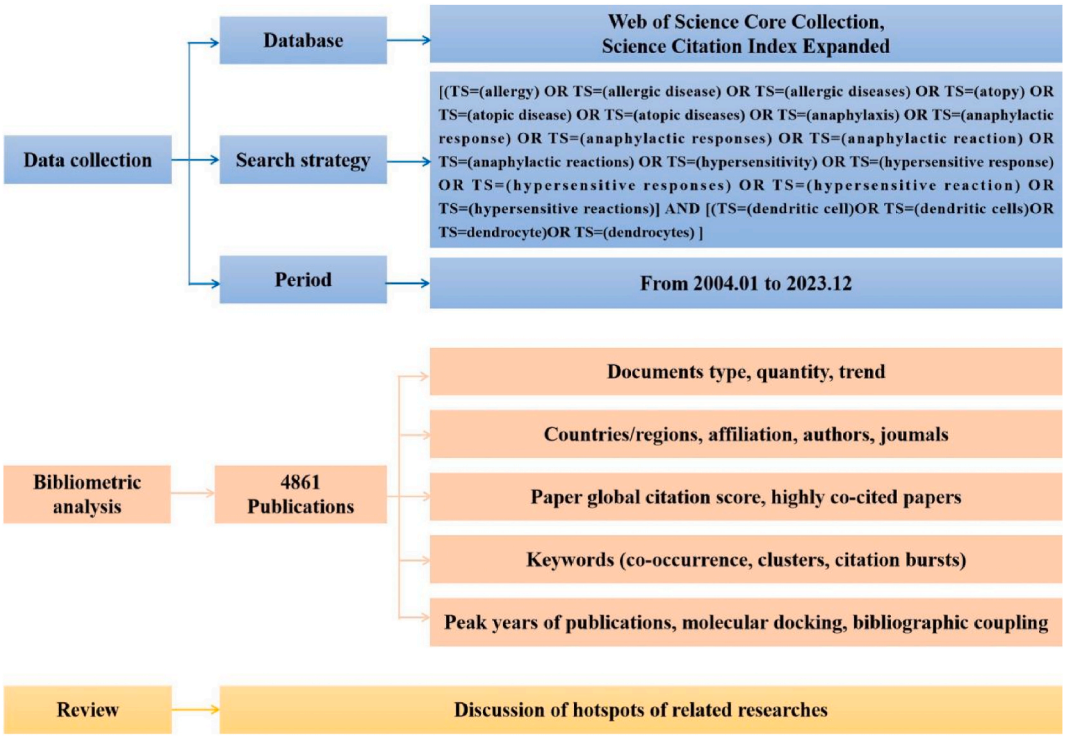



**Fig. 1.** Flowchart of screening process and article framework.

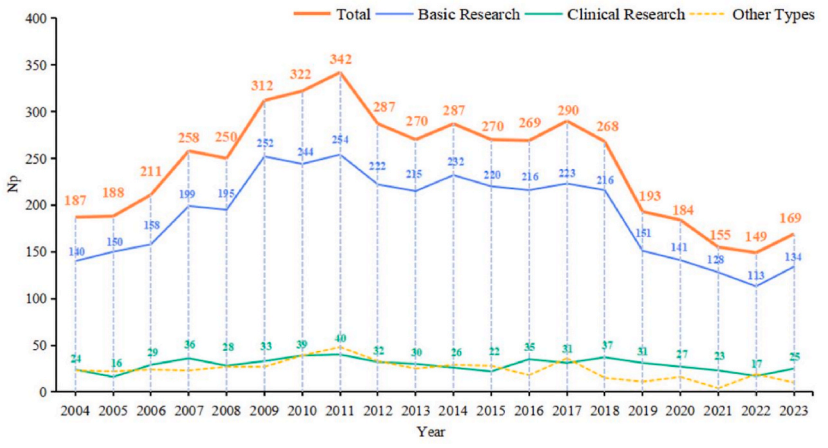



**Fig. 2.** The total annual trend of publications by year from 2004 to 2023. The solid line in orange represents the number of publications (Np) of all research types; the solid line in blue represents the Np of basic research; the solid line in green represents the Np of clinical research; the dashed line in yellow represents the Np of other research types. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

%), followed by Germany (697/14.34 %) and Japan (592/12.18 %). The top 5 nations accounted for 78.36 % of the 4861 articles. Papers from the USA were cited 100,373 times, accounting for 33.22 % of the total citations, followed by Germany (34,088) and Japan (20,847). Besides, the USA achieved the highest H-index (151), followed by Germany (93) and England (78). The England ranked first in average per item (66.99), followed by Netherlands (65.75) and USA (63.87). England had a slightly lower NP but a higher H-index and average per item, showing that its articles were of high quality, similar to the Netherlands.

Fig. 3A shows how the total number of papers on this topic from all countries and regions were distributed geographically. Fig. 3B lists the top 10 nations by number of publications in accordance with the annual publications on the connections between DCs and research on allergy diseases from 2004 to 2023. The largest number of publications (2022/45 and 2023/46) were published in China, followed by the USA (2022/42 and 2023/44). The USA had the most significant number of articles written from 2004 to 2023 but rated second in 2022 and 2023. Its annual Np was in accordance with the annual Np of all countries/regions. This finding suggested that the USA maintained high focus on research, and China showed increasing attention. Close cooperation between nations was obvious. As seen in Fig. 3C–a network of international collaboration was found. Fig. 3D demonstrates that the USA, Germany, Japan, England, and France conducted research prior to other nations.

### *3.4. Analysis of affiliations*

The top 10 affiliations with the most Np associated with this research are shown in Table 2. The Institut National De La Sante Et De La Recherche Medicale Inserm possessed the greatest number of publications (207), followed by Harvard University (184) and Harvard Medical School (141). Though ranking second for the Np, Harvard University ranked first for the Nc (14014) and the H-index (65). And the average per item of Harvard University (76.59) was in the top 5. Six of the top 10 affiliations are located in the USA, and two are in France. This finding suggested that the affiliations of France focused on this field and were closely connected with each other, although their Np was not in the top 5. Moreover, the USA made an important contribution to this research.

**Table 1**
The top ten countries/regions with the highest productivity.

| Country/Region | Np | % of (4861) | Nc | H-index | Average per item |
|---|---|---|---|---|---|
| USA | 1615 | 33.22 | 100373 | 151 | 63.87 |
| Germany | 697 | 14.34 | 34088 | 93 | 50.06 |
| Japan | 592 | 12.18 | 20847 | 73 | 36.15 |
| China | 574 | 11.81 | 13209 | 53 | 23.66 |
| France | 331 | 6.81 | 16865 | 70 | 50.24 |
| England | 326 | 6.71 | 21660 | 78 | 66.99 |
| Netherlands | 298 | 6.13 | 19250 | 77 | 65.75 |
| Switzerland | 230 | 4.73 | 16229 | 67 | 71.37 |
| Canada | 221 | 4.55 | 11642 | 59 | 53.53 |
| Australia | 200 | 4.11 | 11069 | 58 | 56.24 |

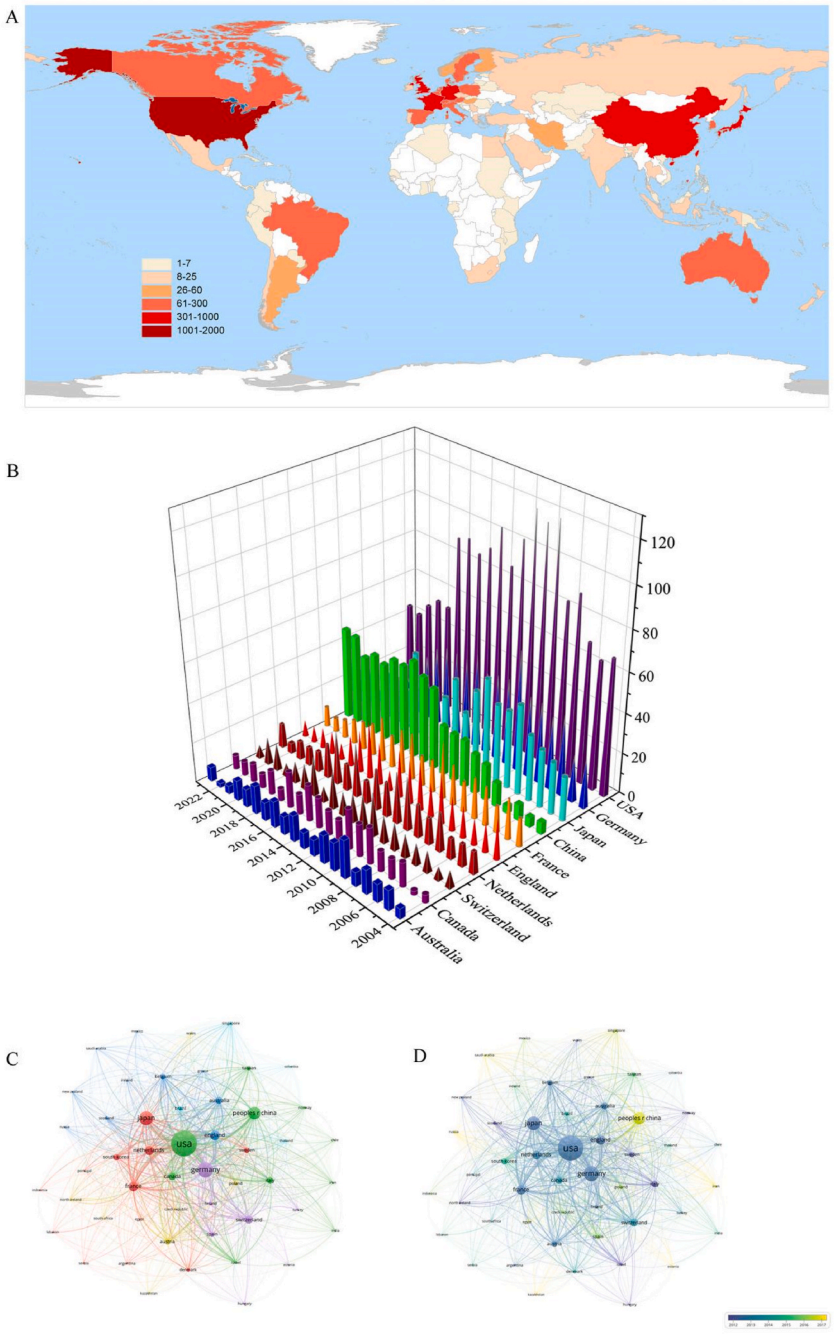



**Fig. 3.** Countries/regions in research of the links between dentritic cells (DCs) and allergic diseases. (A) Geographical distribution of global output; (B) Annual output trend of the top ten productive countries. The pillar's height shows the number of papers. The higher the pillar, the more the number of papers issued in that country. The pillar's colours and forms represent diffierent countries/regions; (C) Visual cluster analysis of cooperation among countries/regions. The different colours of the nodes represent different countries/regions, with larger nodes meaning more frequently countries/regions; (D) Timeline visualization of cooperation among countries. Countries/regions in yellow carried out research in this field later than in blue. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

### *3.5. Analysis of authors*

The top 10 most productive authors are shown in Table 3. They contributed 346 publications, accounting for 7.12 % of the total number of papers. Lambrecht, Bart N (44) from Ghent University in Belgium ranked first in the research of the links between DCs and allergic diseases, followed by Guttman-Yassky, E. (41) and Krueger, James G. (40) from Rockefeller University in USA. As presented in

**Table 2**
The top ten affiliations with the highest productivity.

| Affiliation | Country | Np | Nc | H-index | Average per item |
|---|---|---|---|---|---|
| Institut National De La Sante Et De La Recherche Medicale Inserm | France | 207 | 11461 | 57 | 56.61 |
| Harvard University | USA | 184 | 14014 | 65 | 76.59 |
| Harvard Medical School | USA | 141 | 12206 | 62 | 86.99 |
| University of California System | USA | 127 | 7998 | 45 | 63.27 |
| Centre National De La Recherche Scientifique | France | 110 | 6250 | 39 | 57.55 |
| National Institutes of Health | USA | 110 | 7755 | 43 | 70.82 |
| University of London | England | 107 | 8255 | 44 | 77.4 |
| Helmholtz Association | Germany | 105 | 6232 | 43 | 59.83 |
| University System of Ohio | USA | 95 | 5803 | 39 | 61.53 |
| Icahn School of Medicine at Mount Sinai | USA | 92 | 8765 | 51 | 97.26 |

**Table 3**
The top ten authors with the most publications.

| Author | Affiliations | Country | Np | Nc | H-index | Average per item |
|---|---|---|---|---|---|---|
| Lambrecht, Bart N | Ghent University | Belgium | 44 | 5120 | 32 | 117.91 |
| Guttman-Yassky, E. | Rockefeller University | USA | 41 | 6768 | 36 | 171.39 |
| Krueger, James G. | Rockefeller University | USA | 40 | 6619 | 35 | 171.5 |
| Yang, Ping-Chang | McMaster University | Canada | 38 | 832 | 16 | 23.84 |
| Kabashima, K. | Kyoto University | Japan | 38 | 1985 | 23 | 53.95 |
| Patrick G Holt | University of Western Australia | Australia | 30 | 1259 | 19 | 43.2 |
| Clausen, Björn Erik | Erasmus University Rotterdam | Netherlands | 30 | 2240 | 22 | 77.33 |
| Liu, Zhigang | Shenzhen University | China | 29 | 299 | 10 | 11 |
| Hammad, Hamida | Ghent University | Belgium | 29 | 3930 | 22 | 137.21 |
| Novak, Natalija | University of Bonn | Germany | 27 | 1209 | 18 | 45.74 |

Table 3, Guttman-Yassky, E. (6768) and Krueger, James G. (6619) had a remarkably high Nc. In addition, the H-index of Guttman-Yassky, E. (36) ranked first, followed by Krueger, James G. (35). It is worth noting that the Np and H-index of Hammad, Hamida were not in top 5, but the average per item of his papers (137.21) ranked the third. This demonstrated that one or a few of his papers was in high citation while others in low citation.

### *3.6. Analysis of journals*

The top 10 journals with the most publications are listed in Table 4. The Journal of Allergy and Clinical Immunology (432 publications, IF: 14.2) published the most papers concerning the links between DCs and allergic diseases. The Journal of Immunology (409 publications, IF: 4.4) and the Plos One (146 publications, IF: 3.7) ranked second and third respectively. The Journal of Allergy and Clinical Immunology was also ranked first in Nc, H-index, followed by the Journal of Immunology. About 35.4 % of the retrieved papers were in the 10 journals (1721/35.4 %). Seven of the top 10 journals exhibited a high IF (defined as greater than 5.000).

### *3.7. Analysis of paper global citation score (GCS)*

Fig. 4 depicts the annual number of papers with a high GCS. The paper published in NATURE MEDICINE (IF: 82.9) and written by Trompette, A in 2006 was 1788, ranking first. In this paper, the authors pointed out that metabolites of intestinal microbiota were key determinants of host-microbe mutualism. The short chain fatty acids (SCFAs), as the increased metabolite from fiber metabolizing by gut microbiota, can protect the lung against allergic inflammation through enhancing generation of macrophage and DC precursors [29]. Dhabhar, FS's research ranked second. His research focused on the impact of the stress on innate/primary and

**Table 4**
The top ten most active journals.

| Journal | Np | Nc | H-index | IF(2022) | Average per item |
|---|---|---|---|---|---|
| Journal of Allergy and Clinical Immunology | 432 | 35748 | 103 | 14.2 | 84.45 |
| Journal of Immunology | 409 | 25308 | 89 | 4.4 | 62.49 |
| Plos One | 146 | 4457 | 38 | 3.7 | 30.64 |
| Allergy | 134 | 4601 | 37 | 12.4 | 34.56 |
| Clinical and Experimental Allergy | 133 | 4268 | 37 | 6.1 | 32.31 |
| Journal of Invertigative Dermatology | 119 | 5390 | 41 | 6.5 | 45.67 |
| Frontiers in Immunology | 113 | 1956 | 24 | 7.3 | 17.47 |
| European Journal of Immunology | 94 | 3251 | 31 | 5.4 | 34.79 |
| International Archives of Allergy and Immunology | 78 | 1619 | 23 | 2.8 | 20.92 |
| Journal of Experimental Medicine | 63 | 11987 | 55 | 15.3 | 190.65 |

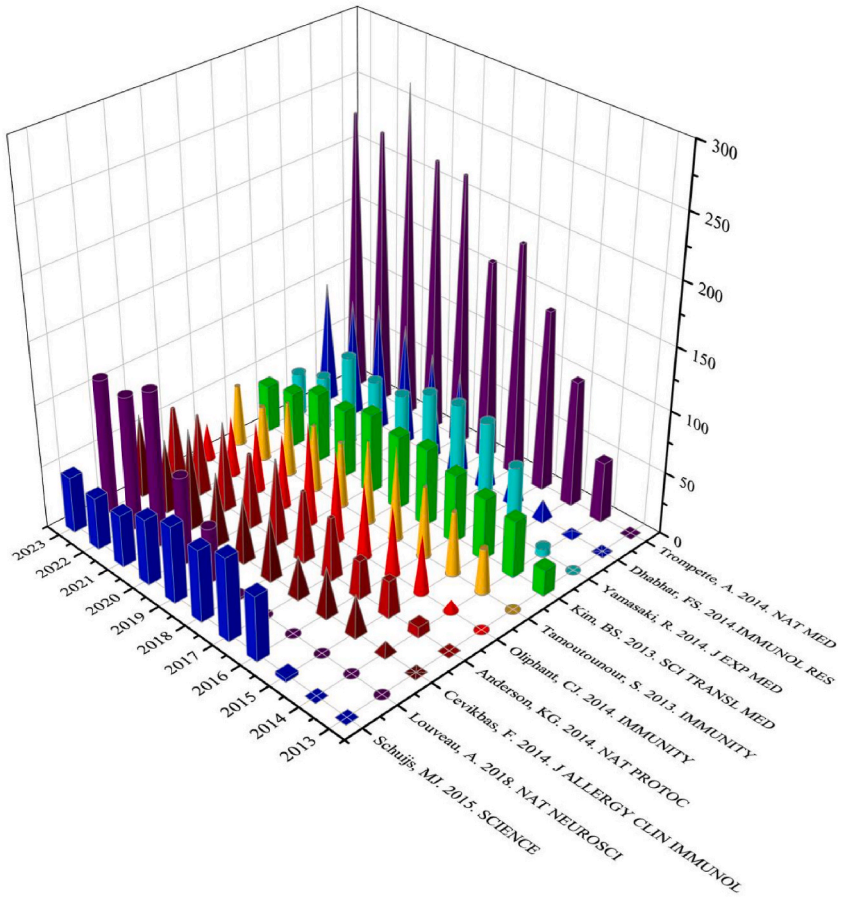


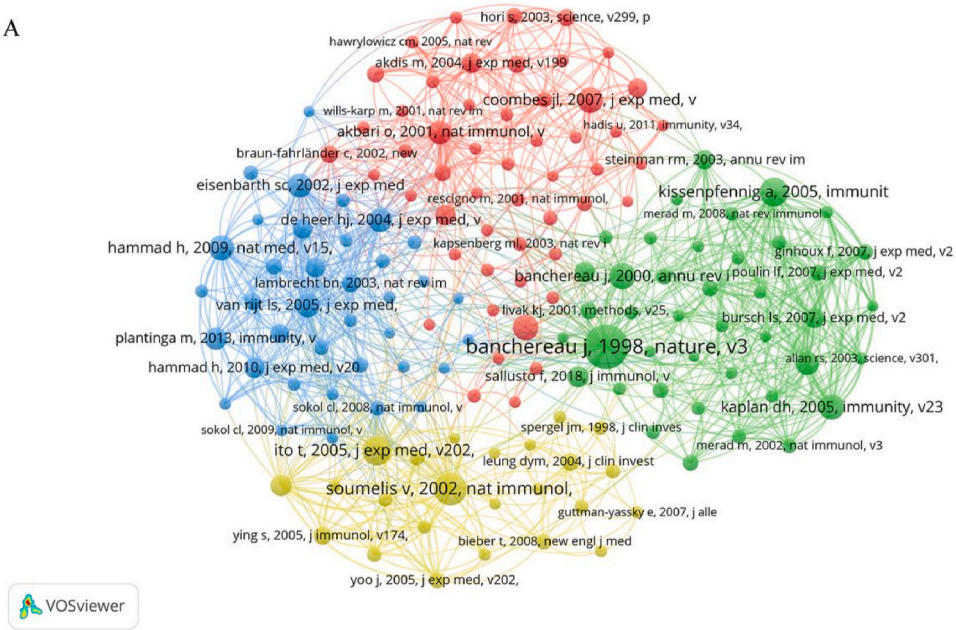

**Fig. 4.** The yearly number of global citations for papers having a high global citation score (GCS). The pillar's height shows the number of citations. The higher the pillar, the more the number of citations of the paper. The pillar's colours and forms represent diffierent papers. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

adaptive/secondary immune responses related to allergic diseases [30]. Yamasaki, R's research ranked third, in which the critical function on inflammation of macrophage activation mediated by T cell was shown [31]. This research confirmed that monocyte-derived macrophages are highly phagocytic and inflammatory and distinguishing tissue resident macrophages from infiltrating monocytes would help to repair in diverse inflammatory pathologies [31]. The papers ranked from fouth to eighth all interpret their views through a mouse model [32–36]. In Kim, BS's research, the mouse model of allergic disease was made to demonstrate that thymic stromal lymphopoietin (TSLP) can promote skin inflammation by eliciting IL-33-independent innate lymphoid cell responses [32]. In Tamoutounour, S's research, origins and functional specialization of macrophages and of conventional and monocyte-derived DCs in mouse skin were identified by combining CD64 and CCR2 staining [33]. Intravascular staining for discrimination of leukocytes was also shown in Anderson, KG's research [34]. In addition, papers of Kim, BS [32], Tamoutounour, S[33] and Oliphant,CJ [35] were all illustrated the relationships between innate lymphoid cell (ILC) and DC in allergic diseases. The researches of Cevikbas, F[36] and Louveau, A [37]. focused the neuroinflammation. In the last one document, the house dust mite (HDM)-induced asthma were presented [38].

### 3.8. Analysis of Co-cited reference

The co-citation network places an emphasis on research topics closely related to particular fields. Considering the masses of cited references, the minimum Nc per reference was set as 40. As shown in Fig. 5A, 154 references were selected for co-citation analysis from the 125,760 references cited by the retrieved publications. The papers were divided into clusters by using various node colours. The relationship between two nodes suggests that a single publication cites two references. [20,24] A shorter line suggests a closer connection between the two items [39]. The total number of co-citations for a reference is represented by the node size. References made up cluster 1 (red), which focused on the mechanism by which inhalation of allergens caused T cells to become tolerant and protected against the emergence of airway hyperreactivity. Cluster 2 (green) comprised 41 references, focusing on the suppression of allergen-driven T cell activation of allergic disease by Treg. Cluster 3 (blue) mainly focused on the function of basophilic granulocytes in allergic diseases. The theme of cluster 4 (yellow) centered on the activation of TSLP in type 2 immune responses. On the basis of the

A

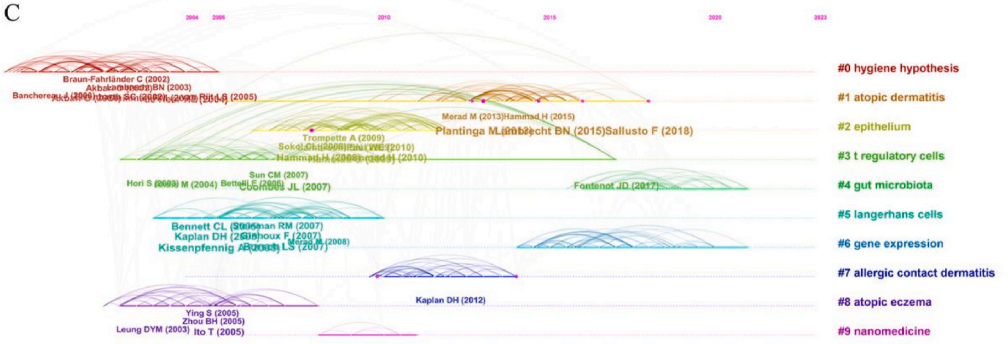



B

**Top 20 References with the Strongest Citation Bursts**

| References | Year | Strength | Begin | End | 2004 - 2023 |
|---|---|---|---|---|---|
| Akbari O, 2001, NAT IMMUNOL, V2, P725, DOI 10.1038/90667, DOI | 2001 | 20.76 | 2004 | 2006 | |
| Eisenbarth SC, 2002, J EXP MED, V196, P1645, DOI 10.1084/jem.20021340, DOI | 2002 | 15.25 | 2004 | 2007 | |
| Akbari O, 2002, NAT MED, V8, P1024, DOI 10.1038/nm745, DOI | 2002 | 14.78 | 2004 | 2007 | |
| Banchereau J, 2000, ANNU REV IMMUNOL, V18, P767, DOI 10.1146/annurev.immunol.18.1.767, DOI | 2000 | 14.03 | 2004 | 2005 | |
| de Heer HJ, 2004, J EXP MED, V200, P89, DOI 10.1084/jem.20040035, DOI | 2004 | 18.01 | 2005 | 2009 | |
| Steinman RM, 2003, ANNU REV IMMUNOL, V21, P685, DOI 10.1146/annurev.immunol.21.120601.141040, DOI | 2003 | 15.71 | 2005 | 2008 | |
| Lambrecht BN, 2003, NAT REV IMMUNOL, V3, P994, DOI 10.1038/nri1249, DOI | 2003 | 13.98 | 2005 | 2007 | |
| Kissenpfennig A, 2005, IMMUNITY, V22, P643, DOI 10.1016/j.immuni.2005.04.004, DOI | 2005 | 24.17 | 2006 | 2010 | |
| Kaplan DH, 2005, IMMUNITY, V23, P611, DOI 10.1016/j.immuni.2005.10.008, DOI | 2005 | 21.6 | 2006 | 2010 | |
| Bennett CL, 2005, J CELL BIOL, V169, P569, DOI 10.1083/jcb.200501071, DOI | 2005 | 19.4 | 2006 | 2010 | |
| Ito T, 2005, J EXP MED, V202, P1213, DOI 10.1084/jem.20051135, DOI | 2005 | 14.85 | 2007 | 2010 | |
| Bursch LS, 2007, J EXP MED, V204, P3147, DOI 10.1084/jem.20071966, DOI | 2007 | 18.61 | 2008 | 2012 | |
| Hammad H, 2008, NAT REV IMMUNOL, V8, P193, DOI 10.1038/nri2275, DOI | 2008 | 16.29 | 2009 | 2012 | |
| Poulin LF, 2007, J EXP MED, V204, P3119, DOI 10.1084/jem.20071724, DOI | 2007 | 14.89 | 2009 | 2011 | |
| Hammad H, 2009, NAT MED, V15, P410, DOI 10.1038/nm.1946, DOI | 2009 | 21.3 | 2010 | 2014 | |
| Paul WE, 2010, NAT REV IMMUNOL, V10, P225, DOI 10.1038/nri2735, DOI | 2010 | 15.18 | 2011 | 2014 | |
| Hammad H, 2010, J EXP MED, V207, P2097, DOI 10.1084/jem.20101563, DOI | 2010 | 21.46 | 2012 | 2015 | |
| Plantinga M, 2013, IMMUNITY, V38, P322, DOI 10.1016/j.immuni.2012.10.016, DOI | 2013 | 32.93 | 2014 | 2018 | |
| Lambrecht BN, 2015, NAT IMMUNOL, V16, P45, DOI 10.1038/ni.3049, DOI | 2015 | 32.11 | 2015 | 2020 | |
| Hammad H, 2015, IMMUNITY, V43, P29, DOI 10.1016/j.immuni.2015.07.007, DOI | 2015 | 14.52 | 2016 | 2018 | |

C




*(caption on next page)*

**Fig. 5.** Visualization of the co-cited reference analysis. (A) Co-occurrence network of co-cited reference. The different colours of the nodes represent different references, with larger nodes meaning more frequent co-cited references; (B) Top twenty representative burst co-cited references. The different colours of line segments represent different states. Red represents burst years of co-cited references; cyan represents the co-cited references are not in a burst state; light cyan represents the co-cited references hasn't been occurrent; (C) Timeline distribution of cluster analysis of the co-cited references. The different colours of lines represent different references and keywords clusters. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

clusters, most studies were found to focus on the basic research of pathogenesis of the contact dermatitis and airway hyperreactivity in allergic diseases. Citation bursts of references can indicate the trends of hotspots over time in a certain field [20]. Fig. 5B depicts the most typical references in terms of burst length, burst strength, and burst time. As shown in Fig. 5B, the top 9 clusters of co-cited references were "hygiene hypothesis," "atopic dermatitis," "epithelium," "t regulatory cells," "gut microbiota," "langerhans cells," "gene expression," "allergic contact dermatitis," "atopic eczema" and "nanomedicine." Fig. 5C illustrates the top 20 references with the most powerful citation bursts. The article with the strongest burst (32.93), entitled "Conventional and monocyte-derived CD11b (+) dendritic cells initiate and maintain T helper 2 cell-mediated immunity to house dust mite allergen," was published in Immunity by Plantinga M et al., in 2012 [40]. In addition, the paper entitled "The immunology of asthma" had a burst lasting until 2020 [41].

### *3.9. Analysis of highly Co-cited articles*

The articles in Table 5 are listed in descending order of the total Nc. More than half of the top 10 highly co-cited papers were published between 2000 and 2005. The writing in Nature ranked first, cited almost 300 times (IF: 64.8; title: Dendritic cells and the control of immunity; type of study: review; citations: 299). This paper systematically introduced the mechanism of action of DCs in immune diseases, including allergic diseases [42]. It was followed by Nature Immunology (IF: 30.5; title: Human epithelial cells trigger dendritic cell mediated allergic inflammation by producing TSLP; type of study: basic research; citations: 192), and Journal of Experimental Medicine (IF: 15.3; title: TSLP-activated dendritic cells induce an inflammatory T helper type 2 cell response through OX40 ligand; type of study: basic research; citations: 160). In addition, the Journal of Experimental Medicine covered three highly cited papers among the top 10. This finding suggested that the research results this journal provided were not only copious but also of high quality. Moreover, studies related to the links between DCs and allergic diseases were published in the Journal of Experimental Medicine, indicating the significant importance of researchers for the study of the pathogenesis of allergic diseases related to DC.

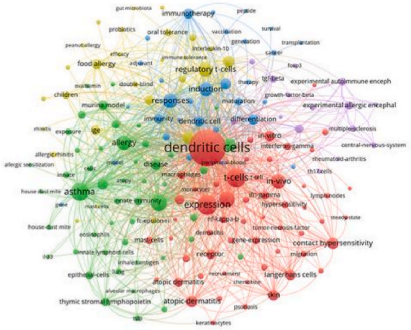
### *3.10. Analysis of hotspots in research*

The analysis of co-occurring keywords can identify research hotspots within a certain knowledge base [20]. 13,338 keywords were extracted, of which 176 keywords occurred more than or equal to 45 times. According to Fig. 6A, cluster 1 (56 items, red) focused on the hypersensitivity in allergic deseases (allergic asthma, atopic dermatitis) activated by contact antigens and immune cells involved in this pathogenesis. Cluster 2 (48 items, green) primarily reflected the effects of generation and external environment in the regulation of allergic response. Cluster 3 (29 items, blue) was mainly about the experimental researches related to allergy. Cluster 4 (27 items, yellow) focused on the function of DCs in the development and differentiation of T cells. Cluster 5 (16 items, purple) was mainly about TSLP, toll like receptors and the immune therapy. The top frequent keywords were "dendritic cells," "expression," "t-cells," "asthma," and "inflammation." The color depth in Fig. 6B demonstrated the distribution of keywords in chronological order. Before 2014, most

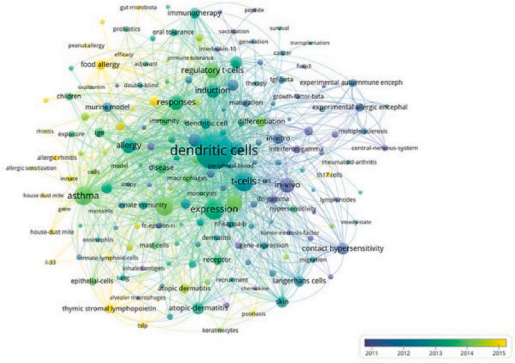
**Table 5**
The top ten highest co-cited articles.

| Year | Article | Total Citations | IF (2022) | Type of study |
|---|---|---|---|---|
| 1998 | Banchereau J et al. Dendritic cells and the control of immunity. Nature. 1998 Mar 19; 392(6673):245-52. | 299 | 64.8 | Review |
| 2002 | Soumelis V et al. Human epithelial cells trigger dendritic cell mediated allergic inflammation by producing TSLP. Nat Immunol. 2002 Jul; 3(7):673-80. | 192 | 30.5 | Basic Research |
| 2005 | Ito T et al. TSLP-activated dendritic cells induce an inflammatory T helper type 2 cell response through OX40 ligand. J Exp Med. 2005 Nov 7; 202(9):1213-23. | 160 | 15.3 | Basic Research |
| 2005 | Kissenpfennig A et al. Dynamics and function of Langerhans cells in vivo: dermal dendritic cells colonize lymph node areas distinct from slower migrating Langerhans cells. Immunity. 2005 May; 22(5):643-54. | 156 | 32.4 | Basic Research |
| 2000 | Banchereau J et al. Immunobiology of dendritic cells. Annu Rev Immunol. 2000; 18:767–811. | 138 | 29.7 | Basic Research |
| 1999 | Lutz MB et al. An advanced culture method for generating large quantities of highly pure dendritic cells from mouse bone marrow. J Immunol Methods. 1999 Feb 1; 223(1):77–92. | 135 | 2.2 | Basic Research |
| 2007 | Coombes JL et al. A functionally specialized population of mucosal CD103+ DCs induces Foxp3+ regulatory T cells via a TGF-beta and retinoic acid-dependent mechanism. J Exp Med. 2007 Aug 6; 204(8):1757-64. | 132 | 15.3 | Basic Research |
| 2005 | Kaplan DH et al. Epidermal langerhans cell-deficient mice develop enhanced contact hypersensitivity. Immunity. 2005 Dec; 23(6):611-20. | 131 | 32.4 | Basic Research |
| 2009 | Hammad H et al. House dust mite allergen induces asthma via Toll-like receptor 4 triggering of airway structural cells. Nat Med. 2009 Apr; 15(4):410-6. | 130 | 82.9 | Basic Research |
| 2002 | Eisenbarth SC et al. Lipopolysaccharide-enhanced, toll-like receptor 4-dependent T helper cell type 2 responses to inhaled antigen. J Exp Med. 2002 Dec 16; 196(12):1645-51. | 122 | 15.3 | Basic Research |

A




B




C

## Top 20 Keywords with the Strongest Citation Bursts

| Keywords | Year | Strength | Begin | End | 2004 - 2023 |
|---|---|---|---|---|---|
| interferon gamma | 2004 | 24.21 | **2004** | 2009 | |
| delayed type hypersensitivity | 2004 | 16.44 | **2004** | 2009 | |
| necrosis factor alpha | 2004 | 11.86 | **2004** | 2009 | |
| lymphocytes | 2004 | 11.41 | **2004** | 2009 | |
| epidermal langerhans cells | 2004 | 10.97 | **2004** | 2007 | |
| antigen | 2004 | 10.16 | **2004** | 2005 | |
| colony stimulating factor | 2004 | 10.18 | **2007** | 2009 | |
| multiple sclerosis | 2004 | 10.25 | **2008** | 2010 | |
| experimental allergic encephalomyelitis | 2004 | 9.7 | **2008** | 2009 | |
| th17 cells | 2011 | 11.85 | **2011** | 2014 | |
| infection | 2005 | 15.06 | **2012** | 2017 | |
| peripheral blood | 2008 | 10.62 | **2012** | 2014 | |
| house dust mite | 2012 | 21.28 | **2013** | 2019 | |
| innate lymphoid cells | 2014 | 19.33 | **2014** | 2023 | |
| allergic asthma | 2010 | 11.46 | **2016** | 2018 | |
| food allergy | 2007 | 32.88 | **2017** | 2023 | |
| mechanisms | 2009 | 15.5 | **2017** | 2023 | |
| gut microbiota | 2017 | 15.47 | **2017** | 2023 | |
| allergic rhinitis | 2006 | 14.43 | **2018** | 2023 | |
| protein | 2004 | 10.83 | **2018** | 2023 | |

D

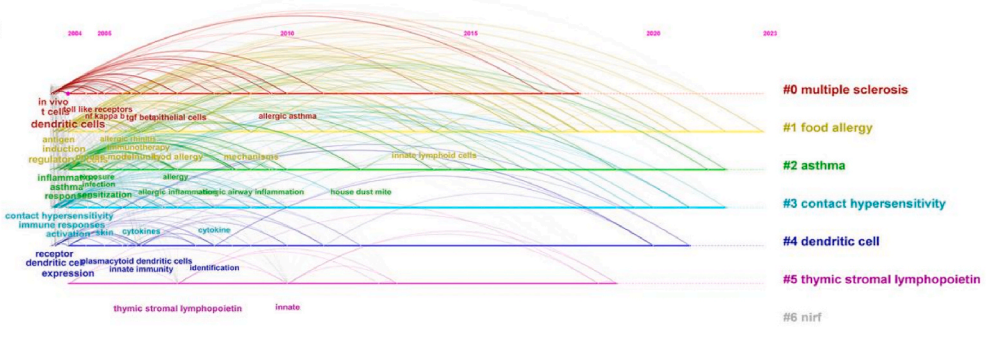



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**Fig. 6.** Visualization of the keywords analysis. (A) Network of keywords. The different colours of the nodes represent different keywords, with larger nodes meaning more frequent keywords; (B) Timeline visualization of keywords. Keywords in yellow appeared later than that in blue; (C) Top twenty representative burst keywords. The different colours of line segments represent different states. Red represents burst years of keywords; cyan represents the keywords are not in a burst state; light cyan represents the keywords hasn't been occurrent; (D) Timeline distribution of cluster analysis of the keywords. The different colours of lines represent different keywords clusters. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

research focused on "t-cells," "contact hypersensitivity," "foxp3," "interferon-gamma," "langerhans cells," "expression," whereas the latest identified research hotspots indicated "food allergy," "peanut allergy," "asthma," "allergic rhinitis," "thymic stromal lymphopoietin," "early life," and "children" as emerging fields. The distribution reflected that the research on allergic diseases changed from basic immune mechanisms to clinical diseases. Fig. 6C shows the 20 most representative keywords in terms of burst strength, burst duration, and burst time. The findings shows that in the early stage of research on the relationship between DCs and allergic diseases, the "interferon gammar," "delayed type hypersensitivity," "necrosis factor alpha," "epidermal langerhans cells," and "antigen" were the research hotspots. "innate lymphoid cells," "allergic asthma," "food allergy," "mechanisms," "gut microbiota," "allergic rhinitis," and "protein" were the new research hotspots. Except for "allergic asthma," other keyword bursts lasted until 2023. In Fig. 6D, "multiple sclerosis," "food allergy," "asthma," "contact hypersensitivity," "dendritic cell," "thymic stromal lymphopoietin," and "nirf" were the research hotspots for a long time. Fig. 6C and D reflect that the lasting research hotspots had a close relation with the noted keywords in the early and late years.

### 3.11. Analysis of peak years

The years 2011 and 2017 are the two peak years of Np. The publications of the two years are screened and analyzed separately to further understand the phenomenon. The top 10 productive categories associated with the links between DCs and allergic diseases of 2011 are shown in Fig. 7C and Supplementary Table 1 (Table S1). The most prevalent study category was immunology (167 papers; 48.83 %), followed by allergy (63 papers; 18.42 %), multidisciplinary sciences (24 papers; 7.02 %), biochemistry molecular biology (23 papers; 6.73 %), and cell biology (23 papers; 6.73 %). A total of 342 papers about the study of DCs and allergic diseases in 2011 were screened and analyzed, with 1992 keywords in total. As shown in Fig. 7A, except for DCs, T cells, expression, in vivo, and inflammation most frequently occurred. Fig. 7D and Table S2 depicts the 2017's top 10 productive categories. The top 3 categories were still immunology (141 papers; 48.62 %), allergy (53 papers; 18.28 %) and multidisciplinary sciences (33 papers; 11.38 %). The fourth prevalent category was cell biology (31 papers; 10.69 %), followed by biochemistry molecular biology (20 papers; 6.9 %). Immunology, allergy, and cell Biology were always the most prevalent categories related to DCs and allergic diseases. In the Np of 2017, 290 papers about the study were screened and analyzed, with 1959 keywords in total. Except for DCs and cytokines related to immunity, Fig. 7B shows that asthma appeared more frequently in 2011. In addition, allergic asthma, food allergy, mechanism and gut mcriobita became the emerging hotspots, consistent with the results shown in Fig. 6C. The research degree of allergic diseases such as asthma became more and more intensive.

### 3.12. Molecular docking of active compounds of Saposhnikovia divaricata and TLRs

*S. divaricata* is a herb that was demonstrated to have a positive effect on allergic diseases [43,44]. Cleomiscosin A [45–48], vanillic acid [45,49–53], prim-*O*-glucosylcimifugin [45,54–56], and 5-*O*-methylvisammioside [45,56,57] are bioactive components of *S. divaricata* and these components play an important role in inhibiting allergic inflammation. In innate and adaptive immunity, TLRs have developed into essential molecules [58]. TLRs are known to contribute to the development of Th2 responses according to epidemiological studies and recent findings [58]. The main ligand of TLR1 is bifidobacterium. TLR3 is expressed on the surface of DCs specifically, whereas TLR1 is expressed on kinds of immune cells. As the keywords burst frequently in this study, TLR1 and TLR3 were selected for molecular docking analysis with the bioactive components of *S. divaricata*. The structures of the components are shown in Supplementary Fig. 1. The molecular docking of TLRs with components is shown in Fig. 8, incluing binding mode of TLR1 with Cleomiscosin A (Fig. 8A), TLR1 with Vanillic acid (Fig. 8B), TLR1 with Prim-*O*-glucosylcimifugin (Fig. 8C), TLR1 with 5-*O*-Methylvisammioside (Fig. 8D), TLR3 with Cleomiscosin A (Fig. 8E), TLR3 with Vanillic acid (Fig. 8F), TLR3 with Prim-*O*-glucosylcimifugin (Fig. 8G) and TLR3 with 5-*O*-Methylvisammioside (Fig. 8H). As depicted in Fig. 8 and Table 6, most of the binding free energy of the key active components of *S. divaricata* docked with the TLR proteins well. The binding sites may be the potential therapeutic targets in allergic diseases.

### 3.13. Analysis of bibliographic coupling

Bibliographic coupling depicts that if two documents cite the same references, they have a coupling relationship. The more the Nc coupling, the stronger the correlation between the two articles. Bibliographic coupling can be applied to fields such as information science and bibliometrics. It includes article coupling, country coupling, author coupling, and journal coupling. Fig. 9 shows the network of bibliographic coupling analysis of countries/regions (Fig. 9A), affiliations(Fig. 9B), authors (Fig. 9C), journals (Fig. 9D) and documents (Fig. 9E). In addition, the related information is shown in the supplementary tables. In the top 10 bibliographic coupling countries (Table S3), the USA had the greatest number of documents, citations, and total link strength. Germany ranked second. Japan

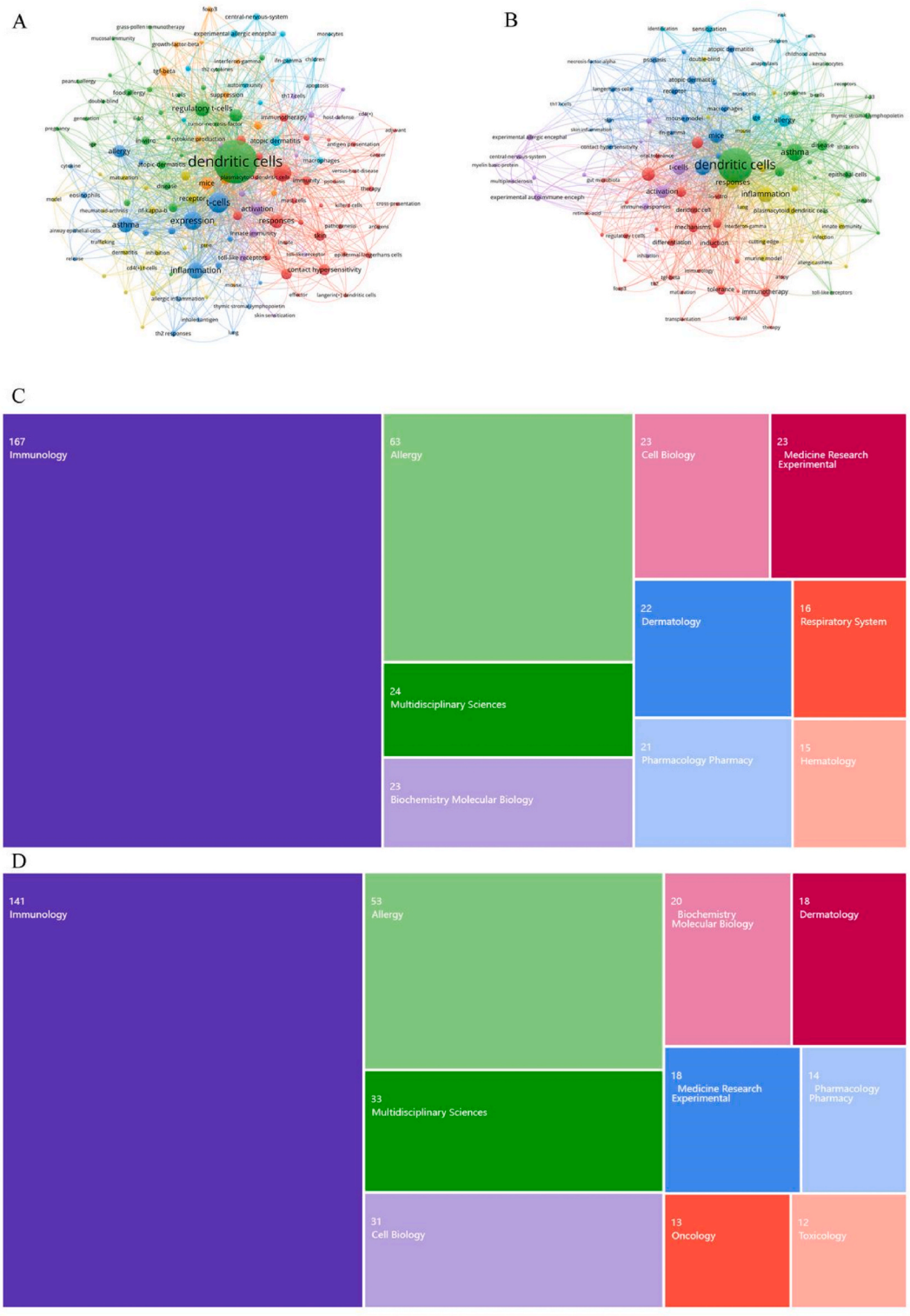


**Fig. 7.** Visualization of the peak years. (A) Network on keywords of the papers published in 2011; (B) Network on keywords of the papers published in 2017; (C) The top ten productive categories in 2011; (D) The top ten productive categories in 2017.

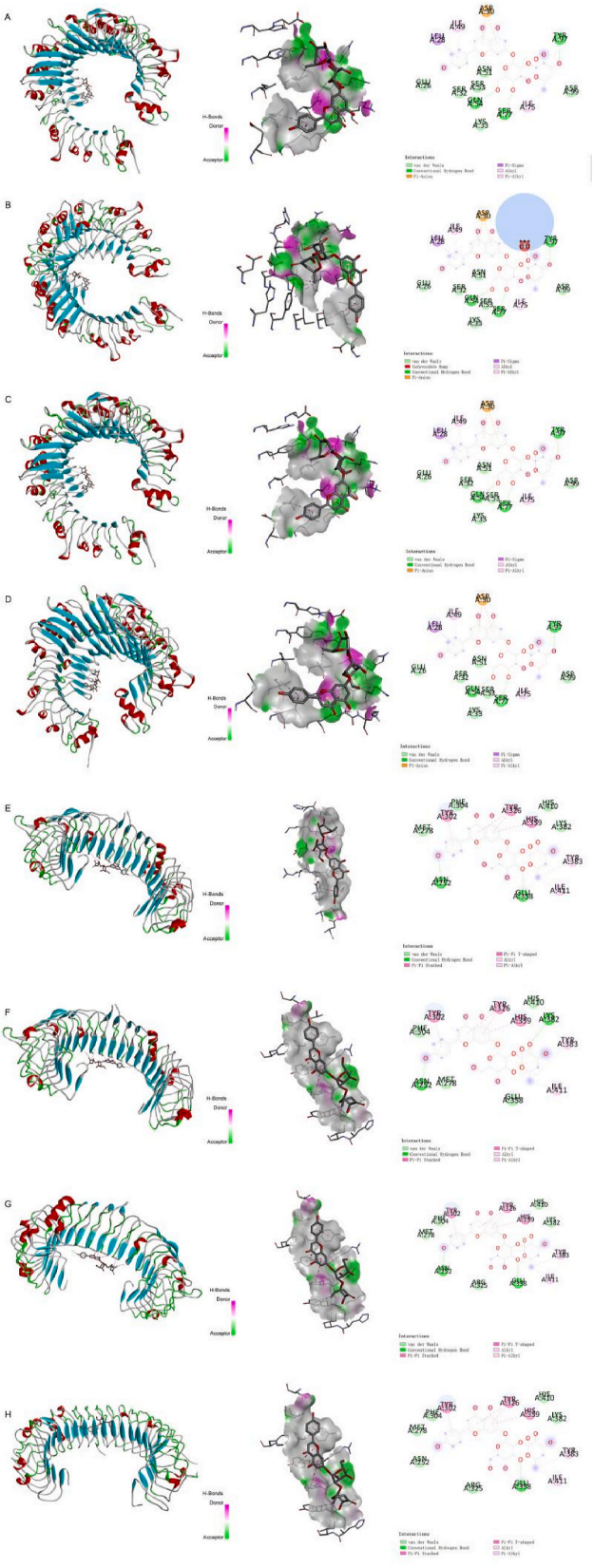


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**Fig. 8.** Molecular docking. Binding mode of (A) Toll-like receptor 1 (TLR1) with Cleomiscosin A; (B) TLR1 with Vanillic acid; (C) TLR1 with Prim-*O*-glucosylcimifugin; (D) TLR1 with 5-*O*-Methylvisammioside; (E) TLR3 with Cleomiscosin A; (F) TLR3 with Vanillic acid; (G) TLR3 with Prim-*O*-glucosylcimifugin; (H) TLR3 with 5-*O*-Methylvisammioside.

ranked third in documents and total link strength. China ranked fourth in documents, but its citations and total link strength were not in the top 5. Except for the USA, the documents of other countries were <1000. The top 10 affiliations are shown in Table S4. Harvard University ranked first in terms of documents, citations, and total link strength, followed by Rockefeller University and Ghent University. Although Ghent University ranked third in total link strength, its documents was not in top 5. In terms of authors (Table S5), Guttman-Yassky, Emma had the most total link strength, whereas his documents and citations ranked second. Krueger, James G. ranked second in total link strength, but the author's citations were the first of the top 10. As shown in Table S6, the Journal of Allergy and Clinical Immunology published the greatest number of documents, which have the most citations and total link strength, followed by the Journal of Immunology. The article written by Mübeccel. Akdis published in 2011 had the most total link strength, and the article written by Guttman-YaSsky, Amma in 2011 ranked second in total link strength (Table S7).

## 4. Discussion

A significant medical and financial burden has been placed on the world due to the rising prevalence of allergic diseases [59]. However, the exact processes that give rise to allergic disorders remain largely unclear [20]. DCs act as a bridge between the innate and adaptive immune systems and are heavily involved in cellular and humoral immune responses through the presentation of antigens to trigger T cell reactions, cytokine and chemokine secretion, T cell differentiation and expansion, B cell activation and regulation, and the mediation of immune tolerance [60]. The process of functioning of DCs may play an important role in the precise mechanisms leading to the development of allergic diseases.

This study attempted to reveal the hotspots and research trends in the field of DCs and allergic diseases. A dataset including 4861 publications from 2004 to 2023 was analyzed through bibliometric methods. Based on the searching reports of the WOSCC database, the publication and citation trends over the years and the contributions of different countries/regions and affiliations were evaluated. The research categories (Fig. 1) and the collaboration relationships, keyword bursts, and co-cited references were detected by bibliometric tools. In the period of 2004–2023, the Np of basic research has a significant impact on the overall situation, because the Np of basic research was close to the total Np. Besides, the Np of total and basic research had almost the same change trend, while there is not much trend fluctuation of clinical and other types research. Two peaks in publication quantity were found (Fig. 2): 2011 (n = 342) and 2017 (n = 290). Besides, in the years around 2011, the publication quantity was in a high level (2009, n = 312; 2010, n = 322; 2012, n = 287). In 2011, the cell biologist Ralph M. Steinman, who discovered the immune system's sentinel DCs, won the Nobel Prize. This situation may cause DCs to be the focus of allergic disease research. Furthermore, the ipilimumab injection (anti-CTLA4), as the first immune checkpoint inhibitor, was ratified by the Food and Drug Administration (FDA) in 2011 [61]. Then, in 2016, the second immune checkpoint inhibitor pembrolizumab (anti-PD1) was ratified [62]. They were all related to the mechanism of antigen presentation [63,64]. Though the annual Np was not in an increasing trend from 2004 to 2023, the publication quantity was in a high state with the annual Np higher than 100. This finding reflected that DCs, as the strongest and most professional APCs, had always been the focus of allergic disease research.

Publications were dispersed worldwide, while productivity in many locations was modest (Fig. 3A). The USA rated first in terms of Np, Nc, H-index and average per item among the top 10 countries/regions, indicating that the country is very prolific in the research of DCs and allergic diseases (Table 1). Though the NPs of England and Netherlands were not in high levels, the H-index of the two countries ranked third and fourth. And the average per items of the two countries ranked first and second. These findings reflected that the publications of England and Netherlands were of high quality. By contrast, the Nc and H-index of China were the last among the top 10 countries/regions, whereas the Np was in the top 5, indicating that the quality of papers in China needs to be improved. As shown in Fig. 3B, China published the highest number of articles in 2022 and 2023, suggesting the increasing attention of China on this research. Meanwhile, the USA made the most important contribution to the publication trend in Fig. 3B.

Nine of the top 10 institutions were from the top 5 countries with the most publications, six of which were in the USA, demonstrating the country's good scholarly competence in this field (Table 2). Lambrecht, Bart N, Guttman-Yassky, E. and Krueger, James G. were the top 3 scholars in the research of DCs and allergic diseases with the most publications. Lambrecht, Bart N, as a scholar of

**Table 6**
Free binding energy and RMSD of four components of Saposhnikovia divaricata and TLRs.

| Component | Chemical formula | Receptor | Free binding energy (kcal/mol) | RMSD |
|---|---|---|---|---|
| Cleomiscosin A | $C_{20}H_{18}O_8$ | TLR1 | −6.3 | 1.537 |
| | | TLR3 | −8.1 | 1.877 |
| Vanillic acid | $C_8H_8O_4$ | TLR1 | −6.4 | 1.527 |
| | | TLR3 | −8.1 | 1.870 |
| Prim-*O*-glucosylcimifugin | $C_{22}H_{28}O_{11}$ | TLR1 | −6.3 | 1.103 |
| | | TLR3 | −8.0 | 1.859 |
| 5-*O*-Methylvisammioside | $C_{22}H_{28}O_{10}$ | TLR1 | −6.3 | 1.552 |
| | | TLR3 | −8.1 | 1.840 |

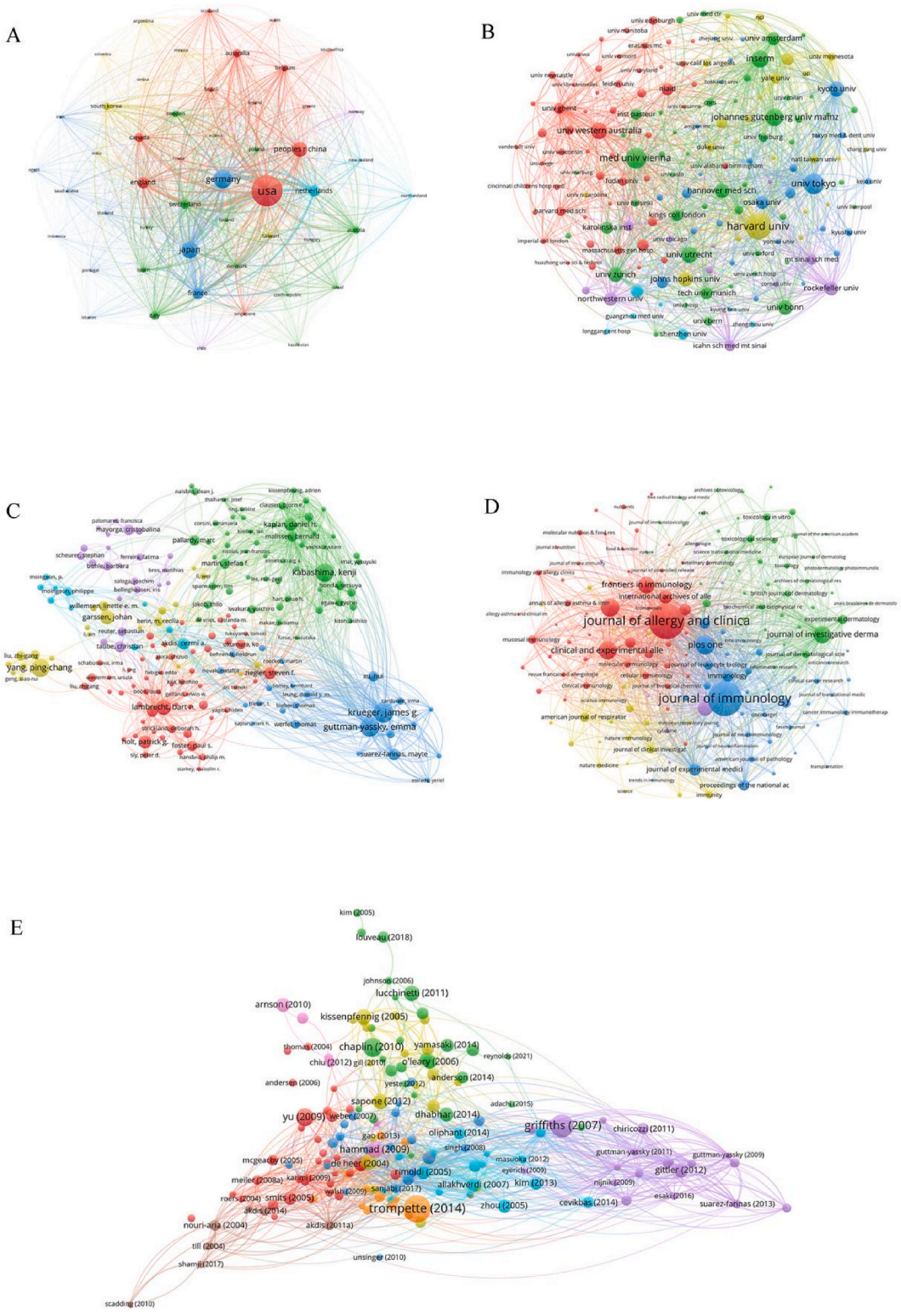


**Fig. 9.** Bibliographic coupling analysis of the links between dentritic cells (DCs) and allergic diseases. The different colours of the nodes represent different categories (countries/regions; affiliations; authors; journals; documents), with larger nodes meaning more frequent occurrence. (A) Network of bibliographic coupling countries/regions; (B) Network of bibliographic coupling affiliations; (C) Network of bibliographic coupling authors; (D) Network of bibliographic coupling journals; (E) Network of bibliographic coupling documents. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Erasmus University Rotterdam of Netherlands (he is also a scholar worked in Ghent University as shown in Table 3), published the most papers with high Nc and H-index in the field, which helped explain why the quality of Netherlands' publications was in a high level. A notable detail that Guttman-Yassky, E. and Krueger, James G., who are among the USA's top 10 scholars, worked in Rockefeller University. However, this university was not ranked among the five institutions of the USA in the top 10 institutions, indicating that the two scholars from Rockefeller University specialized in this field. The studies of Guttman-Yassky, E. and Krueger, James G. were almost focused on allergic dermatosis (especially atopic dermatitis) and the related pathogenesis [65–70]. In addition, Hammad, Hamida achived the third average per item because of his low Np and high citation of individual papers compared with other top 10 scholars.

Notably, seven of the top 10 most prolific journals had a high IF, so the publishing papers related to these fields in high-quality publications was not a challenge. The Journal of Allergy and Clinical Immunology, Journal of Immunology and Plos One made significant contributions. The Journal of Allergy and Clinical Immunology (IF: 14.2) was among the top 10 in terms of Np, Nc and H-index. Its average per item and IF ranked second among the top 10 journals with the most publications. This journal publishes high-impact, cutting-edge basic, clinical, and translational research papers, with topics covering AS, food allergy, AR, AD, primary immune deficiencies, occupational and environmental allergy, and other allergic and immunologic diseases. The Journal of Immunology (IF: 4.4) publishes peer-reviewed papers outlining fresh discoveries in all fields of experimental immunology, including basic and clinical studies. The topics of published studies include allergic reactions and other hypersensitivities, antigen identification, and reactions. The subjects covered in the course include autoimmunity clinical and human immunology, immune regulation, immune system development, immunogenetics, immunotherapy, and vaccines, infectious diseases and host responses, innate immunity and inflammation, molecular and structural immunology, mucosal immunology, systems immunology, transplantation, tumor immunology, and novel immunological technique. Though the Journal of Experimental Medicine was the last in the top 10 journals of Np, its average per item and IF were the highest, which indicated this journal has a significant influence. Since its inchoative in 1896, this journal focuses on the field of medical biology and prefers to reports ranging from atomic-level analysis to clinical interventions that illustrate new mechanisms. Besides, the Allergy (IF: 12.4) made an important contribution. It is the official publication of the European Academy of Allergy and Clinical Immunology. It aims to advance, influence, and communicate all facets of the discipline of allergy/immunology, including educational, basic, translational, and clinical research, and maintain communication between basic and clinical allergy/immunology. These journals enable academics to discuss and exchange their ideas with colleagues to raise their academic standards and scientific proficiency because of their professionalism and high level of popularity and effect. Additionally, these journals have a swift review process. Therefore, the journals shown in Table 4 may continue to be major channels for future research in this field and offer the latest research results for scholars.

The paper titled "Gut microbiota metabolism of dietary fiber influences allergic airway disease and hematopoiesis" ranked first among the top10 GCS. It is a basic research that demonstrated dietary fermentable fiber and SCFAs can change the composition of the gut and lung microbiota and influence the severity of allergic inflammation through a mouse experiment [29]. Among the papers with GCS, 50 % (5/10) focused on the research of immune mechanism in allergic diseases, and interpret their views through a mouse model [32–36]. Kim, BS made a mouse model of allergic disease to demonstrate that TSLP can elicit IL-33-independent innate lymphoid cell responses to promote skin inflammation [32]. In Kim, BS's paper, the relationships between innate ILC and DC in allergic diseases were also illustrated [32]. Researches of Tamoutounour, $S^{33}$ and Oliphant,CJ [35] showed smilar viewpoints of the relationships between innate ILC and DC. Yamasaki, R's research showed the critical function on inflammation of macrophage activation mediated by T cell [31]. This research also confirmed that distinguishing tissue resident macrophages from infiltrating monocytes would help to repair in

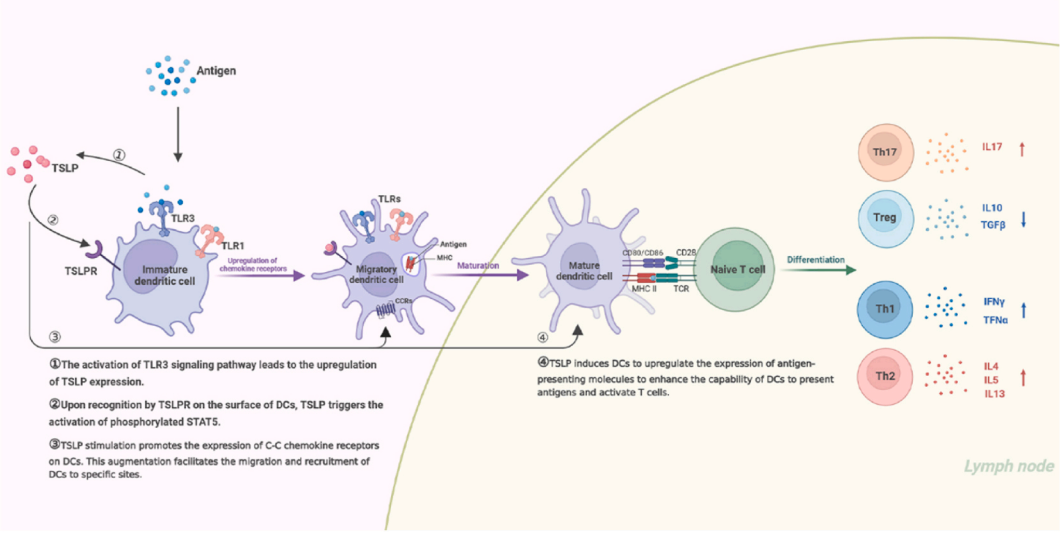


**Fig. 10.** Mechanisms of thymic stromal lymphopoietin (TSLP) and Toll-like receptors (TLRs) pathways interacting with DCs in allergic diseases (created with BioRender.com).

diverse inflammatory pathologies [31].

The paper (IF: 64.8; title: Dendritic cells and the control of immunity; type of study: review; citations: 299) published in Nature were co-cited the most. It introduced how DCs in the periphery captured and processed antigens, expressed lymphocyte co-stimulatory molecules, migrated to lymphoid organs, and secreted cytokines to trigger immune responses [42]. Additionally, DCs may minimize autoimmune reactions by tolerizing T lymphocytes to body-innate antigens [42]. This paper systematically and clearly introduced the mechanism of action of DCs in immune responses, including hypersensitivity. The following two papers with the most citations centered on the activation of DCs by TSLP in allergic responses [71,72]. In addition, the Journal of Experimental Medicine covered three highly cited papers of the top 10 cited papers, showing the importance of understanding the etiology of allergy disorders linked to DCs to researchers.

Combining the bursts and network of cited references and keywords (Figs. 5 and 6), the links between DCs and allergic diseases could be summarized in four main parts. First, as the sentinels of the immune system, DCs continually monitor their environment, presenting antigens to T cells and co-operatively regulating tolerance or immunity [73]. When DCs are in an immature state, they distribute in tissues and organs, including Langerhans cells (LCs) in the mucosal epithelium. Immature DCs express kinds of pattern recognition receptors (PRRs), such as TLRs. These PRRs could recognize various antigen–antibody complexes or pathogenic microorganisms and intake antigens recognized to initiate innate immune response through patterns of pinocytosis, engulfing and mediated receptor [8]. Second, the cytokine TSLP was shown to be essential for preserving immunological homeostasis and controlling type 2 inflammatory responses at mucosal barriers in various allergic disorders [74]. Not come singly but in pairs, in this study of the links between DCs and allergic diseases, TSLP and TLRs are the research focus running through the entire process. As shown in Fig. 10 (Created with BioRender.com), TSLP is an important activator of DCs. It can activate phosphorylated STAT5 signals by recognizing TSLPR on the surface of DCs, inducing DC maturation [75]. TSLP can also promote the transfer and maturation of DCs by promoting the expression of C–C chemokine receptors of DCs [76]. In addition, TSLP can induce DCs to upregulate the expression of antigen-presenting molecules and co-stimulatory molecules [77]. TLR3 is expressed on the surface of DCs specifically, and its ligands can activate the TLR3 signaling pathway through NF-kB and IRF3 to promote the expression of TSLP. TLR1, as one of the surface markers of DCs [78], can also activate the NF-kB signaling pathways cooperating with TLR2 through their ligands [79,80]. House dust mites enhances the innate immune system of keratinocytes to cause complex allergic diseases, and TLR1 activation on keratinocytes may promote Th2 cell responses through ILC2 activation [81]. Meanwhile, as key members of PRRs, TLRs can upregulate the expression of CD40, CD80 and CD86 to mature DCs [82]. The bioactive components of Chinese herb *S. divaricata*, which was demonstrated to have an effective function in antianaphylaxis, were selected to dock with TLR1 and TLR3 proteins to further explore this key mechanism. Cleomiscosin A is one member of coumarinolignoids. Coumarinolignoids belong to the cycloalkylpropanoic acid class of compounds, and its pharmacophoric region is similar to the non-steroidal anti-inflammatory drugs [83]. In Abha Meena's research, a possible anti-inflammatory mechanism of action of cleomiscosin molecules was hypothesized which constitutes TLRs, CDs, iNOS, COX-2 and STAT-6 proteins as potential anti-inflammatory targets [46]. Also, in Meena's research, cleomiscosins A, B and C were showed to be the anti-inflammatory zones, the mechanisms involving NF-kB signaling pathway, MAPK pathway, etc. [46] In addition, the expression of anti-inflammatory mediator IL-4 was found to increase with cleomiscosins A, B and C [84]. Vanillic acid, an oxidized form of vanillin, is a phenolic antioxidant which has been reported with numerous pharmacological properties incluing anti-inflammatory [49,85]. According to more than one study, vanillic acid can decrease the expression of inflammatory markers incluing TLRs [86,87]. Though there was not the direct research between TLRs and the components of prim-*O*-glucosylcimifugin and 5-*O*-methylvisammioside, the function in anti-allergy of prim-*O*-glucosylcimifugin and 5-*O*-methylvisammioside has been reported more than once [53–56]. Molecular docking is established to discover new drug based on 3D structure in silico [88]. Without knowing a priori chemical structure of other target modulators, docking is able to identify novel compounds of therapeutic interest, delineate structure-activity relationships and predict ligand-target interactions in a molecular level [88,89]. The analysis of molecular docking showed a good binding between components and receptors (Fig. 8 and Table 6). After molecular docking, we found the ligands of cleomiscosin A, vanillic acid, prim-*O*-glucosylcimifugin and 5-*O*-methylvisammioside could directly interact with the receptors of TLR1 and TLR3. The RMSD of them were all less than 2, which demonstrated the conformations were ture. And their binding energy values were all less than −5 kcal/mol. Both of these showed that the components can regulate TLR1 and TLR3 well and the Chinese herb *S. divaricata* may has a curative effect on allergic diseases. In addition, the binding energy value of cleomiscosin A with TLR3 was the minimum (−8.1 kcal/mol), so were the vanillic acid with TLR3 and 5-*O*-Methylvisammioside with TLR3. These binding sites may be the potential therapeutic targets in allergic diseases, providing a new path for immunotherapy research. Third, a paper published in 2012 showed that cancer immunotherapy based on DC has been widely used [90]. Sensitizing DCs with cancer antigens and cancer cell lysates is the most widely used approach for creating DC vaccines [91]. Treg, a subgroup of $CD4^+$ T cell, expresses the transcription factor Foxp3 in its nucleus, and it is involved in the maintenance of immune tolerance and immune homeostasis [92]. Different forms of Treg can be generated when DCs are conditioned by external signals, pathogens, and microbes [93]. The mechanism of Treg involves in kinds of cell surface molecules, such as CTLA-4 and PD-1. In the analysis of peak years, the occurrence of immune checkpoint inhibitors (ipilimumab injection and pembrolizumab) attracted the study on sensitization and DCs. Combining the second point and relevant literature, drug blocking of TSLP with its related pathways may be of great significance for the treatment of allergic diseases [94]. Finally, except for immune tolerance, gut microbiota and food allergy were research hotspots. Cancers escape recognition by the immune system through CTLA-4 and PD-1 [95,96]. Gut microbiota can enhance the body's anticancer immune response by regulating these cell surface molecules [97]. The "hygiene hypothesis" was first to point out the potential role of microorganisms in the development of allergic diseases in 1989 [98]. The gut is the main site of host–microbial interaction, and the gut flora is crucial for the development of the host immune system [99].

Probiotics can provide health benefits to the host by changing the gut microbiota [100]. The cellular components of probiotics and

their metabolites can stimulate DCs and macrophages of the innate immune system, regulating Th1/Th2 balance to reduce allergic symptoms to prevent and cure allergic diseases, such as AR, AS, AD, and food allergy [101]. Furthermore, as shown in the time of hotspots' distribution, the research on allergic diseases changed from basic immune mechanisms to clinical diseases. Despite the publications of the links between DCs and allergic diseases were not in an increase trend, the important role of DCs in allergic diseases did not change.

The hotspots and trends in the research on the relationships between DCs and allergic diseases can be better explained by using literature visualization and bibliometric analysis. However, this research has limitations. First, the data from SCI-expanded were included only for articles. Second, by failing to analyze the full text of a publication, VOSviewer and Citespace may overlook some information. Finally, this study could have a slight lag because fresh papers from 2024 were excluded.

## 5. Conclusion

From this bibliometric analysis, we found that DC was always the research hospot in allergic diseases. Though the main type of the related researches is still the basic experimental research, the research contents have changed to clinical diseases. As a bridge between innate immunity and adaptive immunity, DC may regain direct attention in the new hotspots in allergic diseases, such as gut microbiota, food allergy, immune tolerance, and immunotherapy. The findings of our study, which also include the information of global research trends, scholars, affiliations and Journals, could assist academics to further understand the current research state of linkages between DCs and allergic disorders from a macro perspective.

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## Data availability statement

The data used to support the findings of this study were derived from the Web of Science Core Collection, URL at http://www.webofscience.com/wos/woscc/advanced-search.

## CRediT authorship contribution statement

**Xianghe Meng:** Writing – original draft, Visualization, Formal analysis, Data curation, Conceptualization. **Yi Wang:** Writing – original draft, Supervision, Conceptualization. **Zhuqing Li:** Writing – review & editing, Supervision, Conceptualization. **Fan Yang:** Writing – review & editing, Supervision, Conceptualization. **Ji Wang:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization.

## Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Ji Wang reports financial support was provided by National Natural Science Foundation of China. Ji Wang reports financial support was provided by National Administration of Traditional Chinese Medicine. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e30315.

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