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Knowledge mapping of immunotherapy for allergic rhinoconjunctivitis: a bibliometric study (2002-2021)

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Abstract
Background: Allergic rhinoconjunctivitis (ARC) is a common chronic inflammatory disease. Numerous studies on the treatment of ARC have been published. By contrast, there are few bibliometric studies on immunotherapy for ARC. The purpose of this article is to describe the current treatments for ARC and to identify the trends in immunotherapy for ARC.
Methods: Publications were searched from the Web of Science (WOS) Core Collection on April 25, 2022. CiteSpace and Microsoft Excel software were used for further bibliometric analysis.
Results: A total of 969 publications on immunotherapy for ARC in English were retrieved. The number of relevant publications has been continuously increasing over the past 20 years, with many of the publications coming from Germany and the United States of America. In terms of institutions, the ALK Company in Denmark, Imperial College London in United Kingdom, and Charite-Universitatsmedizin Berlin in Germany published the most articles on immunotherapy for ARC. Meanwhile, *Allergy* and *Journal of Allergy and Clinical Immunology* published the most number of studies, and Oliver Pfaar from Germany authored the most number of articles. "Subcutaneous immunotherapy," "international consensus," "allergen immunotherapy," and "recommendation" were the most popular subjects. Thus, directions in research can be predicted as studies regarding mechanisms of ARC, clinical trials, and extracts have reported high-quality results.
Conclusion: Over the past 20 years, the overall quality of research on immunotherapy for ARC has gradually improved, allowing the introduction of specific and targeted treatment. Currently, the main focus of ARC research is the novel routes of drug delivery and combined treatment with biological agents.

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Introduction

Allergic rhinoconjunctivitis (ARC) is a common chronic inflammatory disease[1] that includes allergic rhinitis (AR) and allergic conjunctivitis (AC) and affects approximately 20% of the global population. AR is characterized by clinical symptoms, such as nasal congestion, rhinorrhea, paroxysmal sneezing, or itching of the nose[2] and is usually accompanied by AC, which manifests as itching of the eyes, conjunctival redness, and swelling.[3] Patients with ARC often visit otolaryngology or ophthalmology clinics. ARC affects the quality of sleep, occupational activities, and quality of life of patients, with severe ARC increasing the economic burden on the patients and healthcare systems.

During the past two decades, researchers around the world have made great advances in the epidemiology, diagnosis, and therapy of ARC. Currently, the management of allergic diseases includes environmental control, immunotherapy, and pharmacotherapy. Modern medicine is effective in the treatment of ARC, but long-term control is difficult. In 2011, a paper published in *The Lancet* suggested that allergen immunotherapy alone has the potential to alter the natural history of AR.[4] Allergen immunotherapy, which can be classified as subcutaneous (SCIT) or sublingual (SLIT), is the only currently available treatment that may modify the disease by modulating the innate and adaptive immune responses of the body.[5,6] In the recent years, new molecules and biomarkers for allergen immunotherapy and their combination with biological agents have been the focus of research.[7]

There have been numerous reports regarding the pathophysiology, diagnosis, and treatment of ARC, with many articles reporting on allergen immunotherapy.[8,9] However, no bibliometric study focusing on the current knowledge and trends in the development of immunotherapy for ARC has been conducted. Bibliometric analysis is a method used to visually reveal numerous facets and research trends in a field of study and is widely used to summarize research hotspots and trends.[10-11]

The present study aims to evaluate the literature on immunotherapy for ARC from 2002 to 2021 and to describe and reveal trends in the current state of research on ARC.

Material and Methods

Search strategy

Relevant publications on immunotherapy for ARC were searched from Science Citation Index-Expanded (SCI-Expanded) in the Web of Science (WOS) Core Collection on 25 April 2022. The main search terms were "allergic rhinitis," "allergic conjunctivitis," "ARC," and "immunotherapy". The search strategy was used: ((((TS = ("allergic rhinitis")) OR (TS = ("hay fever"))) AND ((TS = ("allergic conjunctivitis")) OR (TS = (conjunctivitis)))) OR ((TS = ("allergic rhinoconjunctivitis")) OR (TS = (rhinoconjunctivitis)))) AND TS = (Immunotherapy OR Immunotherapies OR immunotherapeutic OR "immunological therapy" OR SLIT OR SCIT OR "immune therapy"). Restrictions: (1) Languages (English), (2) Document types (article or review), and (3) Timespan (2002~2021).

Bibliometric analysis

The searched publications were downloaded, which included a full record and all cited references and then imported to Microsoft Excel (2016) and CiteSpace (5.8.R4, Chaomei Chen, Drexel University, Philadelphia, PA, USA) for further analysis. Microsoft Excel was used to draw the line graph for showing the trend of published articles by year. Visualization analysis including annual publications, authors, institutions and countries, keywords, and keywords with the strongest citation bursts were carried out by CiteSpace. The parameters of CiteSpace were as follows: time span (2002~2021), year of slice (1 year), selection criteria (Top 50), and visualization (cluster view-static and show-merged network).

Ethical approval

Ethical approval was not applicable in the present study.

Results

Annual publications

A total of 969 publications on immunotherapy for ARC in English published between 2002 and 2021 were retrieved, including 727 articles and 242 reviews. The line graph shows that the number of publications related to immunotherapy for ARC over the past 20 years has increased and has a steady growth rate (Figure 1A). The annual trend in the number of publications associated with immunotherapy for ARC per country is shown in Figure 1B. Notably, the number of published studies from 2011 to 2018 remarkably increased from previous years.

Analysis of countries/regions and institutions

From 2002 to 2021, there were 969 publications from 72 countries and 321 cooperations on ARC (Figure 2). As shown in Table 1, the countries with the most number of publications were Germany (n = 215, centrality = 0.11), the United States (n = 213, centrality = 0.06), and Italy (n = 129, centrality = 0.13). Additionally, among all countries, less than half published more than 10 papers. Notably, extensive cooperation between several countries/regions was also observed (Figure 2A).

The CiteSpace software was used to analyze 544 institutions that published studies on immunotherapy for ARC (Figure 2B); 6.07% published more than nine papers, and 14.89% published more than four papers. Table 2 shows the institutions with the most number of studies published from 2002 to 2021. The ALK Company in Denmark (n = 90, centrality = 0.19), Imperial College London in the United Kingdom (n = 61, centrality = 0.07), and Charite-Universitatsmedizin Berlin in Germany (n = 53, centrality = 0.21) were the institutions with the most number of studies published. Additionally, 10 institutions published 416 studies, accounting for 42.93% of the 969 publications from 2002 to 2021; four of these institutions are in Germany.

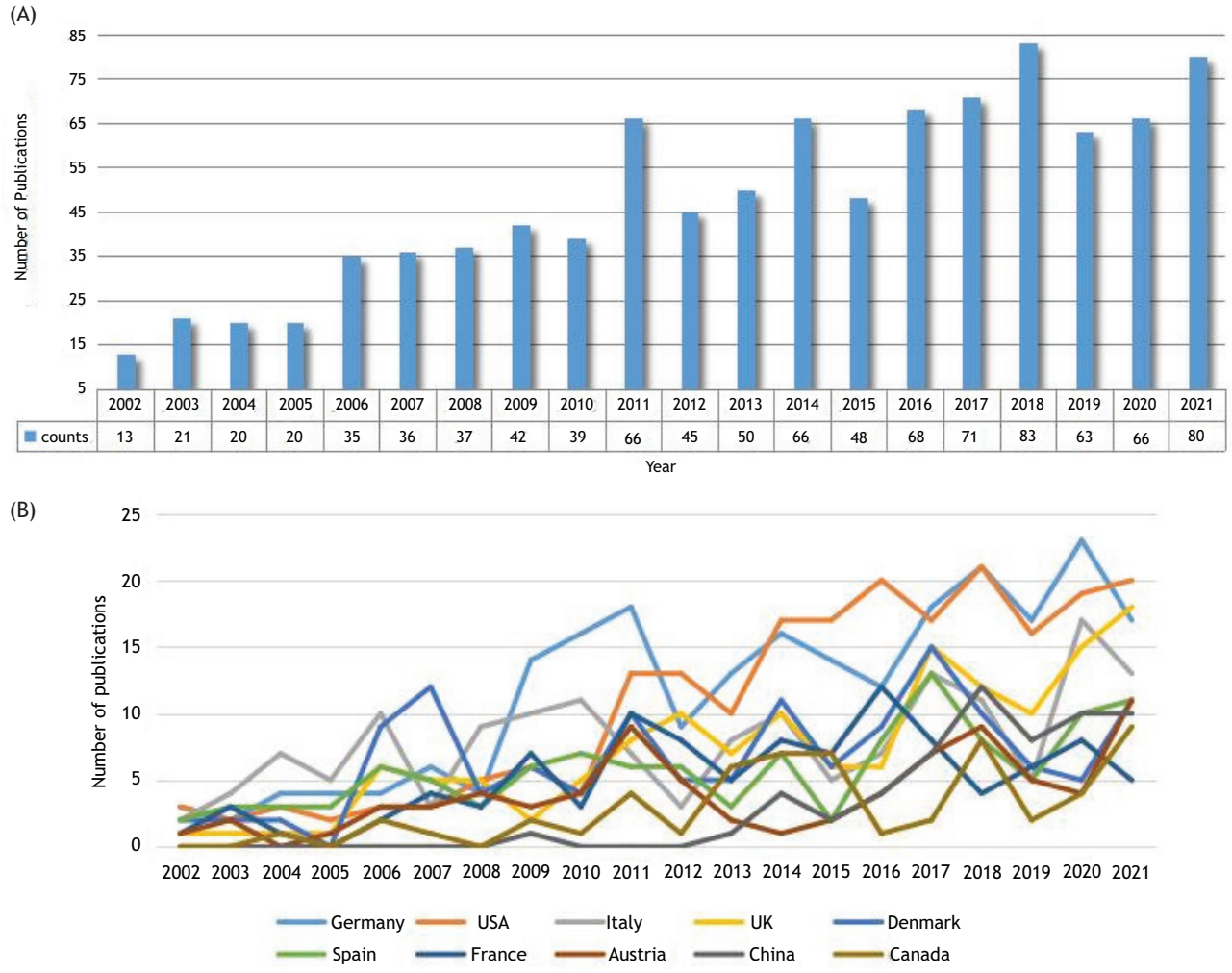


Figure 1 (A) Annual number of studies on immunotherapy for ARC published from 2012 to 2021. (B) Annual number of studies on immunotherapy for ARC per country published from 2012 to 2021.

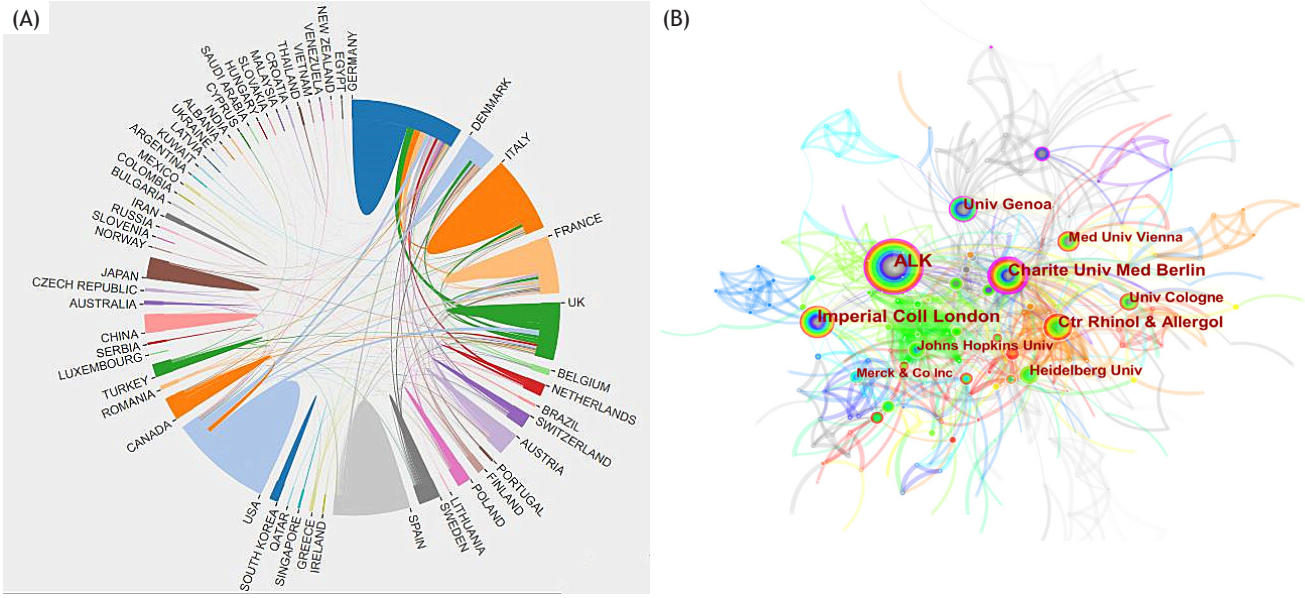


Figure 2 (A) Cooperation map of countries involved in research on immunotherapy for ARC. (B) Network map of the institutions involved in research on immunotherapy for ARC.

Table 1 Top 10 countries with the most publications from 2002 to 2021.

Rank	Country	Counts	Centrality
1	GERMANY	215	0.11
2	USA	213	0.06
3	ITALY	129	0.13
4	UK	126	0.03
5	DENMARK	105	0.15
6	SPAIN	95	0.05
7	FRANCE	94	0.02
8	AUSTRIA	75	0.09
9	PEOPLES R CHINA	54	0
10	CANADA	53	0.04

Table 2 Top 10 institutions with the most publications from 2002 to 2021.

No.	Institution	Country	Counts	Centrality
1	ALK (ALK Company)	Denmark	90	0.19
2	Imperial Coll London (Imperial College London)	UK	61	0.07
3	Charite Univ Med Berlin (Charite-Universitatsmedizin Berlin)	Germany	53	0.21
4	Ctr Rhinol & Allergol (Centre of Rhinology & Allergology, Wiesbaden)	Germany	43	0.04
5	Univ Genoa (University of Genoa)	Italy	39	0.15
6	Univ Cologne (University of Cologne)	Germany	31	0.05
7	Heidelberg Univ (Heidelberg University)	Germany	28	0.02
8	Med Univ Vienna (Medical University of Vienna)	Austria	26	0.04
9	Johns Hopkins Univ (Johns Hopkins University)	USA	23	0.05
10	Merck & Co Inc (Merck Company)	USA	22	0.01

Analysis of journals and co-cited journals

The 969 articles were published in 213 different journals. Table 3 shows the 10 journals and co-cited journals that published the most number of studies on immunotherapy for ARC during the past 20 years. Among them, *Allergy* (n = 116), *Journal of Allergy and Clinical Immunology* (n = 83), *Clinical and Experimental Allergy* (n = 52), *Annals of Allergy and Asthma Immunology* (n = 45), and *Current Opinion in Allergy and Clinical Immunology* (n = 38) published the most number of studies, with *Allergy* having the highest Impact Fact (IF) of 13.146.

The most frequently co-cited journal was the *Journal of Allergy and Clinical Immunology* (927 citations), followed by *Allergy* (909 citations) and *Clinical and Experimental Allergy* (752 citations). Among the most co-cited journals, *New England Journal of Medicine* had the highest IF of 91.245. As shown in Figure 3, there were active mutual relationships between these journals.

The dual-map overlay of journals demonstrates the topic distribution of the journals (Figure 4). The mapping identifies three colored citation pathways: two green citation paths suggested that studies from molecular/biology/genetics journals and health/nursing/medicine journals were frequently cited in studies from medicine/medical/clinical journals, whereas the orange path suggested that studies from molecular/biological/genetics journals were frequently cited from studies in molecular/biological/immunology journals.

Analysis of authors and co-cited authors

Authors who wrote the most number of studies as well as the most cited authors are listed in Table 4, and the author and co-cited author network are shown in Figure 5. The authors who wrote the most number of studies on immunotherapy for ARC were Oliver Pfaar (n = 67), Ludger Klimek (n = 47), and Ralph Mösges (n = 38), who were all from Germany, followed by Stephen R Durham (n = 38) from the United Kingdom, Hendrik Nolte (n = 29) from the United States, and Giorgio Walter Canonica (n = 19) from Italy.

The most cited author was Bousquet J (554 citations) from France, who focused on asthma and AR, followed by Durham SR (434 citations) and Canonica GW (339 citations).

Analysis of references

The most co-cited references are summarized in Table 5. Most of them (7/10) were published in the *Journal of Allergy and Clinical Immunology*. Among them, the article "Pollen immunotherapy reduces the development of asthma in children with seasonal rhinoconjunctivitis (the PAT-study)" published by Möller C et al. was the most cited (n = 744).

We used CiteSpace to construct the network of co-cited references and found eight clusters (Figure 6A). The clusters were as following: #0 "clinical trials," #1 "phleum pratense," #2 "allergy immunotherapy," #3 "intralymphatic immunotherapy," #4 "cytokines," #5 "children," #6 "allergy prophylaxis," and #7 "blocking IgG antibodies." The references with the strongest citation bursts are shown in Figure 6B. Among them, three clusters (#0 "clinical trials," #3 "intralymphatic immunotherapy," and #6 "allergy prophylaxis") have bursts that have persisted until the present.

Analysis of keywords

CiteSpace was used to construct a network map of keywords (Figure 7A and Table 6) and keywords with the strongest citation bursts (Figure 8). Figure 7B shows a network of nine clusters of keywords as follows: #0 "allergic rhinitis," #1 "sublingual immunotherapy," #2 "recombinant allergens," #3 "allergen immunotherapy," #4 "grass

Table 3 Top 10 productive journals and co-cited journals from 2002 to 2021.

Rank	Journal	Article counts	Impact factor	Rank	Cited journal	Citations	Impact factor
1	*Allergy*	116	13.146	1	*Journal of Allergy and Clinical Immunology*	927	10.793
2	*Journal of Allergy and Clinical Immunology*	83	10.793	2	*Allergy*	909	13.146
3	*Clinical and Experimental Allergy*	52	5.018	3	*Clinical and Experimental Allergy*	752	5.018
4	*Annals of Allergy and Asthma Immunology*	45	6.347	4	*Annals of Allergy and Asthma Immunology*	613	6.347
5	*Current Opinion in Allergy and Clinical Immunology*	38	3.142	5	*International Archives of Allergy and Immunology*	496	2.749
6	*International Archives of Allergy and Immunology*	37	2.749	6	*Journal of Investigational Allergology and Clinical Immunology*	339	4.333
7	*Journal of Investigational Allergology and Clinical Immunology*	33	4.333	7	*New England Journal of Medicine*	333	91.245
8	*Allergy and Asthma Proceedings*	29	2.587	8	*Current Opinion in Allergy and Clinical Immunology*	316	3.142
9	*Pediatric Allergy and Immunology*	28	6.377	9	*Pediatric Allergy and Immunology*	304	6.377
10	*Immunotherapy*	26	4.196	10	*Allergy and Asthma Proceedings*	301	2.587

Figure 3 A network map of the co-cited journals involved in research on immunotherapy for ARC.

pollen," #5 "subcutaneous immunotherapy," #6 "regulatory T," #7 "transforming growth factor beta," and #8 "treatment efficacy."

As shown in Figure 8, the strongest burst (house dust mite) occurred in 2003, with a burst strength of 9.18 that lasted for 3 years. However, what we were more concerned about were the current hotspots, including "SCIT" (strength 7.62, 2015–2021), "international consensus" (strength 4.8, 2018–2021), "allergen immunotherapy" (strength 4.02, 2018–2021), and "recommendation" (strength 4.86, 2019–2021).

Discussion

In this study, we searched for articles and reviews regarding immunotherapy for ARC from 2002 to 2021 from the WOS Core Collection. A total of 969 publications comprising 213 journals from 544 institutions in 72 different countries were retrieved and used to perform a bibliometric analysis. As can be observed from the number of annual publications, the number of studies on immunotherapy for ARC is gradually increasing, indicating that this field has received sustained and significant attention during the past years.

In terms of countries/regions, Germany, the United States, and Italy contributed the most number of studies on immunotherapy for ARC in the last 20 years. Additionally, Oliver Pfaar, Ludger Klimek, and Ralph Mösges, who authored the most articles, were all from Germany. Notably, although Denmark had only one institution (ALK Company) among the 10 countries with the most number of studies published, this institution published the most number of studies among all institutions worldwide. Additionally, 4 of the 10 institutions that published the most studies are in Germany. Moreover, most of these papers were published in *Allergy*, *Journal of Allergy and Clinical Immunology*, and *Clinical and Experimental Allergy*, which belong to allergy and immunology. Meanwhile, the *Journal of Allergy and Clinical Immunology* and *Allergy* were the most cited journals.

Keywords are the summary and generalization of the article, and keyword clusters can classify the degree of similarity between indicators. Therefore, keywords and clusters serve as important indices to reflect research hotspots and the focus of the literature in a field of study. Co-cited references and keyword analyses showed that research on immunotherapy for ARC revolved around different immunotherapy pathways and mechanisms. "International consensus," "allergen immunotherapy," and "recommendation" are the keywords with the strongest citation bursts that are currently still active. Therefore, research directions for immunotherapy for ARC can be predicted as follows:

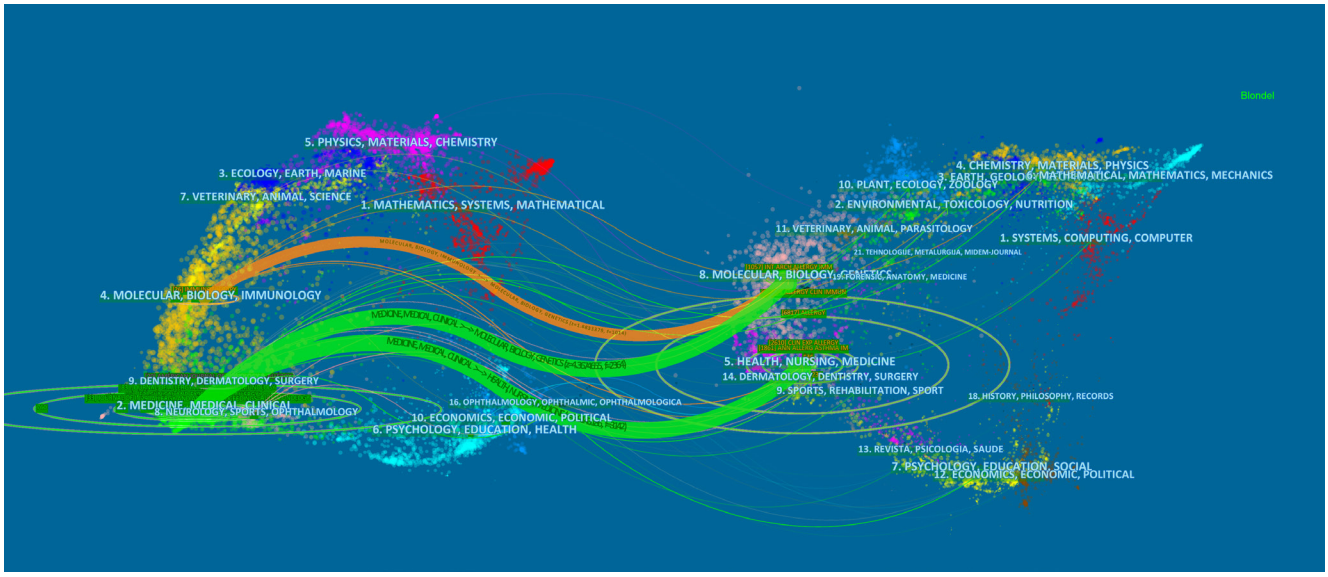


Figure 4 A dual-map overlay of journals related to research on immunotherapy for ARC[a].
[a]From left to right, the colored lines depict the citation paths. The citing journals are on the left of the map and the cited journals are on the right.

Table 4 Top 10 productive authors and cited authors from 2002 to 2021.

Rank	Author (Country)	Counts	Centrality	Rank	Cited Author (Country)	Citations
1	Oliver Pfaar (Germany)	67	0.16	1	Bousquet J (France)	554
2	Ludger Klimek (Germany)	47	0.04	2	Durham SR (UK)	434
3	Ralph Mösges (Germany)	38	0.05	3	Canonica GW (Italy)	339
4	Stephen R Durham (UK)	38	0.15	4	Calderon MA (UK)	304
5	Hendrik Nolte (USA)	29	0.04	5	Pfaar O (Germany)	229
6	Giorgio Walter Canonica (Italy)	19	0.03	6	Passalacqua G (Italy)	229
7	Pascal Demoly (France)	13	0.01	7	Cox L (USA)	223
8	Giovanni Passalacqua (Italy)	13	0.01	8	Didier A (France)	205
9	Moises A Calderon (UK)	12	0.01	9	Dahl R (France)	195
10	Harold S Nelson (USA)	12	0.02	10	Moller C (Denmark)	180

mechanism research related to different pathways, clinical trials and allergen extracts that meet standards, and the recommended international consensus.

The European Academy of Allergy and Clinical Immunology (EAACI) is an association dedicated to improving the health of people affected by allergic diseases. In 2010, the GA(2)LEN/EAACI pocket guide,[12] which has been presented in several meetings, offered comprehensive recommendations on the daily use of immunotherapy in ARC and asthma. In the latest guidelines prepared by the EAACI,[13] allergen immunotherapy is recommended as first-line treatment.

Currently, in clinical practice, allergen immunotherapy includes classical SCIT and SLIT.[14,15] Allergen immunotherapy reduces the immune response through long-term repeated exposure to specific allergens. The efficacy of conventional allergy immunotherapy in ARC has been established, and both SCIT and SLIT are effective. The gold standard in the treatment of allergic diseases is SCIT due to its long-term benefits for patients. However, only 5% receive SCIT mainly

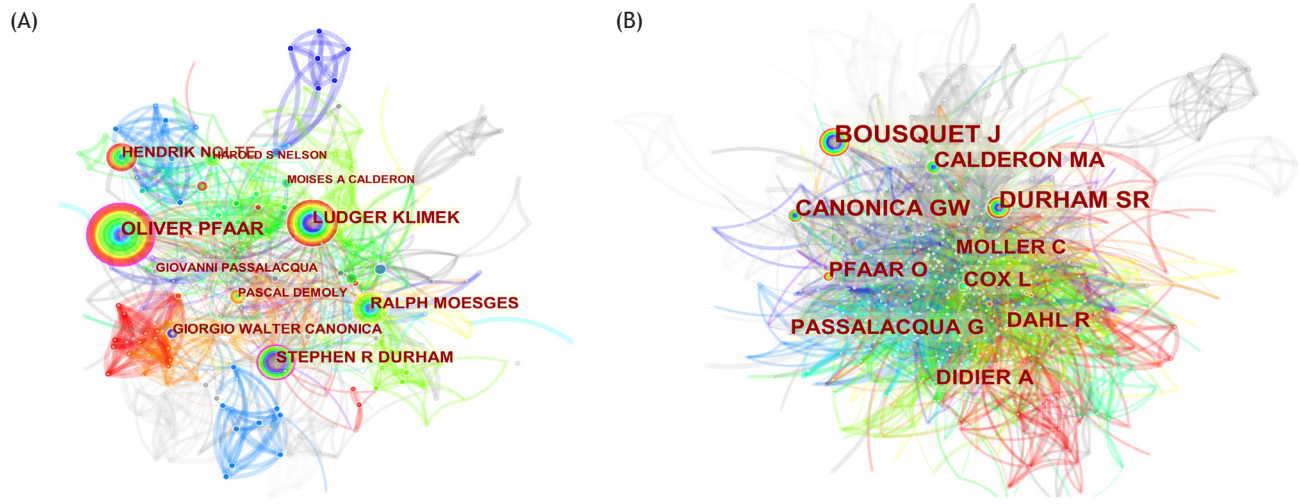


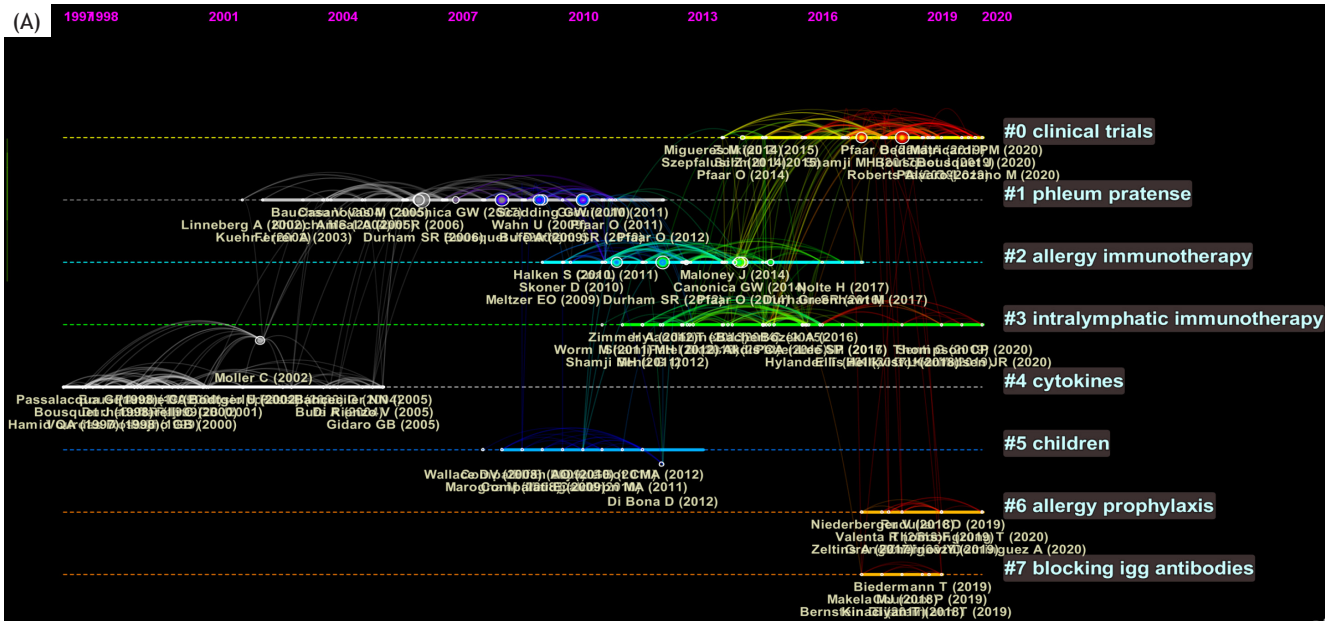
Figure 5 (A) A network map of the authors involved in research on immunotherapy for ARC. (B) A network map of the cited authors involved in research on immunotherapy for ARC.

Table 5 Top 10 co-cited references from 2002 to 2021.

Rank	Article title	First author	Citations	Journal (Impact factor)
1	Pollen immunotherapy reduces the development of asthma in children with seasonal rhinoconjunctivitis (the PAT-study)	Möller C[29]	744	*Journal of Allergy and Clinical Immunology* IF=10.793
2	Specific immunotherapy has long-term preventive effect of seasonal and perennial asthma: 10-year follow-up on the PAT study	Jacobsen L[30]	666	*Allergy* IF=13.146
3	SLIT with once-daily grass allergen tablets: A randomized controlled trial in seasonal ARC	Durham SR[31]	429	*Journal of Allergy and Clinical Immunology* IF=10.793
4	Allergen-specific immunotherapy with recombinant grass pollen allergens	Jutel M[32]	396	*Journal of Allergy and Clinical Immunology* IF=10.793
5	Optimal dose, efficacy, and safety of once-daily SLIT with a 5-grass pollen tablet for seasonal AR	Didier A[33]	389	*Journal of Allergy and Clinical Immunology* IF=10.793
6	Coseasonal SLIT reduces the development of asthma in children with ARC	Novembre E[34]	362	*Journal of Allergy and Clinical Immunology* IF=10.793
7	Efficacy and safety of SLIT with grass allergen tablets for seasonal ARC	Di Bona D[35]	354	*JAMA Internal Medicine* IF=21.873
8	SQ-standardized sublingual grass immunotherapy: Confirmation of disease modification 2 years after 3 years of treatment in a randomized trial	Durham SR[36]	351	*Journal of Allergy and Clinical Immunology* IF=10.793
9	Clinical Practice Guideline: AR	Seidman MD[37]	340	*Otolaryngology Head & Neck Surgery* IF=3.497
10	SLIT for hazelnut food allergy: A randomized, double-blind, placebo-controlled study with a standardized hazelnut extract	Enrique E[38]	326	*Journal of Allergy and Clinical Immunology* IF=10.793

due to its frequency of administration that must be performed in a hospital, unpredictable adverse reactions, and long duration of treatment.[16,17] For some patients, especially children and those afraid of needles, SLIT is an alternative option. However, there may be issues with compliance due to long-term oral medication.

In recent years, intralymphatic immunotherapy (ILIT)[18,19] was developed as a novel route of delivery. ILIT induces tolerance after only three administrations and delivers lower doses of an allergen to a highly immunocompetent lymph node to maximize chances for tolerance induction with fewer adverse events.[20] ILIT is deemed safe and promising based on the results of clinical trials, although long-term follow-up with standard scoring criteria is needed.[21] Witten et al. revealed that intralymphatic injections with grass pollen allergen extracts induced a regulatory T-cell response and increased IgG4 levels but there was no improvement in clinical symptoms;[22] hence, they



(B)

Top 10 References with the Strongest Citation Bursts

References	Year	Strength	Begin	End	2002 - 2021
Moller C, 2002, J ALLERGY CLIN IMMUN, V109, P251, DOI 10.1067/mai.2002.121317, DOI	2002	30.67	2003	2007	
Wilson DR, 2005, ALLERGY, V60, P4, DOI 10.1111/j.1398-9995.2005.00699.x, DOI	2005	29.12	2006	2010	
Durham SR, 2006, J ALLERGY CLIN IMMUN, V117, P802, DOI 10.1016/j.jaci.2005.12.1358, DOI	2006	32.27	2007	2011	
Dahl R, 2006, J ALLERGY CLIN IMMUN, V118, P434, DOI 10.1016/j.jaci.2006.05.003, DOI	2006	27.69	2007	2011	
Didier A, 2007, J ALLERGY CLIN IMMUN, V120, P1338, DOI 10.1016/j.jaci.2007.07.046, DOI	2007	26.38	2008	2012	
Bousquet J, 2008, ALLERGY, V63, P8, DOI 10.1111/j.1398-9995.2007.01620.x, DOI	2008	30.29	2009	2013	
Bufe A, 2009, J ALLERGY CLIN IMMUN, V123, P167, DOI 10.1016/j.jaci.2008.10.044, DOI	2009	24.98	2010	2014	
Roberts G, 2018, ALLERGY, V73, P765, DOI 10.1111/all.13317, DOI	2018	32.29	2018	2021	
Dhami S, 2017, ALLERGY, V72, P1597, DOI 10.1111/all.13201, DOI	2017	26.15	2018	2021	
Shamji MH, 2017, ALLERGY, V72, P1156, DOI 10.1111/all.13138, DOI	2017	25.2	2018	2021	

Figure 6 (A) A line map of the cluster of co-cited references involved in research on immunotherapy for ARC. (B) References with the strongest citation bursts[a].
[a]The blue line represents the period from 2002 to 2021, and the periods of each burst keyword are plotted by the red line.

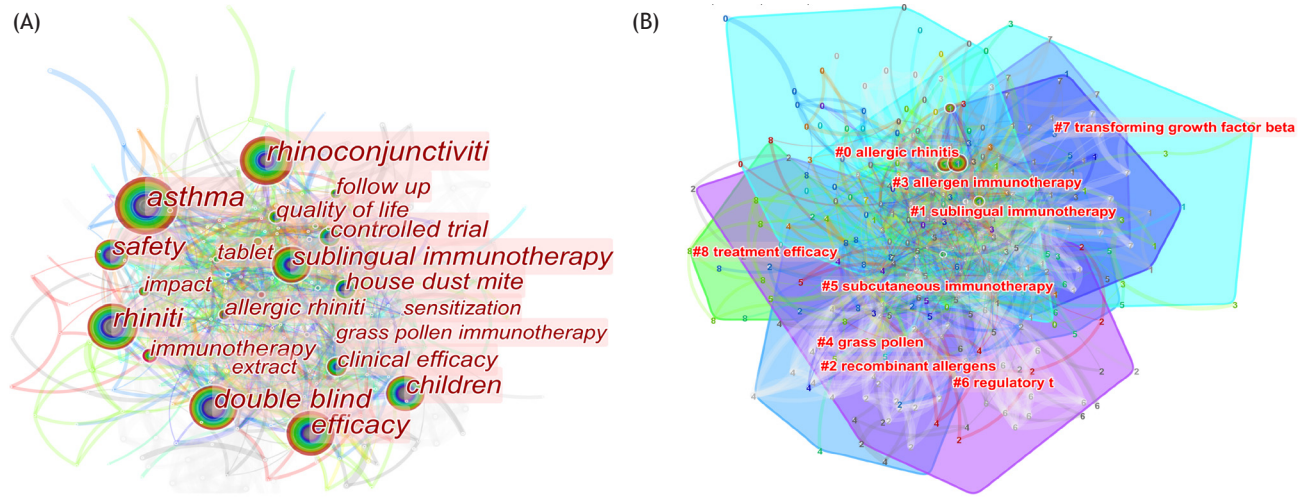


Figure 7 (A) Network map of the keywords involved in research on immunotherapy for ARC. (B) Map of the clusters of keywords involved in research on immunotherapy for ARC.

Table 6. Top 20 keywords in 2002–2021.

No.	Keyword	Counts	No.	Keyword	Counts
1	Rhinoconjunctiviti	346	11	Immunotherapy	115
2	Asthma	334	12	Clinical efficacy	111
3	Rhiniti	295	13	Quality of life	100
4	Double blind	290	14	Allergic rhiniti	97
5	Efficacy	290	15	Follow-up	95
6	Children	232	16	Impact	86
7	Sublingual immunotherapy	205	17	Tablet	74
8	Safety	202	18	Extract	65
9	House dust mite	146	19	Sensitization	64
10	Controlled trial	132	20	Grass pollen immunotherapy	61

doubted whether ILIT can already be introduced for clinical use. Currently, there are no officially approved commercial allergen extracts for intravenous administration. Meanwhile, epicutaneous immunotherapy is also a novel form of immunotherapy, but further research is required to determine its efficacy and safety.[23]

Immunoglobulin E (IgE), which acts as the central mediator in the pathogenesis of type I allergic reactions, plays an important role in the occurrence and development of AR and ARC. Twenty years ago, Kuehr et al. designed the first clinical trial to investigate the effects of anti-IgE with specific allergen immunotherapy.[24] Thereafter, several studies have shown that the anti-IgE monoclonal antibody omalizumab is effective for the treatment of allergic diseases, especially asthma.[25,26] A clinical trial conducted by Larenas-Linnemann et al. showed that omalizumab use with allergen immunotherapy alleviated clinical symptoms and reduced treatment time while having fewer adverse reactions.[27] It is thought that omalizumab binds to the CH3 domain of the Fc portion of IgE, preventing IgE from binding to the high-affinity IgE receptor FcεRI.[28]

Limitation

A few limitations of this visualization analysis must be considered. First, all publications were retrieved from the WOS Core Collection database, and articles in other databases were excluded. Our findings in this study may not be comprehensive because of the limited amount of literature. Second, the publications were limited to those in English, which can lead to bias. Third, the CiteSpace software cannot distinguish the first author from the corresponding author. However, we still believe that the results of this study can be used to determine hotspots and emerging trends in this field of study.

Conclusion

The number of publications related to immunotherapy for ARC is gradually increasing. Germany and the United States published the most studies on immunotherapy for ARC. Oliver Pfaar from Germany authored the most number of studies, and Bousquet J from France was the most cited author. Allergen immunotherapy includes classical SCIT and SLIT and the novel ILIT, with omalizumab emerging as a novel biological therapy. Currently, research regarding

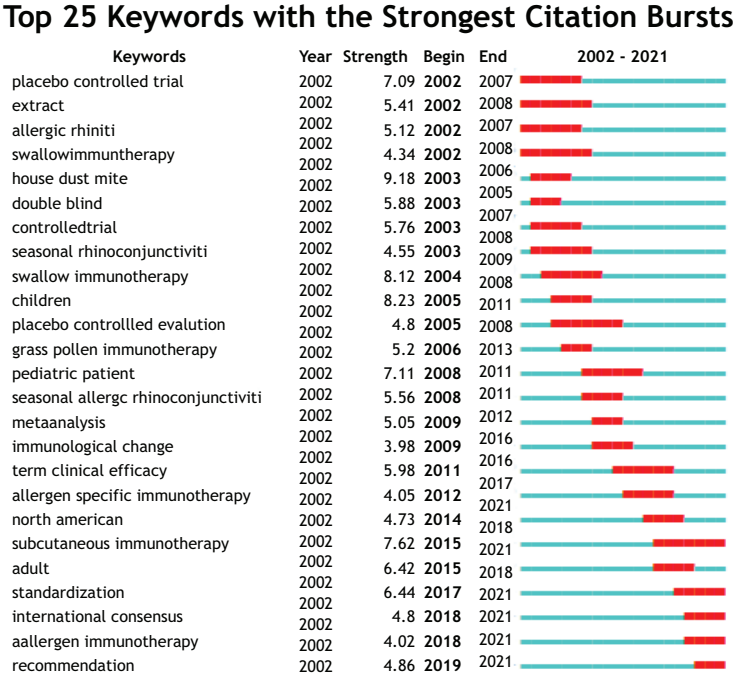


Figure 8 Keywords with the strongest citation bursts[a].
[a]The blue line represents the period from 2002 to 2021, and the periods of each burst keyword are plotted by the red line.

immunotherapy for ARC is now focusing on specific and targeted treatment. Additionally, the direction of future research on allergen immunotherapy includes new routes of drug delivery and combined application with biological agents. Meanwhile, improving the efficacy of allergen immunotherapy and reducing side effects need further exploration and research.

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