ORIGINAL RESEARCH

Emerging Trends and Focus in Human Skin Microbiome Over the Last Decade: A Bibliometric Analysis and Literature Review

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Background: Human skin microbiome is the first barrier against exogenous attack and is associated with various skin disease pathogenesis and progression. Advancements in high-throughput sequencing technologies have paved the way for a deeper understanding of this field. Based on the bibliometric analysis, this investigation aimed to identify the hotspots and future research trends associated with human skin microbiomes studied over the past decade.

Methods: The published research on skin microbiome from January 2013 to January 2023 was retrieved from the Web of Science Core Collection. Data cleaning processes to ensure robust data and the bibliometrix packages R, CiteSpace, VOSviewer, Origin, and Scimago Graphica for bibliometric and visual analyses were utilized.

Results: A total of 1629 published documents were analyzed. The overall publication trend steadily increased, with relatively fast growth in 2017 and 2020. The United States of America has the highest number of publications and citations and shows close collaborations with China and Germany. The University of California, San Diego, indicated a higher number of publications than other institutions and the fastest growth rate. The top three most publishing journals on this topic are Microorganisms, Frontiers in Microbiology, and Experimental dermatology. Gallo RL is the most influential author with the highest h- and g-index and most publications in skin microecology, followed by Grice EA and Kong HH. The top 10 most frequently used keywords in recent years included skin microbiome, microbiome, staphylococcus aureus, diversity, atopic dermatitis, skin, bacteria, infections, gut microbiota, and disease.

Conclusion: The skin microbiome is an area of research that requires continuous analysis, and even with much-achieved progress, future research will further be aided as technology develops.

Keywords: skin microbiome, bibliometric, trends, skin barrier, skin immune

Introduction

The skin is the largest heterogeneous organ in the human body, responsible for water homeostasis and surface thermoregulation. It also acts as the first host barrier against exogenous aggressions. Human microecosystem mainly includes oral, skin, urinary and gastrointestinal microecosystems, among which human skin microecosystem is the second largest microecosystem after intestinal microecosystem.[1,2] Many symbiotic microbes - including bacteria, fungi, viruses, and parasites – coexist with humans,[3] and most of them are beneficial and non-pathogenic, residing in a specific ecological site and working together to ensure skin balance.[4] There are tens of thousands of microorganisms inhabiting human skin, most of which are harmless or even beneficial to the human body. The complex ecosystem composed of these microorganisms in human skin is called skin microecology. The microbe's colonization is closely

linked with skin immunity and metabolism.[5] The colonized commensal bacteria stimulates the epidermis to produce antimicrobial peptides that are ineffective against themselves, thereby preventing the invasion by external pathogens.[6] The diversity and community structure of skin microecology is impacted by a variety of parameters, including the local skin anatomy and conditions (including pH, sweat secretion, and sebum content), as well as gender, social environment, clothing material, etc.[7–11]

The Human Microbiome Project, launched in 2007, has dramatically advanced the field of microbiology.[12] Humans are born with microbes, various delivery methods facilitate different colonization patterns on the skin.[13] The past decade has indicated the importance of skin microecology in the etiology, severity, treatment strategies, and skin disorders prognosis.[14,15] The association of skin microecology with skin disease initiation might be earlier than expected, with predictions since infancy.[16,17] Moreover, compared with previous traditional microbial detection protocols, high through-put technologies such as 16S rRNA and metagenomic sequencing have emerged.[18] However, microbiome research on gastrointestinal dominates more and skin microecology has not yet received sufficient attention. With the heated debate about the gut-skin axis and the resistance studies arising from topical antibiotics, it is essential to further elucidate the correlation of microorganisms with skin.

The bibliometric analysis targets academic publications and provides a comprehensive review of a specific topic by analyzing published documents for their country, institution, journal, author, keywords, and references during a particular period.[19,20] By analyzing the citation relationship and publication trend of the literature related to skin microecology, bibliometrics can reveal the research trends and hotspots in academic circles. This is very helpful for researchers to choose research direction, discover new research areas and understand the development of academia. These aspects assess multiple dimensions, including frequency, co-occurrence, burst words, and co-citation analysis, to provide quantitative data to quickly understand the relevant topic. The human skin microbiome has not yet been the subject of any bibliometric analysis. Therefore, this study aims to illustrate the skin microbiome research hotspots in the past decade and visualize the overall landscape based on bibliometric analysis and data-cleaning methods.

Materials and Methods
Data Collection
We obtained the data for the bibliometric analysis from the Web of Science Core Collection database (WoSCC, Clarivate Analytics), a widely recognized and used literature search database.[21,22] To avoid bias caused by daily database updates, all WoSCC screenings were carried out on February 01, 2023, for the period starting from 2013-01-01 to 2023-01-31. The search strategy included the mandatory word "skin" to avoid the impact of gastrointestinal flora. The search strategy was TS = (("skin microbiome") or ("skin microbiota") or ("skin microflora") or ("skin flora") or ("skin microbiology") or ("skin microecology") or ("skin microorganism") or ("skin micro-ecosystem") and ("human")). Subsequently, we utilized the page filtering feature of WoSCC and selected "articles" and "reviews" as the document types. The language of the publications was "English". Finally, a total of 1949 documents were preprocessed and exported as Excel files for manual exclusion (Figure 1).

Data Pre-Processing
This study utilized data-cleaning techniques such as missing value supplementation, duplicate literature analysis, and merging synonyms. First, manual data cleaning was performed by Microsoft Excel software. Based on titles and abstracts, 320 papers on non-relevant topics were excluded. Because of the remarkable uniqueness of human skin microecology,[23] all animal categories (including amphibians, marine mammal, horse, bat, canine, feline, insect, etc.) except for experimental mice and rats were excluded (n=304). Non-animal categories (n=16) included living environment, building, and plant categories. We retained 2 articles from 2012, despite them not strictly fitting the criteria, to avoid introducing human bias. Finally, 1629 articles were selected. A plain-text file was exported with all the full records and cited references in WoSCC for further analysis. A test using R revealed 26 missing publication year values, which were added manually. Cite Space software was used to check duplicates (n= 0). The keywords merging was carried out by thesaurus_terms.txt file (VOSviewer software) and citespace.alias file (CiteSpace software). Data collection and preprocessing were done by 2 researchers independently. In case
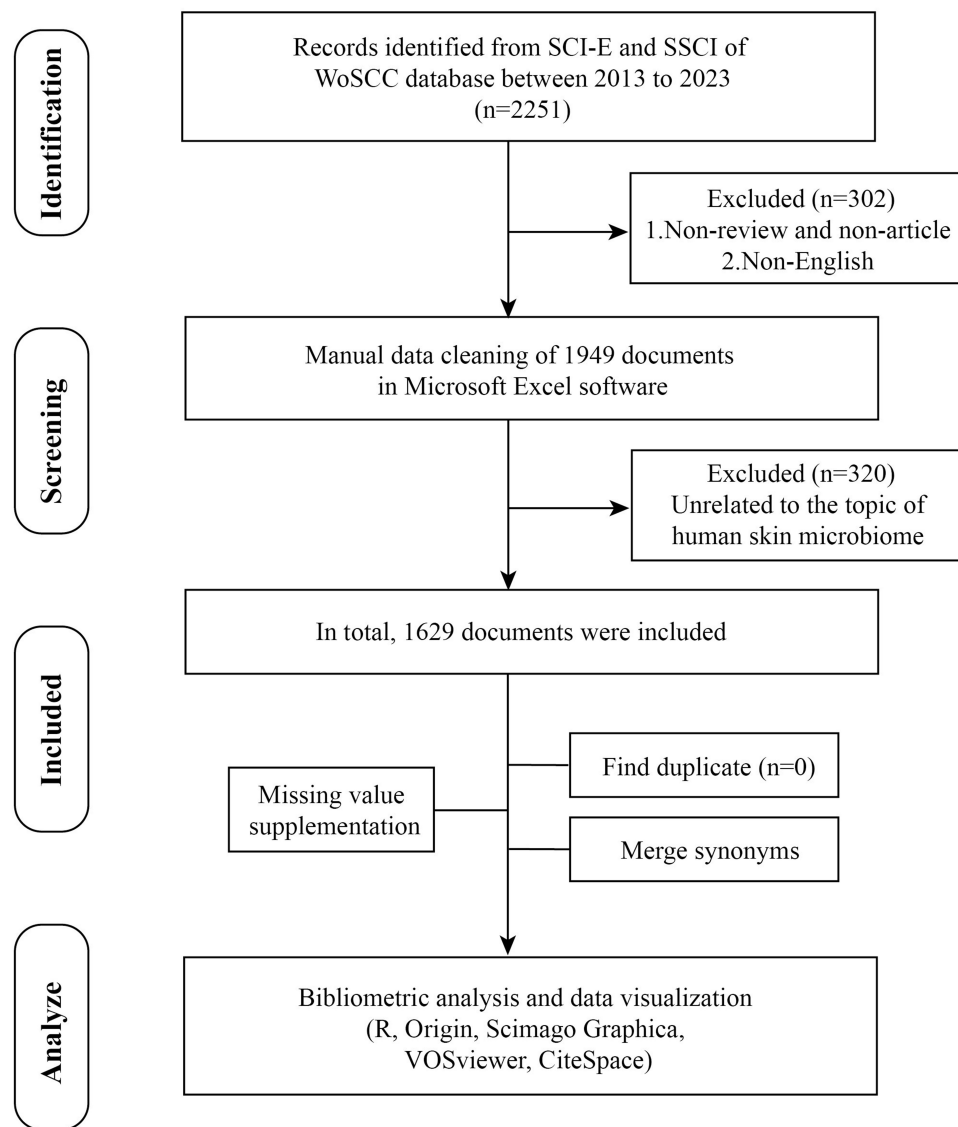
Figure 1 Flowchart for literature filtration and data analysis.

of disagreement on the nesting of the documents, the decision was made by the 3rd researcher. The journal information was acquired from the 2022 Journal Citation Report (Clarivate Analytics, Philadelphia, PA, United States).

Data Analyses

The bibliophile website[24] in the bibliometric R-package was used for frequency statistics and plotting. The relevant information was summarized in a table using Microsoft Excel (version 16.58). For bibliometric and visual analyses following software were used: CiteSpace (version 6.1.R6, Chaomei Chen,[25,26]), VOSviewer (version 1.6.19, van Eck and Waltman, 2010,[27,28]), Origin (version 2022) and SCImago Graphica (version 1.0.26, Yusef Hassan-Montero, V. Guerrero-Bote, and Félix De-Moya-Anegón,[29,30]).

Results

General Trend of Production and Citation

Altogether, 8458 authors published 1629 studies from 578 sources during 2013–2023, comprising 55,327 references through the main information panel in R analysis. 1207 articles and 422 reviews were found. Regarding authors and

collaborations, there were 41 single-authored documents and 6.69 co-authors per other documents. International co-authorships were 28.18%, indicating very close international cooperation.

Supplementary Table 1 and Figure 2 show the annual scientific publication and citations trend. Since 2013, substantial growth has been observed twice in total in 2017 and 2020. After each rapid growth, steady growth was observed for two to three years. The average number of articles in the last 3 years was 267, while that in January 2023 was 16, indicating the gradual increase of attention to skin microecology as a research topic. Notably, despite a slight decrease in the number of publications in 2018, average citations/year peaked. However, a downward trend started afterward, suggesting that more attention is required on publication quality.

Analysis of Countries/Regions, Institutions, and Their Cooperation

To determine which countries/regions and institutions have made significant contributions to skin microecology research in the last decade, the frequency and network co-occurrence analyses were conducted (Figure 3).

Figure 3A shows the top 10 highest publishing countries. The United States of America (USA) has ranked 1st with 1798 studies. China ranked 2nd, but only at 31.03% of the USA's. Germany and France participated in relatively high numbers of studies until 2020, but China overtook them. The total number of published articles by the top 10 countries is plotted using SCImago software (Figure 3C). Since Denmark and Spain have the same number of articles (n=137), both have been listed. It is seemed that 60% of the top 10 countries are concentrated in Europe. The USA also ranked 1st in terms of total citations (>1000), with 6.32 times more citations than Germany and France (2595), China (1554), and Denmark (1258) (Supplementary Table 2). According to the visual analysis of network co-occurrence (Figure 3D and E), the USA cooperated closely with China and Germany. Each circle = country/region, circle color = clustering result, and link thickness = degree of cooperation.
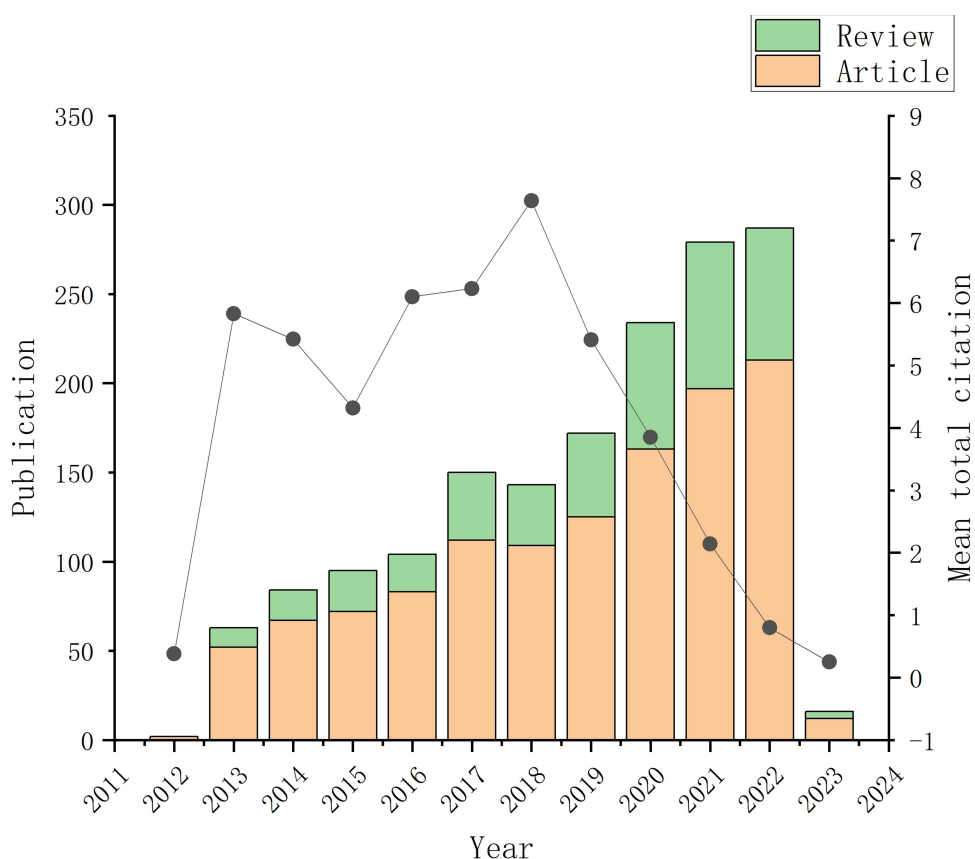

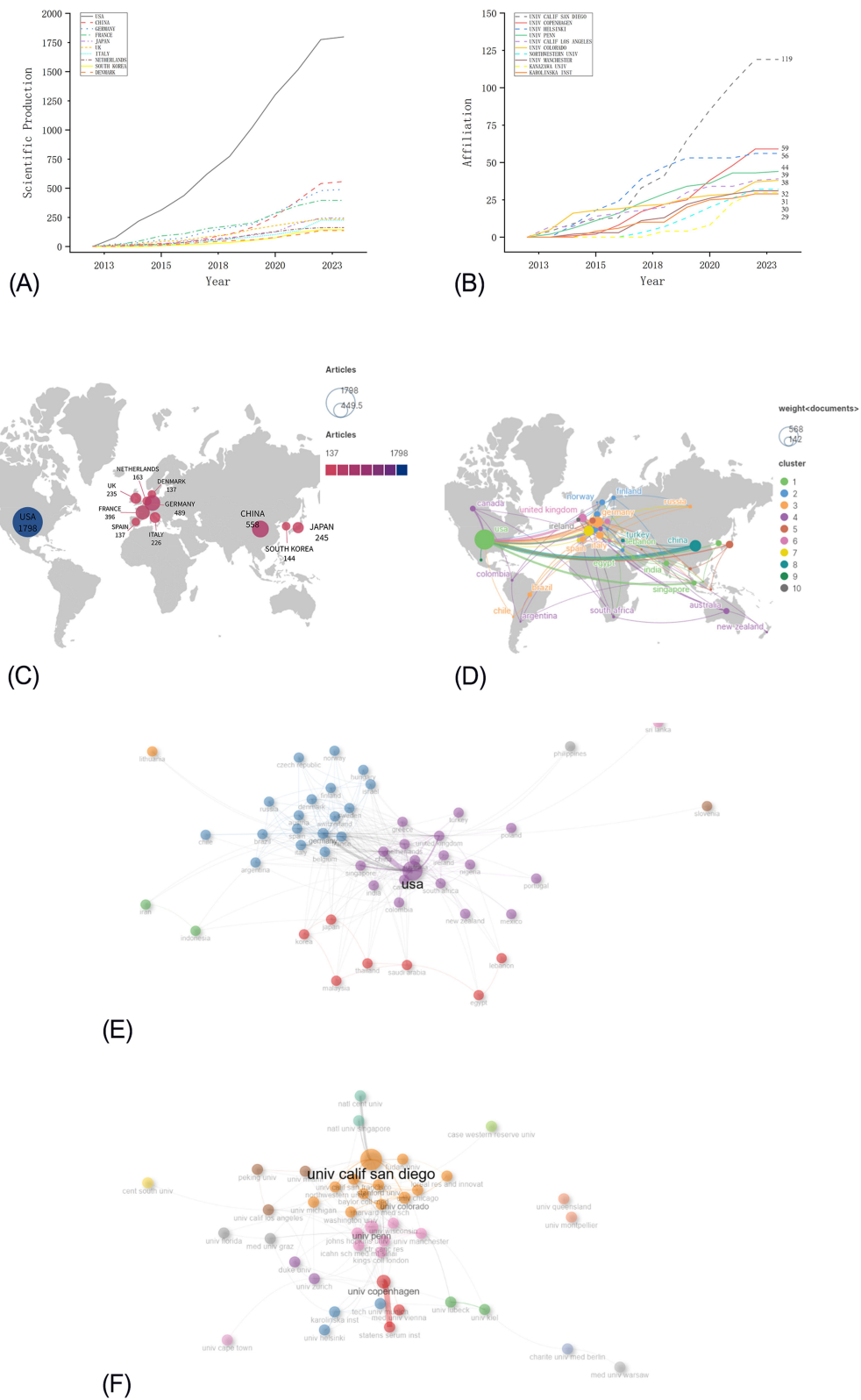**Figure 2** The trends of annual scientific production and citation.

Figure 3 The analysis of countries/regions, institutions, and their cooperation. (**A**) The top 10 highest publishing countries. (**B**) Annual publication trends of the top 10 organizations. (**C**) The total number of published articles by the top 10 countries is plotted using SCImago software. (**D** and **E**) Visual analysis of network co-occurrence of research cooperation in different countries. (**F**) Analysis of the cooperative relationship between institutions.

Figure 3B depicts the annual publication trends of the top 10 institutions. Half of the top 10 institutions were from the USA, with the University of California, San Diego (UCSD) having the highest publication number and the fastest growth rate. The University of Copenhagen from Denmark ranked 2nd with a publishing rate of 10 or more per year since 2019. The University of Helsinki, a leading Nordic institution, ranked 3rd. Regarding inter-institutional collaboration, three large groups (UCSD, the University of Copenhagen, and the University of Pennsylvania) and other smaller groups were observed (Figure 3F).

Analysis of Journals

The core and co-cited journals were analyzed. Bradford's law states that 21 journals are core (Figure 4A, Table 1). The top five core journals in terms of publications include Microorganisms (52), Frontiers in Microbiology (47), Experimental Dermatology (46), Scientific Reports (44), and PLOS ONE (40).

The journal impact evaluation was based on the h-index, g-index, impact factor (IF), and journal citation reports (JCR). H-index, introduced by Jorge Hirsch in 2005, refers to a journal/author with h articles cited at least h times.[31] G-index, proposed by Leo Egghe in 2006, refers to a journal/author with g articles and at least g citations on average.[32] As a derivative index of the H-index, it helps to identify single highly cited journals/authors. Although the Journal of Investigative Dermatology ranked 6th in the number of articles issued, it had the highest h-index (20) and was the highest locally cited journal (3986). British Journal of Dermatology and Frontiers in Microbiology showed the same h-index of 18; the latter had the highest total citation and g-index, suggesting that it has more highly cited articles. The top 10 core journal publication volumes (annual and cumulative) were also evaluated. According to Figure 4B and C, Microorganisms published 25 relevant papers in 2021, making it not only the highest-publishing journal in the calendar year but also the most-published journal in that year. However, its number of citations (642) and h-index (13) were not similar. Most journals are on a steady upward trend, with the number of articles published increasing in the last 3 years.

Supplementary Table 3 shows that all the top 10 locally cited journals have >1000 citations. Furthermore, a co-citation analysis was also carried out of 147 locally cited sources and >100 citations (Figure 4D and E), where nodes = a total number of citations, color = clustering result, and the line between two items = co-citation relevance. The intensity and thickness of the line increase as the number of co-citations increases. It can be divided into 4 clusters: (a) Dermatology field: Journal of Investigative Dermatology, Journal of Allergy and Clinical Immunology, British Journal of Dermatology, etc.; (b) Molecular biology field: Nature, PLOS One, Genome Research, etc.; (c) Microbiology field: Journal of Clinical Microbiology, Journal of Bacteriology, Infection, and Immunity, etc.; (d) Immunology field: Immunity, Journal of Immunology, Nature Reviews Immunology, etc.
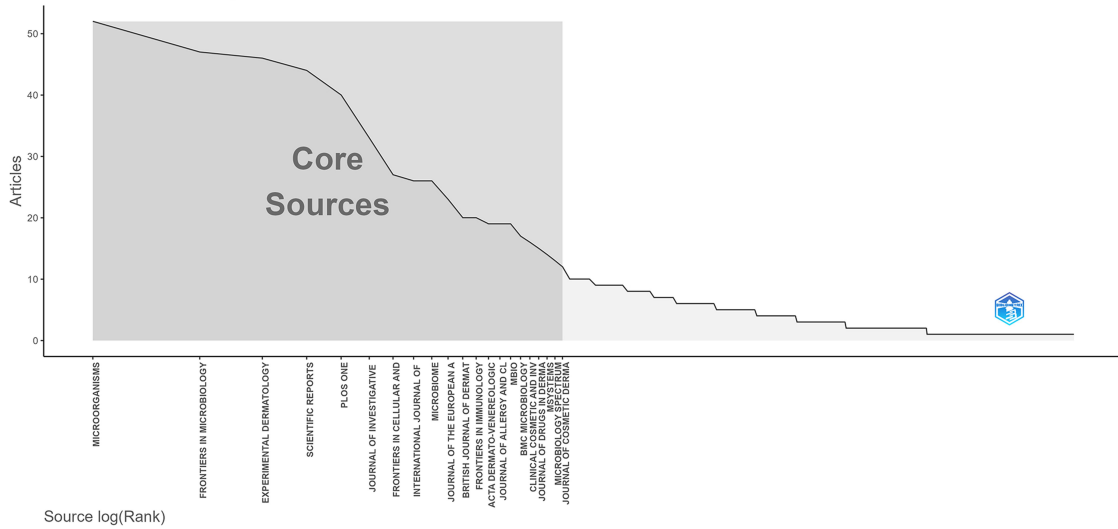
Analysis of Core Author Distribution and Co-Authorship Networks

The core authors and related research in skin microecology were analyzed and clarified. Supplementary Table 4 enlists the top 10 writers' publications, citations, and influence. Gallo RL is the most well-known author, publishes studies annually, and has the most publications among the 8458 writers with the highest h- and g-index. (Figure 5A). Grice EA (20) was the 2nd most published author, comparable to Gallo RL in impact, despite having no relevant publications in 2022. Kong HH (19) ranked 3rd and started publishing in 2014. Although Segre JA is 4th in terms of the number of publications and did not produce in 2015, he had the most local citations (n=1210), with Gallo RL (n=916) in 2nd and Kong HH (n=831) in 3rd position. Supplementary Table 5 shows the top 10 authors' articles with total citations >300. Co-occurrence analysis revealed a close relationship between Kong HH and Segre JA, forming a core group of authors (Figure 5B). This group of authors has collaborative ties with Gallo RL, Grice EA, and Knight R, respectively. Gallo RL and Knight R belong to UCSD and contribute to most of the paper output (Figure 5C). Most authors are from the USA, contributing greatly to their publication volume.
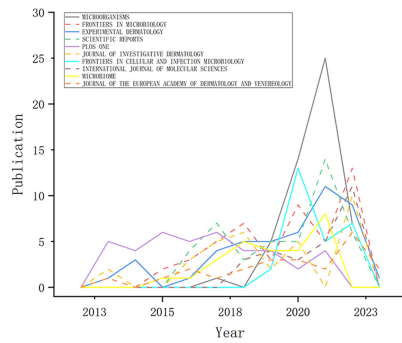
Analysis of Keywords

To understand the hot spots of research and future directions in the last decade, keywords distribution, clustering, burst words, and timeline graph analysis was conducted. According to the statistics, the top 10 highly frequent keywords were
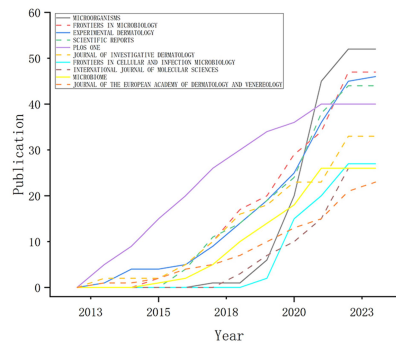
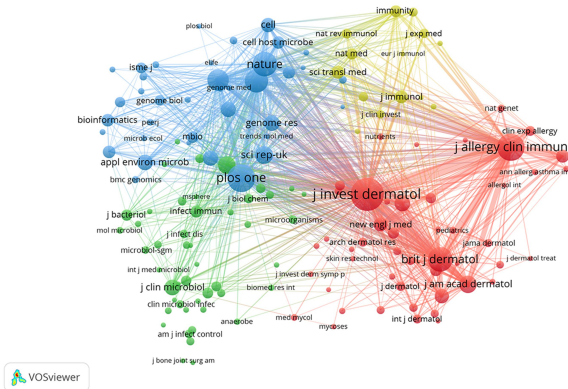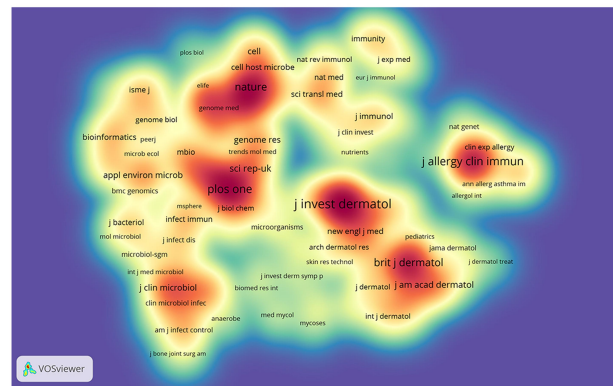**Figure 4** The analysis of journals. (**A**) The 21 core journals and influence. (**B** and **C**) Evaluation of the publication volume (annual and cumulative) of the top 10 core journals. (**D** and **E**) Co-citation analysis was carried out of 147 locally cited sources and >100 citations.

Table 1 The 21 Core Journals and Influence

Rank	Journal	Article Count	Total Citations	H-Index	G-Index	Journal Citation Reports (2021)	Impact Factor (2021)
1	Microorganisms	52	642	13	23	Q2	4.926
2	Frontiers In Microbiology	47	1386	18	37	Q1	6.064
3	Experimental Dermatology	46	754	17	26	Q1	4.511
4	Scientific Reports	44	967	17	30	Q2	4.996
5	PloS One	40	1117	16	33	Q2	3.752
6	Journal Of Investigative Dermatology	33	1346	20	33	Q1	7.590
7	Frontiers In Cellular And Infection Microbiology	27	421	11	20	Q1	6.073
8	International Journal Of Molecular Sciences	26	774	9	26	Q1	6.208
9	Microbiome	26	910	17	26	Q1	16.837
10	Journal Of The European Academy Of Dermatology And Venereology	23	757	11	23	Q1	9.228
11	British Journal Of Dermatology	20	1001	18	20	Q1	11.113
12	Frontiers In Immunology	20	332	9	18	Q1	8.786
13	Acta Dermato-Venereologica	19	329	9	18	Q2	3.875
14	Journal Of Allergy And Clinical Immunology	19	1246	14	19	Q1	11.022
15	mBio	19	862	11	19	Q1	7.786
16	BMC Microbiology	17	218	7	14	Q2	4.465
17	Clinical Cosmetic And Investigational Dermatology	16	156	5	12	Q3	2.765
18	Journal Of Drugs In Dermatology	15	265	7	15	Q4	1.608
19	mSystems	14	420	9	14	Q1	7.324
20	Microbiology Spectrum	13	9	2	2	Q1	9.043
21	Journal Of Cosmetic Dermatology	12	38	5	6	Q3	2.189

skin microbiome, microbiome, staphylococcus aureus, diversity, atopic dermatitis, skin, bacteria, infections, gut microbiota, and disease. The cluster analysis (Figure 6A, Supplementary Table 6) of 100 high-frequency keywords (frequency > 20) indicated that currently, the research focuses on the following five areas: (a) epidemiology and preventive medicine; (b) epidermal barrier and microecology; (c) detection techniques for dermatological diseases and skin flora; (d) acne pathogenesis; (e) allergic diseases and probiotic treatment options. The last two have remained popular in recent years (Figure 6B and C).

Furthermore, the burst words were also assessed (Figure 6D), and the green and red lines indicate the time range and the period of pulse duration, respectively. In 2013, the understanding of skin microecology was mostly focused on identifying and recognizing flora, but by 2014 it was extended to molecular immune mechanisms. 2014 was also the year when sequencing technology 16S rRNA came into the limelight. Figure 6E is a timeline of keywords obtained by
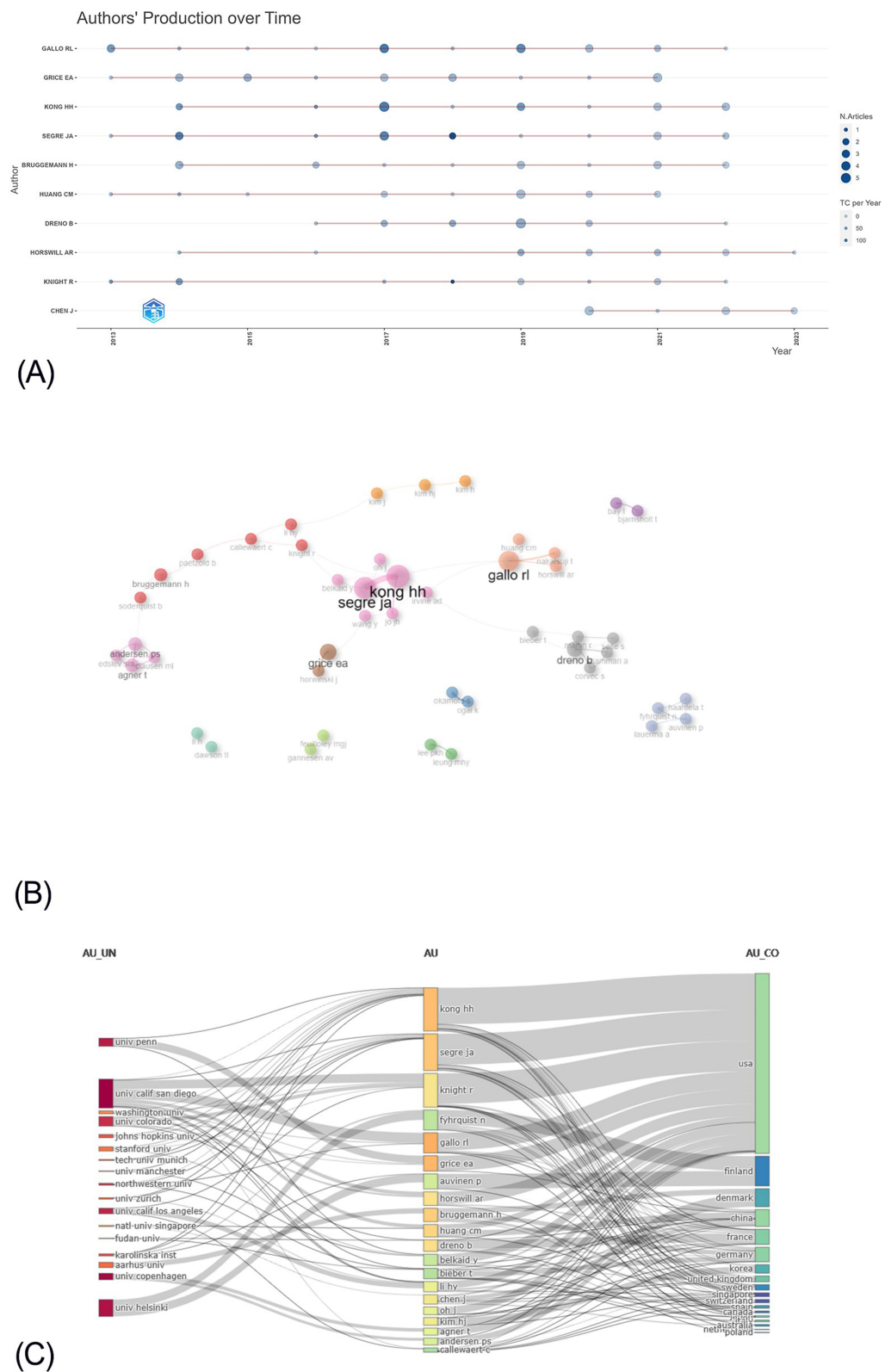
(A)

(B)

(C)

Figure 5 The analysis of core author distribution and co-authorship networks. (**A**) Analysis of core author works over time. (**B**) Co-occurrence analysis of the relationship between the core authors. (**C**) Analysis of the nationality and affiliation of core authors.

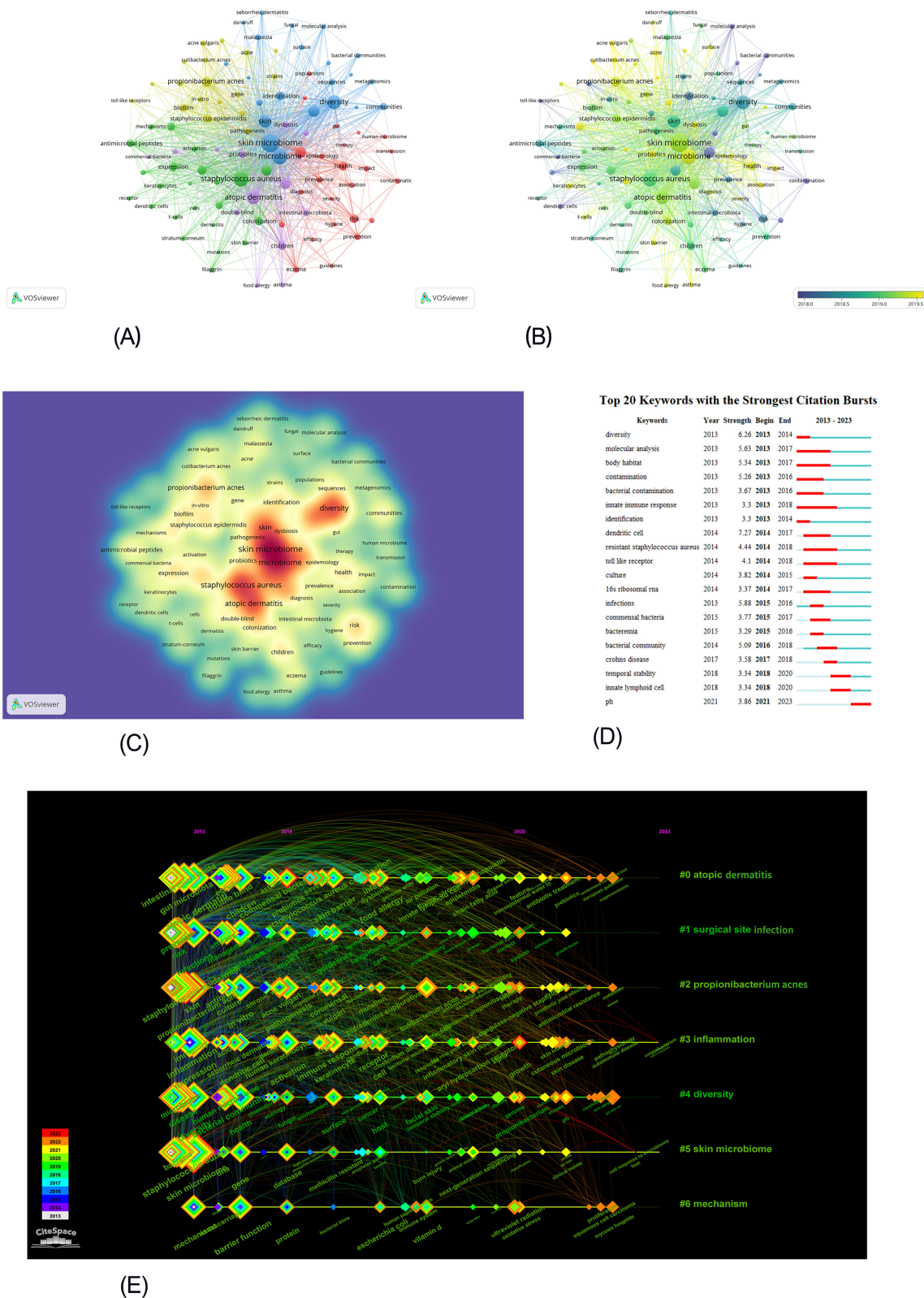(A)

(B)

(C)

(D)

(E)

Figure 6 The analysis of keywords. (**A**) Cluster analysis of 100 high-frequency keywords (frequency>20). (**B** and **C**) Analysis of the popularity of 100 high-frequency keywords (frequency>20) between 2018 and 2019. (**D**) Top 20 keywords with the strongest citation bursts. (**E**) Research hotspots on future skin microecology obtained from Citespace software.

Table 2 Top10 Global Cited Documents

Rank	Title	First Author	Year	Journal	Total Citations	TC per Year
I	Current understanding of the human microbiome[33]	GILBERT JA	2018	NAT MED	871	145.17
2	The human skin microbiome[34]	BYRD AL	2018	NAT REV MICROBIOL	823	137.17
3	Cohabiting family members share microbiota with one another and with their dogs[10]	SONG SJ	2013	ELIFE	617	56.09
4	Biogeography and individuality shape function in the human skin metagenome[35]	OH J	2014	NATURE	580	58
5	Longitudinal analysis of microbial interaction between humans and the indoor environment[11]	LAX S	2014	SCIENCE	541	54.1
6	Antimicrobials from human skin commensal bacteria protect against *Staphylococcus aureus* and are deficient in atopic dermatitis[36]	NAKATSUJI T	2017	SCI TRANSL MED	517	73.86
7	Psoriasis Pathogenesis and Treatment[37]	RENDON A	2019	INT J MOL SCI	507	101.4
8	Atopic dermatitis[38]	WEIDINGER S	2018	NAT REV DIS PRIMERS	491	81.83
9	Temporal Stability of the Human Skin Microbiome[39]	OH J	2016	CELL	468	58.5
10	Geography, Ethnicity or Subsistence-Specific Variations in Human Microbiome Composition and Diversity[40]	GUPTA VK	2017	FRONT MICROBIOL	438	62.57

Citespace software, suggesting future research hotspots in skin microecology, including ultraviolet, oxidative stress, ph, skin aging, ceramide, skin cancer, gut-skin axis, prebiotics therapy, etc.

Analysis of Documents and References

To identify the most influential articles in skin microecology research, the included literature and references were assessed. Table 2 enlists the top 10 globally cited documents, which are the highly cited documents in WoSS. Of these, Gilbert JA's review "Current understanding of the human microbiome", published in Nature Medicine 2018, ranked 1st. The article describes the factors influencing the human microbiome, the dynamic balance of human microbes, and present and future directions of mechanistic research in detail.[33] The 2nd was Byrd AL's review of "The human skin microbiome", also published in the same year in Nature Reviews Microbiology, and analyzed the skin microbiome in health and disease conditions.[34] This is also the first locally cited document (Supplementary Table 7) and the most highly cited document included in this dataset. Byrd AL and Chen YE's review "Skin microbiota-host interactions", published in Nature in 2018, is likely to receive more citations in the future, according to the burst citation analysis (Figure 7B). The Historiography helped us understand the literature with high importance in the dataset (Figure 7A, Supplementary Table 8). Figures 7C and D depict the co-citation analysis of the references, indicating that Grice EA's experimental article "Topographical and temporal diversity of the human skin microbiome", published in Science in 2009, was also in the core position. Table 3 shows the top 10 locally cited references.

Discussion

The skin and the intestines are the sites with the most abundant microbes, but the former has received less published research than the latter.[46] Skin microbes have a different composition than the intestines, comprising predominantly aerobic or partly anaerobic bacteria, whereas the intestines are mostly anaerobic.[35,47] And the distribution of skin
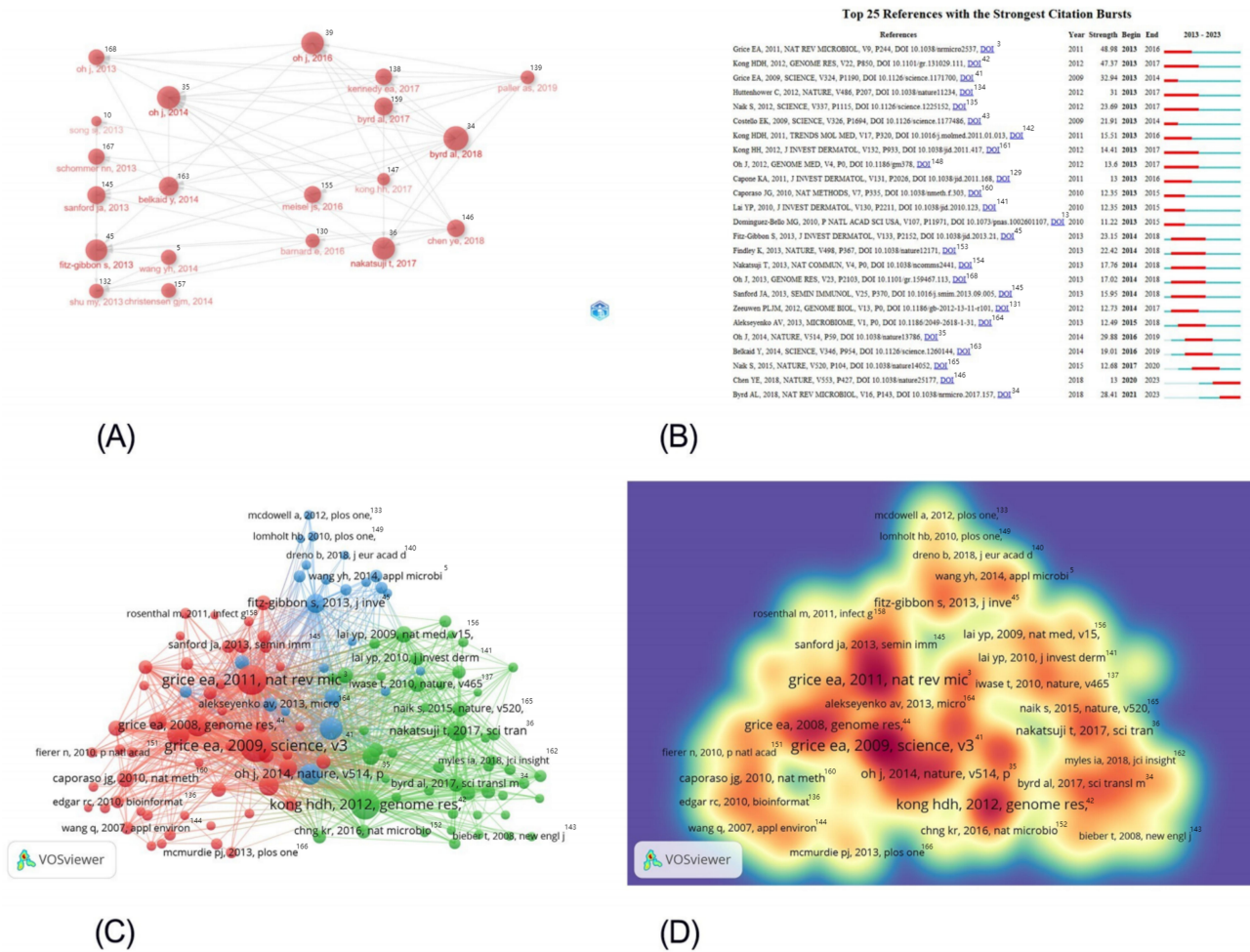
Figure 7 The analysis of documents and references. (**A**) The historiography shows the literature with high importance in the dataset. (**B**) Top 25 references with the strongest citation bursts. (**C** and **D**) depict the co-citation analysis of the references.

microbiota can vary across sites.[41] Staphylococci species are frequently predominant at sebum-secreting and moist sites, where sweat is secreted commonly. Propionibacteria species predominate sebaceous sites, Corynebacteria species predominate moist sites, and β-Proteobacteria and Flavobacteriales predominate dry sites. Among them, the most studied were Staphylococci species, especially the highly pathogenic *Staphylococcus aureus* (*S. aureus*) (Figure 6C). Unlike *Staphylococcus epidermidis*, which seldom causes pathogenesis, *S. aureus* is the major pathogen of skin infections.[48] It can specifically release inflammatory mediators (IL-1α, IL-24β) from keratinocytes to produce skin inflammation.[6] Notably, *S. aureus* is also genetically variable and strengthens itself by genome alteration to expand territory, virulence, and immune evasion.[49,50] Furthermore, it is known to promote wound healing and hair follicle regeneration. It enhances keratinocyte hypoxia, stimulates cellular glutamine metabolism, and exerts beneficial effects through the IL-1β-MyD88 signaling pathway.[51,52] Compared with an 11% incidence in healthy skin, *S. aureus* has a relative abundance of ≥30% in infection-free surgical wounds. Some studies have proposed that the mechanism behind lower *S. aureus* infection may be related to the enrichment of Corynebacterium,[53] implying that the skin microorganisms interactions could have a benign effect on the hosts, like how yin and yang are balanced in traditional Chinese medicine.

The skin barrier is currently a hot research topic for clinicians.[54,55] The skin microorganisms are in a harmonious interaction with the body epidermis on which they depend. At one end, the epidermal barrier integrity determines the diversity and composition of microorganisms,[56] and at the other end, the microorganisms influence the stability of the epidermal barrier. Commensal microbes can rebuild the epidermal barrier by turning on the aryl hydrocarbon receptor and restoring anti-infection function.[57,58] *Staphylococcus epidermidis* helps preserve skin barrier integrity by secreting

Table 3 Top 10 Locally Cited References

Rank	Title	First Author	Year	Journal	Citations
1	Topographical and temporal diversity of the human skin microbiome[41]	GRICE EA	2009	SCIENCE	476
2	The skin microbiome[3]	GRICE EA	2011	NAT REV MICROBIOL	429
3	Temporal shifts in the skin microbiome associated with disease flares and treatment in children with atopic dermatitis[42]	KONG HDH	2012	GENOME RES	389
4	The human skin microbiome[34]	BYRD AL	2018	NAT REV MICROBIOL	248
5	Bacterial community variation in human body habitats across space and time[43]	COSTELLO EK	2009	SCIENCE	232
6	A diversity profile of the human skin microbiota[44]	GRICE EA	2008	GENOME RES	232
7	Biogeography and individuality shape function in the human skin metagenome[35]	OH J	2014	NATURE	209
8	Temporal Stability of the Human Skin Microbiome[39]	OH J	2016	CELL	196
9	Antimicrobials from human skin commensal bacteria protect against *Staphylococcus aureus* and are deficient in atopic dermatitis[36]	NAKATSUJI T	2017	SCI TRANSL MED	195
10	*Propionibacterium acnes* strain populations in the human skin microbiome associated with acne[45]	FITZ-GIBBON S	2013	J INVEST DERMATOL	178

sphingomyelinase, which can produce ceramides that retain water and fight aging.[59] In addition to the most superficial microbial barrier, skin barriers are functionally classified as chemical, physical, immune, and neuronal barriers.[60,61] They exhibit growing networks from the outside to the inside, while neither is entirely independent. Among them, the chemical barrier is the acidic shield composed of lipid membranes (ceramides, cholesterol, and free fatty acids), sweat, and natural-moisturizing factors (amino acids, lactates, urea, and electrolytes, etc.) on the surface of the stratum corneum.[61,62] The ph is the main determinant of the chemical barrier, which increases upon physical barrier disruption and has been the focus of multiple studies since 2021 (Figure 6D). Normal human stratum corneum has a ph range of 4.1 to 5.8.[63] Elevated ph can damage the chemical barrier, reducing the skin's antimicrobial capacity and thereby increasing the skin's risk of infection. Since commensal microbes cannot tolerate a non-acidic environment, their ability to adhere to the skin surface deteriorates.[64–66] This microecological imbalance due to ph alterations can occur because of daily skin cleansing routine.[67] Therefore, a sound understanding of the connection between the skin barrier and microbes can be the foundation for healthy skin hygiene.

Streilein was the first to propose the idea of skin-associated lymphoid tissues in 1983, whereas the concept of the "skin immune system" was introduced by Bos and Kapsenberg in 1986.[68,69] In general, the main cell populations that exert cutaneous immunity include the keratinocytes, epidermal Langerhans cells, dendritic cells, mast cells, and T cell subsets (mainly T regulatory and T resident memory cells) in the dermis.[70,71] Currently, the most studied cells are keratinocytes, associated with innate immunity. It's core immunological role is to produce constitutive epidermal antimicrobial proteins (AMPs) and various hornerin polypeptides-derived cationic intrinsically disordered antimicrobial peptides (CIDAMPs) against invading infections.[72] The first AMP to be discovered was lysozyme.[73] However, defensins are the most researched AMPs and can be classified into human α- and β-defensins.[74–76] Together with cathelicidins, dermcidin, and psoriasis, these molecules have strong anti-inflammatory and antibacterial properties.[77] Furthermore, recent studies have shown that a deficiency of IL-17 receptors in keratinocytes of mice is closely associated with *S. aureus* skin infection and acts as an activator of T cell proliferation.[78] T cells are not only involved in skin immunity but also modulate skin homeostasis and promote wound healing, all of which have attracted the attention of researchers.

It has been shown that there are 2.0×10^{10} T cells in healthy skin, nearly twice the total circulating T cells.[79] Among them, the most discussed are the resident memory T cells (TRMs), which are important for skin immune responses and surveillance.[80–82] Skin infections can encourage CD8 TRMs to produce immunological effectors, enabling long-lasting effects.[83] Whereas CD4 TRMs release IL-17A, IL-22, IFN-γ, and TNF-α to kill *S. aureus*, thereby regulating skin microbes.[84]

Research on skin flora and dermatology is now focused on inflammatory, allergic, and immune skin diseases, and skin cancers are an emerging trend. Acne vulgaris is a widely studied inflammatory skin disease that often occurs in high sebum secretion sites such as the face, scalp, chest, and back.[85,86] *Cutibacterium acnes* or *Propionibacterium acnes* are essentially linked with pathogenic mechanisms of the disease and are the theoretical cornerstone of the current application of antibiotic therapy.[45,87,88] Moreover, *Cutibacterium acnes* interact with *Staphylococcus epidermidis*, and their dysregulation can release inflammatory cytokines.[89] The next most studied skin diseases are atopic dermatitis (AD) and psoriasis.[90] AD is characterized by polymorphic lesions with persistent and intense itching.[38,91,92] Increased *S. aureus* colonization reduces the diversity of skin bacteria at AD-prone sites, which is strongly associated with the onset and severity of AD.[36,42,93] Skin microecology is also involved in the pathogenesis and progression of psoriasis.[14,37,94] Skin microecology had similar differences in healthy or in patients without lesions, as well as between patients' lesion sites and contralateral non-lesion sites.[15] Based on the pro-inflammatory and immune effects of skin microbial dysbiosis, the link between skin cancers and skin microecology has become a topic of interest.[95] Malignant melanoma progression has been correlated with alterations in skin microecology.[96] *S. aureus* has also been correlated with the progression of cutaneous squamous cell carcinoma[97] and T-cell lymphoma.[98] We may aspire for more research in this field, and these findings will also bring hope for cancer immunotherapy sensitization.

Although the study of gastrointestinal flora was excluded, a high frequency of the keyword "gut" was still observed (Figure 6A). Due to the interaction between the skin and the gut, the gut-skin axis notion has steadily evolved.[99,100] For instance, the pathophysiology of acne vulgaris may be influenced by disturbances in the gut microbial metabolism.[101] Individuals with inflammatory bowel disease can also experience dysbiosis of the skin flora and may even indicate post-skin treatment adverse events.[102] This highlights the treatment option of probiotics, prebiotics, and postbiotics, available as supplemental therapies in addition to the commonly used antimicrobial agents. As defined by the International Scientific Association for Probiotics and Prebiotics (ISAPP), probiotics are "live microorganisms which, when administered in adequate amounts, confer a health benefit on the host".[103] At the same time, prebiotics is "a substrate that is selectively utilized by host microorganisms conferring a health benefit".[104] Since these have been around for decades, much research is present. Until 2019, postbiotics were also called "preparation of inanimate microorganisms and, or their components that confer a health benefit on the host".[105] The synergistic probiotics and prebiotics, or synbiotics, were first introduced by Gibson and Roberfroid in 1995.[106] Non-medical topical application of prebiotics-comprising cosmetic serum improves the skin's ability to retain water in women.[107] A moisturizer containing prebiotics and postbiotics has been found to reduce facial wrinkles in women.[108] Oral administration of probiotic and prebiotic fermented milk improved the hydration of healthy women's skin and ensured skin barrier function.[109] Research reveals that clinical oral spore-based probiotic ingestion reduces sebum secretion and acne lesions in acne patients.[110] Topical postbiotic application promoted wound healing in diabetic mice by releasing growth factors, chemokines, and cytokines.[111] Prebiotic or symbiotic baths can alleviate AD severity and ameliorate the symptoms of itching and dryness.[112] Probiotics and prebiotics can also counteract ultraviolet radiation-induced photoaging, immunosuppression, and inflammatory responses.[113] Therefore, using microbiome-associated microorganisms to address skin diseases is a promising strategy.

There are several microbiome studies based on bibliometric analysis. Most publications are focused on gut microbes and their associated diseases, including pain,[114] metabolic-associated fatty liver disease,[115] Alzheimer's disease,[116] and rheumatic diseases.[117] Some studies explored the mechanisms, including microbiome–gut–brain axis, dementia,[118] and miRNA-microbiome interaction.[119] Xingzhu Yuan et al[46] separately focused on the human gastrointestinal microbiome and showed the highlights and recent trends of previous studies in this field. In contrast, the bibliometric articles on skin microbiomes are scant. Only 1 bibliometric study on allergic disease and microbes containing AD was identified, but it did not distinguish between the skin microbiome and gut flora.[120] Another article discussing symbiotic microorganisms

and AD lacked a clear distinction between them.[121] Therefore, this study was designed to differentiate skin and gut microorganisms, making it the first bibliometric study on the skin microbiome.

Through a comprehensive literature review, it was proposed that future skin microecology research will have the following 3 directions: (1) antibiotic resistance and skin microbiome: antimicrobial resistance is a serious global health problem.[122] Scholars have launched an integrated Human Skin Microbial Gene Catalog to describe skin resistome to discover antibiotic resistance genes and human skin flora distribution.[123] This is crucial for the next step in complex skin microecology research. (2) Anti-aging and skin microbiome: human aging is inevitable and associated with gut microbiota dysregulation.[124] With deepening aesthetic concepts and accelerating population aging, skin anti-aging is a key task for dermatologists and aestheticians.[125] *Streptococcus* species have already been found to exert anti-aging effects by secreting spermidine.[126] (3) Artificial intelligence and skin microbiome: the development of skin microecology is accompanied by new technologies. Next-generation sequencing and artificial intelligence technologies are now gradually being applied in this field, such as convolutional neural networks and machine learning.[127] One study found that the accuracy rate in diagnosing onychomycosis can be improved with convolutional neural network,[128] and by merging the patient's other information, machine learning may thoroughly analyze the data in next-generation sequencing.

Limitations

There are also certain limitations to this study. 1) Data from only the last 10 years was studied, and earlier literature was not included; therefore, there is a lack of traceability of the research focus. 2) The known studies on skin microecology are still insufficient, common clinical pigmented skin diseases were rarely addressed, and the existing basic experiments still require clinical validation. 3) The limitations of bibliometric analysis were present, such as the inability to exclude data confounding by author renaming.

Conclusion

In conclusion, this bibliometric analysis involves a comprehensive literature review of publications from the past decade on skin microbiomes. Data cleaning processes such as missing value supplementation, and synonym merging were used to ensure data robustness. The results indicated that much had been achieved in this field; however, it still requires continuous progress. Current studies focus on skin microbe diversity, distribution characteristics, interaction with host epidermal immunity, and roles in skin disorders. Artificial intelligence and sequencing technology development will pave the way for future research. This bibliometric study is a reference for researchers to better grasp the trends and priorities of skin microbiology.

Abbreviations

UCSD, University of California, San Diego; IF, impact factor; JCR, journal citation reports; *S. aureus*, *Staphylococcus aureus*; AMPs, antimicrobial proteins; CIDAMPs, cationic intrinsically disordered antimicrobial peptides; TRMs, resident memory T cells; AD, atopic dermatitis; ISAPP, International Scientific Association for Probiotics and Prebiotics.

Data Sharing Statement

The datasets supporting the conclusions of this article are included within the article and its additional files.

Consent for Publication

All authors agree publication.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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