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Redefining the Skin Type: Microbiome-based Segmentation for Efficient Product Development and Personalization

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INTRODUCTION

The skin is the largest organ of the human body, serving as the body's protective barrier. The skin is naturally colonized by various species of microorganisms, together known as the skin microbiome. The human skin microbiome is divided into resident or commensal skin microorganisms that include bacteria, fungi, viruses, archaea, and mites, which live in homeostasis with the host, and also transient pathogenic microorganisms from the environment, which live on the skin temporarily [1, 2].

Microbial imbalances, or dysbiosis between the commensal and pathogenic microorganisms, have been suggested to be involved in aberrant immune responses, disrupted skin barrier function, and consequent inflammatory and allergic skin diseases [2-5]. Research on human microbiome dysbiosis continues to progress, focusing on individual bacterial, viral, and fungal species typically associated with common skin disorders and providing valuable information on the role of the microbiota in various health conditions [1, 3].

Abstract

Despite available educational resources, people often misdiagnose skin conditions and select ineffective solutions that potentially worsen skin sensitivity. Therefore, relying solely on self-reported information without objective measurements can be misleading. To tackle this, we employed hierarchical clustering of species-level resolution bacterial and fungal microbiome data from 323 forehead samples and associated the clusters with self-reported data on skin health, age, gender, and lifestyle. Results revealed Cutibacterium acnes abundance to be a main driver of differences between different facial skin profiles. Clusters featuring > 80% C. acnes abundance contained the majority of samples (63%) and were associated with oily skin. Clusters exhibiting lower C. acnes abundance were dominated by other taxa, such as Corynebacterium kroppenstedtii, and were linked to dry and sensitive skin types, particularly in individuals above their 40s. Overall, this study highlights C. acnes levels as a novel and valuable metric for personalized skincare development. Furthermore, our work emphasizes the value of applying untargeted microbiome profiling to improve the classification of self-reported skin information, particularly in cases where unique microbes might be overlooked with a targeted approach. Future research directions include expanding the analysis to other body regions to explore the broader applicability of microbiome clustering.

For example, it has been demonstrated that *Staphylococcus aureus* colonization has a crucial role in exacerbating atopic dermatitis (AD), while *Staphylococcus epidermidis* modulates AD pathogenesis [3].

People with skin conditions often perceive the severity of their disease subjectively, which may not align with the assessments made by their dermatologists or objective evaluations [6]. Many patients turn to self-diagnosis methods available on the market, such as answering quizzes that appear tailored to their skin type, hoping to find suitable products. Conditions, such as acne, rosacea, and sensitive skin, are often self-diagnosed with the help of educational media content that guides individuals in identifying their skin issues. However, these tools can be misleading when providing personalized regimens without an objective measurement. Due to their subjective nature, these self-diagnosis quizzes are not solving but sensitizing the skin. Studies have demonstrated variability in the correlation between self-assessed and clinician-assessed based on measurements of skin conditions diagnosis [7].

Misdiagnosis and an improper evaluation of the severity of the skin condition could often lead to excess use of skincare and personal care products and the use of products that are not appropriate for the individual-specific microbiome and type of skin condition. Personal care products have been demonstrated to have a long-

term effect, producing highly individualized responses and shaping specific dermal microbial communities by changing their chemical environment. Some of the most significant changes include alterations in steroid and pheromone levels and bacterial and archaeal ecosystem structure and dynamics [7].

Skin conditions have become more prevalent over the years [8], and some of the most critical causes may include individual skin profiles, microbial dysbiosis, inaccurate diagnosis, improper evaluation of the severity of skin conditions, and inadequate and excess use of skin-care products. Excessive cleansing habits were documented as important risk factors for the incidence and aggravation of rosacea. The high frequency of cleansing, the use of a large number of cleansers, deep cleansing habits, oil control, and exfoliating behaviors positively correlated with the occurrence of rosacea. Studies indicated that individuals who prefer deep cleansing were more predisposed to present initial symptoms of papule and pustule associated with rosacea. Exfoliating products positively correlated with the progression of the symptoms from flushing to erythema, papule and pustule, and telangiectasis, and affected areas from a single area to the entire face or pan facial [9].

Recent technology advances have facilitated the in-depth analysis of skin microbiome composition and dynamics in healthy volunteers and those with diseased and injured skin. Results have demonstrated that normal human skin microbiome has a high diversity and variation among individuals with diseased skin but also in those with healthy skin [4]. The advancement of next-generation sequencing (NGS) technologies, coupled with enhanced computing capabilities, has resulted in cost-effective skin microbiome sequencing. This has provided researchers with the opportunity to employ genomic and metagenomic analyses, enabling a deeper understanding of the intricate relationships between host cells and the microbiome. These analyses have proven valuable in studying both healthy individuals and those affected by skin diseases. Key studies in the skin microbiome field have revealed the major impact of the microbiome on skin health and pathophysiology. This discovery opens an excellent potential for personalized therapy and skin care [10].

Current research fusing artificial intelligence (AI) with a comprehensive microbiome dataset offers an improved understanding of the microbiome's role in human health. AI may be an essential tool in understanding the complex relationships between microbial communities and phenotypes, may predict skin or other clinical conditions from microbiome samples, and can potentially set the stage and accelerate the development of microbiome-based personalized therapeutics and non-invasive diagnostics [11].

Understanding the full profile and interaction between commensal and pathogenic microbiota might hold extraordinary potential in treating skin disorders and other conditions. To objectively tackle this issue, we built a microbiome platform that clusters individual test results into more precise skin profiles to allow efficient formulation development and personalized regimen through AI classification [3,12]. Using hierarchical clustering, we focused on bacteria and highlighted the importance of *Cutibacterium acnes* as a determinant species for clustering. Additionally, self-reported data, including demographic information, skin types, issues, and concerns, were incorporated into the microbiome data to reveal possible associations between bacterial composition and skin types and issues.

EXPERIMENTAL

Data Sources

Participants included in the study were selected based on their prior completion of a commercial skin microbiome sampling kit. Participants data was processed in accordance with the Privacy Policy. Deidentified results were used for the study. Data from 323 participant tests in total were used in this study.

Sample Collection: Microbiome Sample

Microbiome samples were self-collected from the forehead region using cotton swabs. Participants were asked to avoid washing their face and using any facial products for at least 24 hours prior to sampling. At the time of sampling, participants swabbed their forehead using the provided swabs for a total of 80 seconds. The swabs were placed into a collection tube containing buffer liquid and were immediately stored in the freezer until shipping. Microbiome samples were shipped to the partner sequencing lab within 4 days of sampling. Typical transportation time averaged 7-10 days.

Sample Collection: Self-reported Quiz

Participants were asked to provide metadata using an online survey to accompany their microbiome sampling with demographic information, including gender, location, and year of birth, as well as information related to their current skin condition, diet, routines, issues, and goals.

Sequencing and Pre-processing

DNA extraction of the swab samples and sequencing of the V1-V3 region of the bacterial 16S ribosomal RNA gene and ITS2 region of the fungal Internal Transcribed Spacer (ITS) region were performed by a third-party CLIA-CAP certified diagnostic lab. The sequencing results were then analyzed for contaminants and cleaned using a proprietary algorithm. All 323 samples processed exhibited high quality bacterial and fungal sequence data.

Microbiome clustering and analysis

Raw bacterial and fungal microbiome data from 326 samples were transformed to relative abundances. Bray-Curtis dissimilarity was computed using the combined bacterial and fungal abundances. R was used as a local analytics environment with the phyloseq package for preprocessing, mia package for relabundance method to transform abundance counts to relative abundance, and vegan package was used for hclust hierarchical clustering with bray distance method. To find the optimal number of clustering, NbClust package was used to obtain the silhouette profile. Each cluster was then described using the grouped averages for the associated metadata and microbiome feature characteristics. For data exploration and visualization, Microsoft Power BI was

Table I: Study demographics

Gender	
Female	290 (89.8%)
Male	23 (7.1%)
Non-binary	6 (1.9%)
Prefer not to answer	4 (1.2%)
Age	
< 20	6 (1.9%)
20-29	78 (24.1%)
30-39	143 (44.3%)
40-49	59 (18.3%)
50-59	28 (8.7%)
> 60	9 (2.8%)

Table II: Reported skin characteristics

Skin type	
Balanced	41 (12.7%)
Oily	23 (7.1%)
Dry	93 (28.8%)
Combination	166 (51.4%)
Skin issues	
Acne	205 (63.5%)
Eczema	49 (15.2%)
Psoriasis	12 (3.7%)
Rosacea	81 (25.1%)
Sensitivity	
Yes	223 (69.0%)

used. 3 samples of the 326 were control samples and were excluded from analyses after hierarchical clustering.

Privacy and Cybersecurity

All personal identifiers (PII) were removed before analysis. Analysis was performed locally on the FileVault [13] / BitLocker [14] encrypted hardware. In instances where the data required download /upload from/to our servers, HTTPS connections with up-to-date SHA-256 with RSA encryption were enforced in the browsers and software. 2-factor Authentication is enforced for key team resources such as GitHub [15], AWS [16], and OneDrive [17].

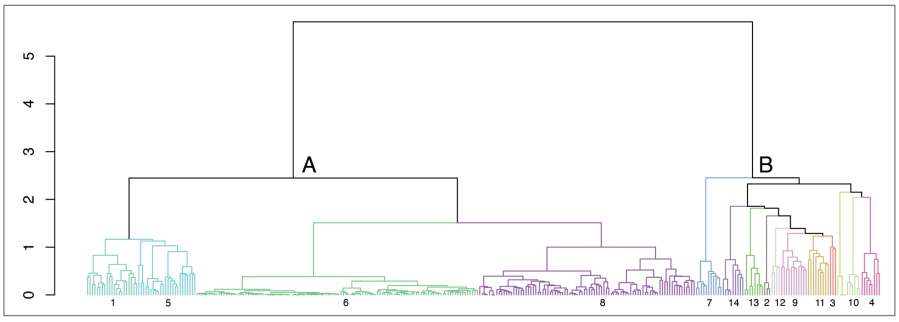

Figure 1: Hierarchical clustering of skin microbiome data – Bray-Curtis dissimilarity was computed for bacterial and fungal skin microbiome data from 326 samples. Hierarchical clustering was performed on the dissimilarity matrix, and the number of optimal clusters was determined using the average linkage method and silhouette index.
The resulting clusters are labelled and colored by cluster designation.

Results

To provide a more objective measurement of skin profile compared to self-reported skin health data alone and to advance product development and personalization, we have developed an at-home skin microbiome collection kit [12] and microbiome platform for scaling microbiome collection and data analysis. With this platform, we employed hierarchical clustering of bacterial and fungal microbiome data from 323 skin forehead samples. Clustering outcomes were then paired with quantitative microbiome measurements that include Shannon diversity, microbial load, and taxonomy as well as self-reported survey data regarding skin health, age, gender, and lifestyle.

Of the 323 individuals, 89.8% identified as female, 7.1% identified as male, and 1.9% identified as non-binary ***(Table I)***. The majority of individuals were in their 30's (44.3%), followed by 20's (24.1%), 40's (18.3%), 50's (8.7%), over 60 (2.8%), or under 20 (1.9%), demonstrating a range of samples representative of the lifespan. Regarding self-reported skin health, over half of individuals reported their skin type as being combination (51.4%), followed by dry (28.8%), balanced (12.7%), or oily (7.1%) ***(Table II)***. Furthermore, a majority of individuals reported experiencing acne (63.5%), and many reported other dermatological skin conditions including rosacea (25.1%), eczema (15.2%), and psoriasis (3.7%). Lastly, 69% of individuals reported having sensitive skin.

Hierarchical clustering of skin microbiome samples

After clustering of the microbiome data, 15 total clusters were identified, forming two

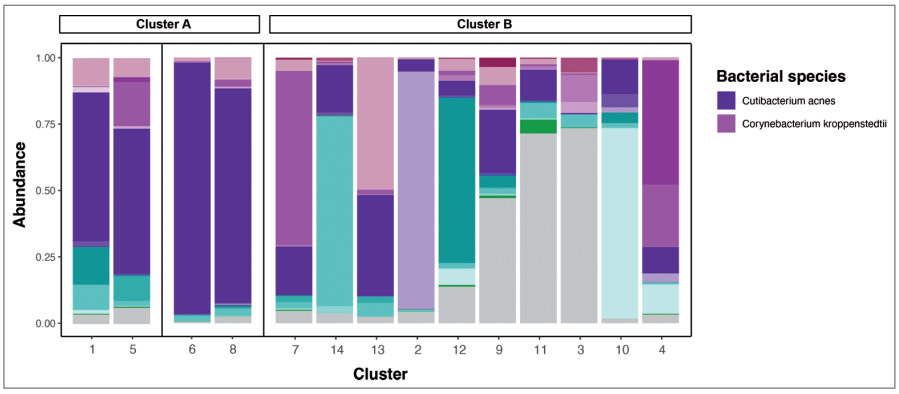

*Figure 2: Bacterial composition of 323 skin forehead microbiome samples grouped by cluster – The relative abundances of the top 20 most abundant bacterial species in the dataset, represented by color, are shown for the clusters identified with hierarchical clustering. Clusters are arranged by their order in **Figure 1**. Any species that are not within the top 20 most abundant species are grouped into "Other". Cutibacterium acnes is displayed as dark purple and Corynebacterium kroppenstedtii is displayed as magenta.*

large clusters A and B containing 250 and 73 samples, respectively ***(Figure 1)***. Across all samples, the average Shannon diversity was 0.94 for bacteria and 1.27 for fungi. The average bacterial load was 1.5E7, and the average fungal load was 7E5, with bacteria existing at a ~ 20-fold higher bioburden than fungi. The most abundant bacteria genera are as follows: *Cutibacterium, Staphylococcus, Atopobium, Corynebacterium, and Lawsonella* ***(Figure 2)***.

Microbiome diversity differences in self-reported acne and eczema

To assess if self-reported skin health data alone would reveal differences in the microbiome, we compared microbiome diversity metrics among individuals with and without skin conditions, as many skin conditions, including acne and atopic dermatitis, have been associated with a disrupted skin microbiome [13,14]. We observed that in individuals with self-reported eczema, there was a significant increase in bacterial Shannon diversity compared to individuals without self-reported eczema ***(Figure 3A)***. Furthermore, in individuals with self-reported acne, a significant decrease in bacterial Shannon diversity was observed compared to those without self-reported acne ***(Figure 3B)***.

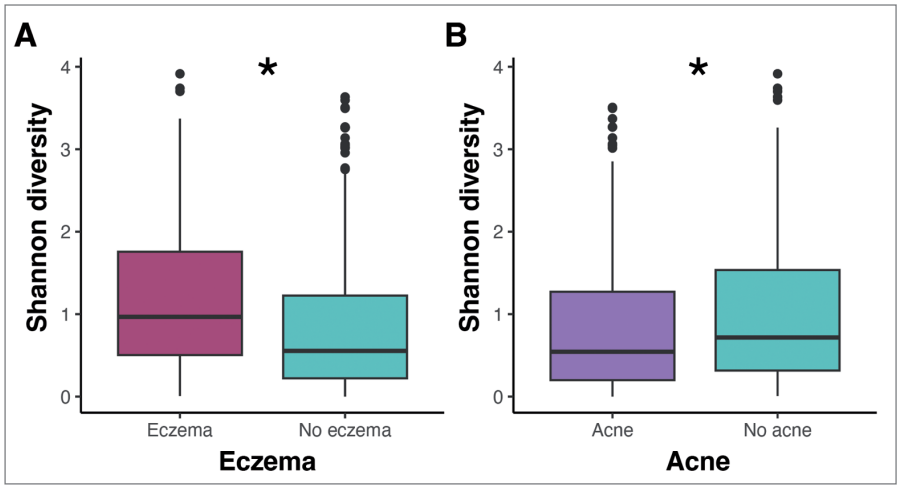

Figure 3: Shannon diversity differences in self-reported eczema and acne – Shannon diversity was calculated for individuals with A) self-reported eczema (n=49) or no eczema (n=274) and B) self-reported acne (n=205) or no acne (n=118). Statistical differences between groups were calculated using the Wilcoxon rank-sum test (, p<0.05).*

Clusters with a high abundance of *C. acnes* are associated with oily skin

Next, we combined microbiome cluster data with self-reported survey data to investigate patterns that may not be observed with microbiome or survey data on their own. We observed that clusters 6 and 8 contain most samples (n=205) and are dominated by on average > 80% *Cutibacterium acnes*, which represent the highest average *C. acnes* abundance of the clusters ***(Figure 2)***. Among the samples in clusters 6 and 8, 71.7% of individuals are in their 30's or younger ***(Figure 4A)***. Additionally, 19 of 22 individuals who reported to have oily skin were found within these clusters, representing 9.3% of the reported skin types within these two clusters ***(Figure 4B)***, and 64.3% (132/205) of individuals have self-reported acne. Our results suggest that skin type, specifically oily skin, may be associated with a high abundance of *C. acnes*. Because a majority of participants in our study exhibit a dominance of *C. acnes* in their skin profiles, this could indicate a potential correlation with oily skin. This aligns with previous research, as *C. acnes* is known to naturally inhabit sebaceous areas of the skin, which are often associated with oily skin conditions [15].

Moderate level of *C. acnes* is linked to non-oily skin types

Contrastingly, clusters 1 and 5 both only contain an average of 55% *C. acnes* across 21 and 24 samples, respectively. Together, these clusters, along with cluster 6 and 8 form a larger cluster separate from the remaining samples, which appears to be driven by higher average relative abundances of *C. acnes*. In these clusters, 68.9% (31/45) of individuals have self-reported acne. To highlight potential insights that can be gleaned from these clusters, we focus on cluster 5 ***(Figure 5)***. In this cluster, the dominant species are *C. acnes* (55%) and *Corynebacterium kroppenstedtii* (17%). 75% of individuals within this cluster are between their 30's and 40's, and 96% of participants reported having combination to dry skin. This cluster exhibits higher bacterial and fungal diversity than the average. Overall, we have identified skin microbiome profiles with a moderate level of *C. acnes* abundance, potentially linking them to combination to dry skin types.

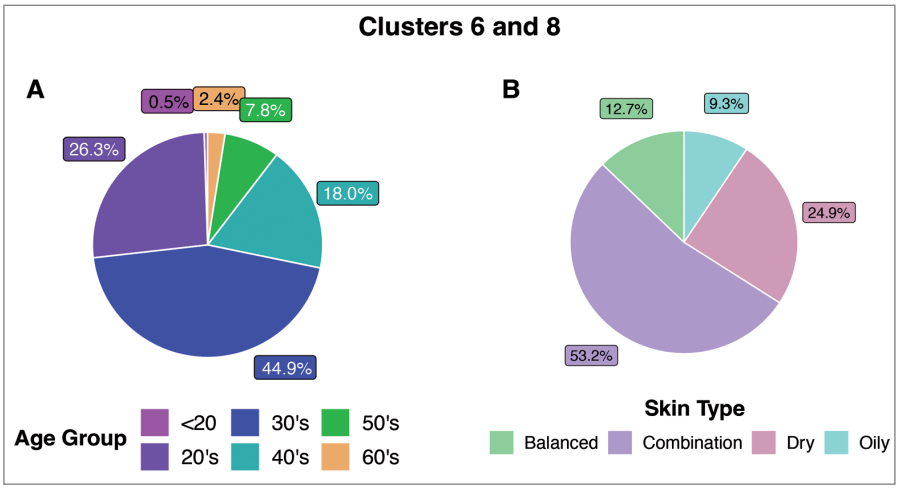

Figure 4: Age group and skin type characteristics in clusters with high level of C. acnes – The proportion of A) age group and B) skin type was calculated for participants (n = 205) within Cluster 6 and 8.

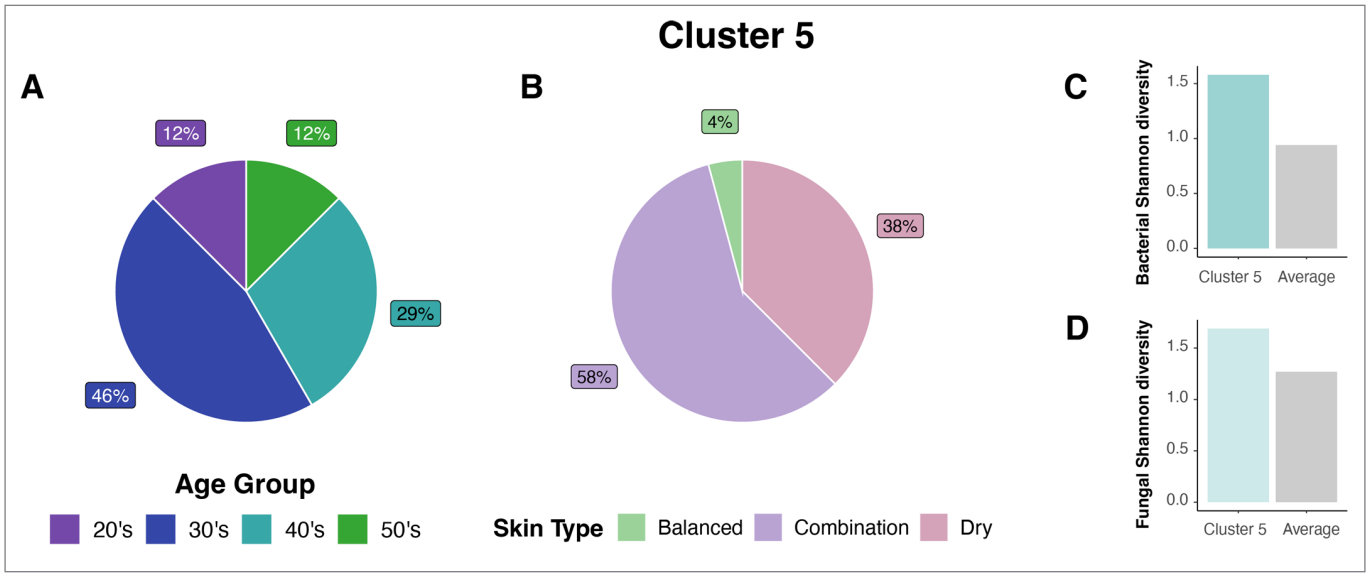

Figure 5: Age group, skin type, and microbial diversity in cluster with moderate C. acnes abundance – Relative proportions of A) age and B) skin type was calculated for individuals (n = 24) who fall into Cluster 5. Shannon diversity was calculated for C) bacteria and D) fungi samples within this cluster.

High levels of *Corynebacterium kroppenstedtii* is associated with dry and sensitive skin

Large cluster B contains 11 smaller clusters, which exhibit unique microbiome and self-reported data patterns. For example, clusters 7, 13, and 14 contain an average of 25% *C. acnes* across 11, 8, and 9 samples, respectively. These clusters are distinct from clusters containing medium to high levels of *C. acnes* ***(Figure 1)***. Combination and dry skin types are dominant in these subclusters. Also, self-reported acne is present in 42/73 individuals (57.5%).

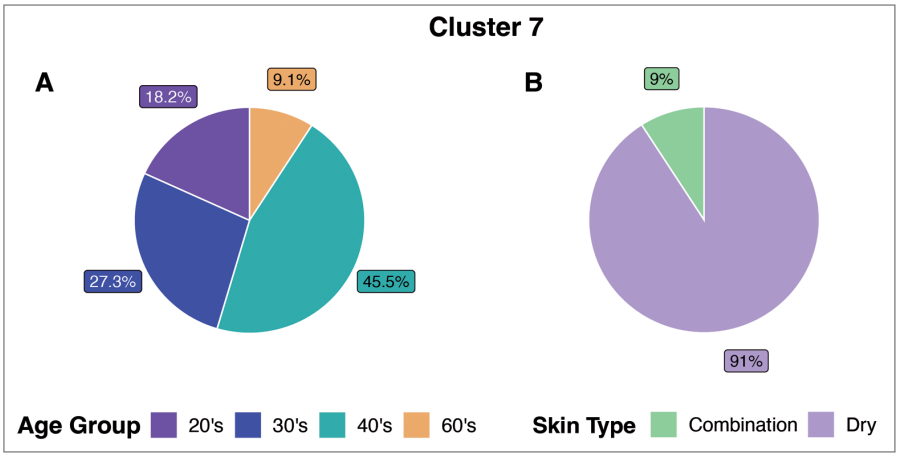

Figure 6: Age group and skin type associated with low level of C. acnes and high level of C. kroppenstedtii – Relative proportions of A) age group and B) skin type was calculated for individuals in Cluster 7.

Within Cluster 7 ***(Figure 6)***, the dominant species are *Corynebacterium kroppenstedtii* (65%) and *C. acnes* (18%). In this cluster, 45.5% of participants are in their 40's. Interestingly, 90% of participants in this cluster reported to have dry skin type. Furthermore, 10/11 (91%) of participants reported to have sensitive skin, and 5/11 (45%) reported to have rosacea. These results suggest that combination to dry skin types could be associated with low *C. acnes* microbial composition. One cluster dominated by *C. kroppenstedtii is* possibly associated with dry skin type and those who are above their 40's. This finding is consistent with a previous study examining the microbiome profiles of individuals with rosacea where *C. kroppenstedtii* was found to be the second most abundant species in those with the skin condition. Furthermore, they found that abundance of *C. kroppenstedtii* peaked in individuals who were in their 40's [16].

DISCUSSION

In summary, our study provides insight into different aspects of skin health and their potential correlation with the composition of the skin microbiome. Importantly, these findings showcase the value of employing microbiome clustering to associate objective microbiome measurements with self-reported skin health, which is often subjective. Although each participant carries unique microbiome characteristics that include differing bacterial and fungal composition, diversity, and dominant species we show that microbiome sequencing data can be effectively clustered to reveal novel insights into skin health and characteristics.

Our findings highlight the significance of *C. acnes* in driving microbial shifts in the skin microbiome and underscore the overall importance of *C. acnes* on the skin. While long considered a commensal, *C. acnes* is more often viewed negatively for its possible role in acne pathogenesis [17]. As such, much work has been aimed at identifying how to control and target

this species on the skin to limit its presence. Here, we demonstrate that a high abundance of *C. acnes* is likely beneficial, as clusters with a low abundance of *C. acnes* were often found to have increased incidence of self-reported skin concerns. This aligns with recent work in the field that highlights the positive role of *C. acnes* on the skin [4,18,19]. We also observe that the abundance of *C. acnes* does not necessarily correlate with the incidence of self-reported acne. Instead, our results suggest that skin type, particularly oily skin, may be associated with higher *C. acnes* abundance. *C. acnes* is well-known for its ability to thrive in sebaceous-rich skin sites and metabolize sebum lipids [20], supporting our findings.

Previous studies that have examined microbial composition along with skin microenvironments have observed moderate to low levels of *C. acnes* in non-sebaceous sites [20]. Interestingly, we also identified clusters with moderate to low levels of *C. acnes* abundance and found that these clusters could possibly be linked to combination and dry skin types. Although the sample size is limited, we identified a distinct cluster dominated by *C. kroppenstedtii*, which may be associated with individuals above their 40's and tendency toward dry skin type. This highlights the potential relationship between specific microbial profiles, such as the dominance of *C. kroppenstedtii*, and the characteristics of combination to dry skin. A study on rosacea, including subtypes erythematotelangiectatic and papulopustular, has found that abundance of *C. kroppenstedtii* could be associated with the skin disorder, with highest relative abundance on the cheek and nose area. Further, relative abundance of the species is correlated with disease severity, where patients who were diagnosed with both subtypes had higher level of *C. kroppenstedtii* [16].

In addition, our findings revealed significant differences in microbiome diversity in the skin conditions eczema and atopic dermatitis. Atopic dermatitis, a type of eczema, has been reported to be associated with reduced skin microbiome diversity [13, 21]. However, we observed an opposite pattern where there was an increase in diversity in individuals with self-reported eczema. Furthermore, previous work has shown that in individuals with acne, microbiome diversity is often similar between acne skin and healthy controls or unaffected skin [2, 22]. Our results, on the other hand, showed decreased diversity in individuals with self-reported acne compared to those without. While our findings may represent true biological signal, both acne and eczema encompass a broad range of dermatological symptoms [23, 24], potentially complicating the self-reporting of skin health. We therefore propose that through combining both objective microbiome data and clustering with self-reported data, this can provide a more comprehensive view of skin health and aid in the selection of products to support the skin, rather than potentially further sensitize it.

CONCLUSION

In conclusion, this study exemplifies the collection of bacterial and fungal skin microbiome communities at scale, at home, and non-invasively. Furthermore, we highlight the application of our skin microbiome platform to enable large-scale, remote data collection and analysis. Through this work, we uncovered distinct skin clusters characterized by specific microbiome fingerprints and driven by microbial composition, diversity, and load. Notably, the integration of self-reported data such as age, skin type, skin issues, and skin concerns facilitated the identification of these clusters. We also observed that *C. acnes* abundance correlated with specific skin types and conditions, highlighting this species as one of the novel metrics for skincare personalization. Our findings emphasize the value of incorporating microbiome data as a standardized measurement approach alongside self-reported information to enhance our understanding of skin condition in a more objective manner. This approach has the potential to enable more effective personalization of skincare regimens and targeted product development. While this study focused on the skin, which is in constant contact with personal care products, future directions involve in expansion to other body regions, such as the scalp and vulva, to explore the applicability of this clustering method in incorporating microbiome and self-reported data.

Conflict of Interest Statement
None

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