



Role Of The Skin Microbiome On Human Health: An Overview

Sujeet Kumar Mritunjay^{1*}, Shruti Patel¹, Shailaja Mohanta¹, Rajesh Kumar Jha¹

¹School of Sciences, P P Savani University, Surat, Gujarat- 394125

Abstract

Numerous different kinds of bacteria, fungi, and viruses reside in the human epidermis. It has been established that these bacteria vary between individuals and between different parts of the skin. Although the causes of the skin microbiome's particular heterogeneity are still not fully understood, the findings indicate that host genetic and environmental factors play a key part. Although the causes of the skin microbiome's particular heterogeneity are still not fully understood, the findings indicate that host genetic and environmental factors play a key part. Recent metagenomic studies that have uncovered a remarkable variety within these ecosystems have prompted a new understanding of commensal microbes as having a significantly broader function in immune control and epithelial health than previously understood.

Keywords: Skin Microbiome, Atopic dermatitis, *Staphylococcus aureus*, *Staphylococcus epidermidis*, Immunity, Metagenomics, Antibiotic

Introduction

Microbes (bacteria, viruses, and fungi) are present in all living things, including humans, animals, plants, and the environment (soil, water, and air). They are frequently regarded as pathogenic because they have the potential to generate infections that, if untreated, can result in major illnesses or epidemics. Microbes are responsible for a variety of useful operations, including the production of medicines, the cleansing and eradication of pests, and the production of cheese, soy sauce, leather, and other goods. Even the maintenance of good health depends on them. The world's microbial population has just a relatively small fraction of it been detected thus far. The identification of the whole variety of a certain microbial community has been constrained by the use of isolation techniques and laboratory conditions that are not universal and are not conducive to the growth of the majority of bacteria. The skin has been known to harbour bacteria, viruses, and eukaryotes like

fungi and arthropods. The microbiome on human skin is more complex than previously believed, though. The functional significance of the microbiota residing on the skin has been shown by recent descriptions of the skin microbiome, and this has significantly advanced our understanding of both healthy physiology and illness (Callewaert et al., 2020). Only lately has the significance of the human skin microbiome for skin health and general human wellbeing been acknowledged (Guo, Xiaoxian, et al. 2023). Most research studies have focused on adult skin, with little attention given to the microbiology of skin during the first few months to years of life. The newborn's skin undergoes a dramatic transformation at the time of birth as it moves from the wet, typically sterile womb to a gaseous environment with ongoing microbial interaction. Rapid surface colonization and considerable changes in skin barrier function occur in the first few days after birth lower trans epidermal water loss, lower skin pH and sebum production, and higher water content (Chiou, , and Peytavi, 2004). The ecological system must, first and foremost, preserve homeostasis between the microbiome and the host in order to function normally. The specific makeup of the skin microbiota varies from person to person but is often constant over time, which complicates the mechanisms causing this equilibrium, which are still mostly unknown (Chiou,, and Peytavi, 2004). Furthermore, interactions that are significant in defining this cutaneous system are not just those between the host and the microorganism. When it comes to intricate ecological interactions with the environment, the skin is remarkable among epithelial surfaces. A healthy microbiome is established and sustained through competition both within and between microbial species. To enhance understanding of the biology and importance of this vital system, this review aims to provide an update on recent discoveries characterizing the skin microbiome and the latest experimental advancements.

1.1 The normal microbiome on human skin

A large number of bacterial species were discovered on a single person after a detailed investigation of the topographical and temporal variety of the microbiome of healthy human skin (Byrd et al., 2018; Einstein, 1935; Grice et al., 2009). Bacteria can be present in the dermis, skin adipose tissue, deeper layers of the epidermis, the skin's surface and appendages, and even (Bay et al., 2020; Dréno et al., 2016; Nakatsuji et al., 2013). The average adult human's skin is thought to have a surface area of about 2 m², but when hair follicles, sweat glands, and sebaceous glands are included, the actual surface area is more than ten times larger, offering at least 30m² of epithelial surface area for interaction with various microbes (Gallo, 2017). Due to the larger anticipated skin surface area, it is possible that the microbial populations that live there could have a major effect on human health. The majority of Microorganisms (bacteria) on the skin are nonpathogenic and saprophytic, however depending on the host environment, some may turn pathogenic. On the skin, there are also mites, viruses, and fungi, with the genus *Malassezia* predominant in seborrheic areas (Byrd et al., 2018). For each of these bacteria to thrive in the various skin microenvironments, they have different metabolic adaptations (Byrd et al., 2018). In order to map the microbiomes of 242 healthy adults, create a reference database of microbial genome sequences, and comprehend how particular habitats in the gut, urogenital system, and skin contribute to health and disease, the National Institutes of Health (NIH) started the Human Microbiome Project in 2007 (Methé et

al., 2012; Turnbaugh et al., 2007). The Human Microbiome Project's findings, which describe their metagenomic techniques and the publicly accessible databases of whole genome and 16S rRNA gene sequences, were recently released (Methé et al., 2012). The skin microbiome of healthy volunteers has been described in this work and other studies over the past decade, along with how it varies among various individuals, time periods, and spatial niches. While the fetus is still in the womb, its skin is sterile, but colonization begins shortly after birth (Capone et al., 2011; Bello et al., 2010). All skin areas on newborns are initially uniformly colonized by a same, weakly diverse microbiome (Capone et al., 2011; Bello et al., 2010). Individual skin habitats with a diverging, progressively diversified microbiota develop as neonates are exposed to the environmental microbiota and as distinct skin patches acquire various moisture, temperature, and glandular properties (Capone et al., 2011). Then, as people age, go through puberty, and are affected by their surroundings, these ecosystems keep changing (Somerville, 1969; Somerville, 1969; Marples, 1982; Fierer et al., 2008). The bulk of skin bacteria and gut-flora fall into four phyla: *Bacteroidetes*, *Actinobacteria*, *Proteobacteria*, and *Firmicutes*, however there are thousands of distinct species within each of these phyla, according to metagenomic studies utilizing 16S rRNA sequencing in adults. In a research of the palm microbiome, for instance, it was shown that 51 healthy participants contained 4,742 distinct species, with an average of 158 species residing on a single palm (Fierer et al., 2008). Comparable habitats, such the axillae and the popliteal fossae, have comparable microbial compositions, according to studies of the microbiomes at 20 different skin sites (Costello et al., 2009; Grice et al., 2009). As a result, *Propionibacterium* species prevail in moist areas like the axillae whereas *Staphylococcus* and *Corynebacterium* species do so in sebaceous areas like the forehead, retro auricular fold, and back in all individuals. Surprisingly, the microbiomes of dry skin areas like the forearm and leg revealed the presence of several Gram-negative microbes, which were previously believed to only sometimes colonize the skin as gastrointestinal pollutants. We now have a much better understanding of the healthy skin microbiome thanks to metagenomics research utilizing 16S rRNA gene sequencing, but there are still many unanswered concerns. A recent study revealed that the bacterial makeup of children's paranasal sinuses, antecubital fossa, volar forearm, and popliteal fossa was generally different from that of the same places in adults (Oh et al., 2012). For instance, *S. aureus* was more prevalent in children's nostrils, and this substantially linked with *S. aureus* colonization in other skin areas. Further research into the skin microbiome composition in various age and ethnic groups may shed light on why some people are more prone to specific disorders and whether hosts or environmental variables affect the skin ecosystem. In-depth research has been done on the topographical and temporal variety of the microbiome of healthy human skin (Byrd et al., 2018; Grice et al., 2009; Grice & Segre, 2011), revealing that thousands of bacterial species are present on a single individual (Grice & Segre, 2011). Bacteria are found on the skin-surface and appendages, in deeper layers of the epidermis, and even in the dermis and skin adipose tissue. Bacteria are present in the dermis, adipose tissue, deeper layers of the epidermis, as well as the skin's surface and appendages. An adult human's skin's entire surface area is typically calculated to be around 2 m². The real surface area is more than 10 times larger when all skin appendages (hair follicles, sweat glands, and sebaceous glands) are considered, offering at least 30 m² of epithelial surface area for contact

with a variety of microorganisms (Gallo, 2017). Due to the larger anticipated skin surface area, it is possible that the microbial populations that live there might have a major effect on human health. The majority of skin-surface bacterial species are saprophytic and nonpathogenic, although some can change depending on the host environment (Callewaert et al., 2020). The skin can also harbour fungi, viruses, and mites, with fungi of the species *Malassezia* predominating in seborrheic areas. For each of these bacteria to thrive in the various skin microenvironments, they have different metabolic adaptations (Byrd et al., 2018). The most abundant bacterial species on human skin belong to only four phyla: *Actinobacteria*, Firmicutes, *Proteobacteria*, and Bacteroidetes. The predominance of these phylotypes on specific skin areas depends on several factors, such as moisture, sebum content, temperature, pH, and UV exposure. Sebaceous sites are colonized mainly by *Cutibacterium* (formerly *Propionibacterium* (Grice, 2015), and their microbiomes are generally less diverse, less evenly distributed, and less abundant than those of moist sites, which harbor mainly *Corynebacterium* and *Staphylococcus* species. Dry sites contain additional *Micrococcus*, *Enhydrobacter*, and *Streptococcus* species (Scholz and Kilian, 2016; Grice et al., 2009). The bacterial composition of adult skin remains relatively stable over a 2-year period (Oh et al., 2016). However, temporal variations in the skin microbiome have been observed and appear to be site-dependent, with the popliteal fossa, volar forearm, and buttocks showing the greatest variation (Grice et al., 2009). Sites that are at least partially occluded, such as the external auditory canal, nostrils, and inguinal crease, are more stable with respect to community composition and structure over time (Kang, 2015). The skin microbiome has the most heterogeneity between persons and the largest fluctuation over time when compared to other habitats (mouth, stomach, or vagina). There is considerable agreement that the less prevalent and unstable taxa exhibit greater intraindividual and interindividual variability than the more common and stable taxa (Grice, 2015). Skin microbial diversity is also influenced by a number of host-specific characteristics, including age, race, and sex. In another section of this supplement, the impact of age is covered in greater detail (Luna, 2020).

1.2 The Composition of the Skin Microbiota

Sequencing research in healthy humans revealed that the physiology of the skin site largely determined the makeup of microbial communities, with the relative abundance of bacterial taxa varying according to moist, dry, and sebaceous microenvironments. While bacteria that thrive in a wet environment, such as *Staphylococcus* and *Corynebacterium* species, were preferentially identified in moist locations, including the crooks of the elbows and feet, lipophilic *Propionibacterium* species dominated sebaceous sites (Fig. 1; Table 1). In contrast to the bacterial communities, the composition of the fungal communities at the central body sites was similar regardless of physiology (Findley, 2013). Fungi of the genus *Malassezia* predominated at arm sites, whereas the foot sites were colonized by a more diverse combination of *Malassezia* spp. and *Aspergillus* sp, *Cryptococcus* sp., *Rhodotorula* sp., *Epicoccum* sp. and others were colonized (Fig. 1). Bacteria were the most abundant and fungi the least abundant species at all sites (Grice et al., 2009); however, many more bacterial reference genomes are available than fungal reference genomes, which may partially contribute to this observed

difference. Remarkably, the overall abundance of fungi was low, even at the feet where fungal diversity was high. In contrast to bacteria and fungus, eukaryotic DNA viruses colonized people rather than specific anatomical sites (Grice et al., 2009). Since viruses do not share a common flag gene, either pure virus-like particles or shotgun metagenome sequencing can be used to identify the diversity of the viral population (Grice et al., 2009; Hannigan et al., 2015). RNA viruses can only be sequenced with RNA sequencing, which was not achievable with skin samples from healthy people. This presents another difficulty. Separately from bacteriophages, particularly those associated with *Propionibacterium* sp. and *Staphylococcus* sp. no central DNA virome has been found to be conserved across individuals (Findley, 2013; Hannigan et al., 2015). To fully comprehend the function of potential predator-prey or co-operative interactions between bacteriophages and bacteria in forming the microbial community, more research is needed in this part of skin microbiome research. The Merkel cell polyomavirus, that causes a rare but severe form of skin cancer, suggests that eukaryotic viruses, in addition to bacteriophages, may potentially be involved in skin illness.

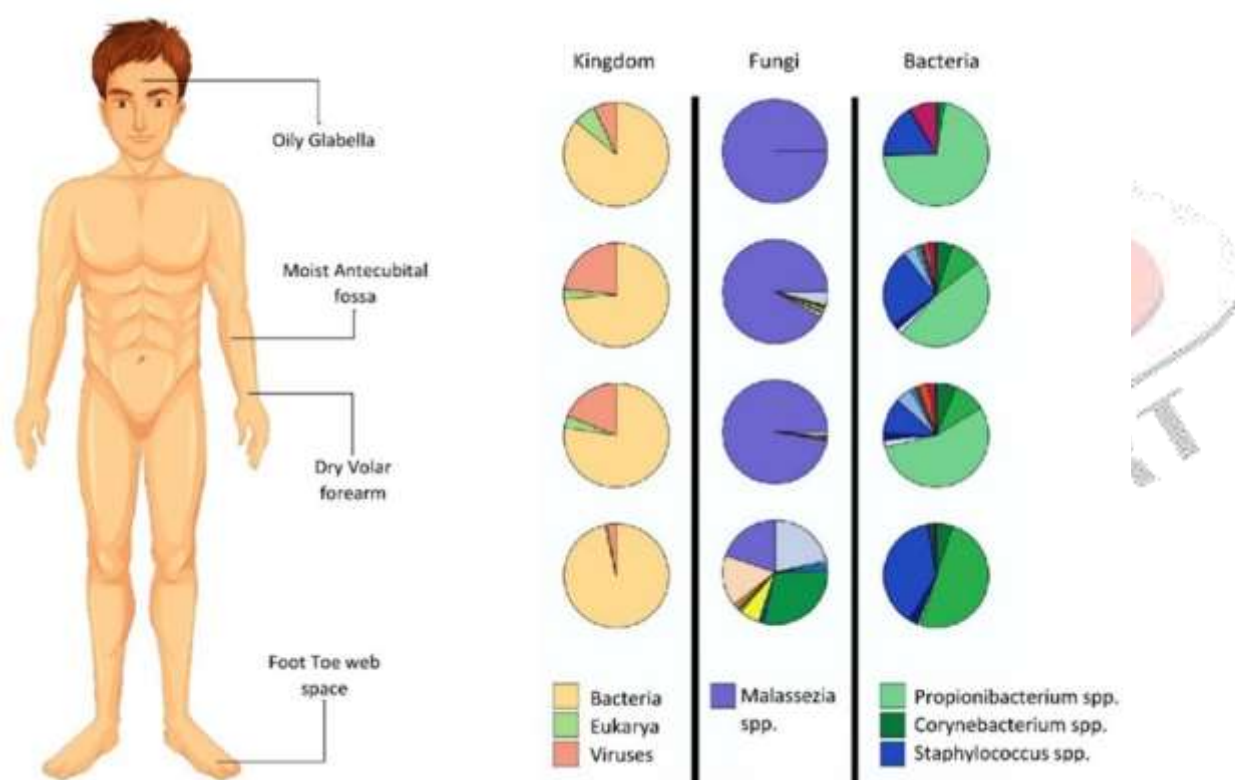


Fig 1:- Skin microbial communities are formed according to physiological characteristics and the individual. There are four venues the main microenvironments of representative skin: glabella (also known as forehead) sebaceous (oily); antecubital fossa (wet); volar forearm (dry); and web space of the toe (foot). Pie charts represent relative consensus abundance of kingdom, fungi and bacteria in healthy adults. The bacterial species *Propionibacterium acnes* and *Staphylococcus epidermidis* and eukaryotic DNA viruses are shown as bar graphs from four representative samples. emphasizes how individuality shapes these communities. Plots of the relative abundance of kingdoms, fungi, bacteria and viruses, key taxon colors are given in the legend. Unmarked colors can be grouped under the "Other" category for *P. acnes* and Bar charts of *S. epidermidis*, similar colors represent closely related strains.

Despite ongoing environmental changes, skin microbial populations were found to be remarkably stable throughout the course of a two-year investigation using longitudinal samples (Grice et al., 2009). Based on strain and single nucleotide level analyses, this stability was determined by the retention of strains over time rather than the reintroduction of common species from the environment (Grice et al., 2009). Similarly, longitudinal studies of the gut have found that certain species of an individual's microbiota persist for a year or longer (Faith, 2013). The most stable microbial and fungus communities were found on the sebaceous glands. Eukaryotic DNA viruses changed the most over time, while the microbial communities on the soles of the feet were the least consistent. The temporary presence of fungi in the environment may be the cause of the relative instability of the microbial communities on the feet.

2.The skin microbiome in disease:

"Colonisation resistance" is a process that describes how interactions among microbiota constituents influence the local microbial population and deter pathogenic bacteria from colonising it (Buffie, 2013). Bacteria that ordinarily benefit their hosts might, change in specific situations to become harmful. A lot of common skin conditions are linked to dysbiosis, or changes in the microbiota (Buffie, 2013). In the cases of acne, eczema, and persistent wounds, common commensal species are frequently to blame for this dysbiosis. It is believed that both uncommon and common skin conditions are brought on by specific species and alterations in the microbial ecology. Microorganisms associated with common acne. Common acne vulgaris in adolescents is a chronic inflammatory skin disease associated with the bacterium *P. acnes* (Iebba et al., 2016) the most abundant organism in the microbiota of healthy adults (Gibbon et al., 2013; Tomida et al., 2013). At the functional level, gene expression profiles of *P. acnes* differ between individuals with and without acne (Kang D, 2015). It is critical to examine disease in the larger context of host genetics, immunological or barrier abnormalities, the microbiome, and the environment. Although a minority of individuals have *P. acnes* colonisation, the majority do not. For instance, as sebum production rates are correlated with the severity of clinical symptoms, higher sebum secretion is linked to the pathophysiology of acne (Picardo, 2009).

2.1 Acne:

A changed bacterial colonisation is thought to be one of the primary factors contributing to the emergence of acne, despite the fact that this chronic inflammatory disease of the pilosebaceous unit is still not entirely understood (Bojar and Holland, 2004). The basic mechanism of disease is thought to include an androgen-induced increase in sebum production, altered keratinization, inflammation, and dysbiosis of the facial skin. The main bacterium associated with the disease is *Propionibacterium acnes*. It colonizes the sebaceous follicles, which contain microcomedones and provide the bacterium with an anaerobic and lipid-rich environment (Dowell et al., 2011; Nakajima et al., 2016). Secretion of various enzymes such as hyaluronidases, lipases and proteases, causing local injury and inflammation (Iinuma et al., 2009). Based on samples of nasal mucosa from 49 acne sufferers and 52 healthy people, a study of *P. acnes* strain and genome levels showed no discernible statistical difference in the relative abundance of *P. acnes*. However, based on their phylotype, only a few *P.*

acnes strains were strongly linked to acne. On healthy skin, however, these strains were less prevalent while other strains were richer (Nakajima et al., 2016). In a different investigation, sebaceous follicles from skin biopsies taken from the face included various *P. acnes* phylotypes. In comparison to control samples, samples from acne patients contained more *P. acnes* and *P. acnes*-containing follicles.

2.2 The Microbiome in Atopic Dermatitis:

Atopic dermatitis (AD) is a condition that metagenomics is widely used to study. Although AD is not contagious, alterations in the skin's microbiota may be the cause of flare-ups. In the United States, AD, a chronic, relapsing condition, affects 15% of youngsters. For the pathophysiology of AD, a number of theories have been put out, including the lack of the epithelial barrier protein filaggrin, *S. aureus* colonisation, and immunological hypersensitivity (Barker et al., 2007; Cramer et al., 2010; Palmer, 2006). Empirically effective treatments for AD include antibiotics, steroids, and dilute bleach baths (Huang, 2009). These substances are believed to lessen bacterial burden and prevent an overactive, malfunctioning immune response to skin flora. Atopic dermatitis (AD) sufferers have significantly different microbial community architectures than healthy participants, according to a number of recent studies. AD Certain antibiotics combined with corticosteroids and diluted bleach baths may occasionally be helpful for patients, but excessive antibiotic use has also drawn criticism for potentially harming the microbiome and interfering with its beneficial functions. Lower skin bacterial diversity and illness aggravation are associated, and microbial changes have been found to be localised in disease hotspots. The latter may imply that microbial populations present in particular ecological niches, such as the antecubital and popliteal crease, also influence the development of sickness. Paradoxically, the best AD therapy is correlated with a larger bacterial diversity, suggesting that existing therapies that support bacterial diversity help the condition get better. Increases in particular bacterial taxa, such *Corynebacterium*, *Streptococcus*, and *Propionibacterium*, are seen throughout treatment, showing more intricate species connections during AD than is known from culture-based approaches (Kong et al., 2012). *Malassezia* may be more frequently linked to AD, according to several research (Gioti et al., 2013; Saunders et al., 2012)

Table - 1			
	Bacteria	Eukarya	Viruses
Dry	<i>Propionibacterium acnes</i> <i>Streptococcus mitis</i> <i>Streptococcus oralis</i> <i>Streptococcus sanguinis</i> <i>Micrococcus luteus</i> <i>Veillonella parvula</i>	<i>Malassezia restricta</i> <i>Malassezia globosa</i> <i>Aspergillus tubingensis</i> <i>Candida parapsilosis</i> <i>Zymoseptoria tritici</i> <i>Malassezia sympodialis</i>	<i>Molluscum contagiosum virus</i> <i>Propionibacterium phage</i> <i>Merkel cell polyomavirus</i> <i>Simian virus</i> <i>Streptococcus phage</i> <i>Stenotrophomonas phage</i> <i>Human papillomavirus (β)</i> <i>Actinomycesphage</i>
Moist	<i>Corynebacterium tuberculostearicum</i> <i>Propionibacterium acnes</i> <i>Staphylococcus epidermidis</i> <i>Corynebacterium fastidiosum</i> <i>Corynebacterium afermentans</i> <i>Corynebacterium simulans</i>	<i>Malassezia globosa</i> <i>Malassezia restricta</i> <i>Tilletia walkeri</i> <i>Malassezia sympodialis</i> <i>Pyramimonas parkeae</i> <i>Parachlorella kessleri</i>	<i>Molluscum contagiosum virus</i> <i>Propionibacterium phage</i> <i>Polyomavirus HPyV6</i> <i>Human papillomavirus (γ)</i> <i>Staphylococcusphage</i> <i>Actinomyces phage</i> <i>Human papillomavirus (β)</i> <i>Acheta domestica densovirus</i>
Sebaceous	<i>Propionibacterium acnes</i> <i>Corynebacterium tuberculostearicum</i> <i>Staphylococcus capitis</i> <i>Streptococcus mitis</i> <i>Staphylococcus hominis</i> <i>Corynebacterium amycolatum</i>	<i>Malassezia restricta</i> <i>Malassezia globosa</i> <i>Malassezia sympodialis</i> <i>Aureoumbra lagunensis</i> <i>Tilletia walker</i> <i>Pycnococcus provasolii</i>	<i>Propionibacterium phage</i> <i>Molluscum contagiosum virus</i> <i>Merkel cell polyomavirus</i> <i>Staphylococcus phage</i> <i>Gammapapillomavirus HPV127</i> <i>Enterobacteria phage</i> <i>Human papillomavirus (β)</i> <i>Acheta domestica densovirus</i>
Common in feet	<i>Corynebacterium tuberculostearicum</i> <i>Staphylococcus warneri</i> <i>Staphylococcus epidermidis</i> <i>Staphylococcus haemolyticus</i> <i>Micrococcus luteus</i> <i>Corynebacterium resistens</i>	<i>Malassezia restricta</i> <i>Trichophyton rubrum</i> <i>Malassezia globosa</i> <i>Pyramimonas parkeae</i> <i>Trichophyton mentagrophytes</i> <i>Parachlorella kessleri</i>	<i>Propionibacterium phage</i> <i>Merkel cell polyomavirus</i> <i>Alphapapillomavirus</i> <i>RD114 retrovirus</i> <i>Molluscum contagiosum virus</i> <i>Stenotrophomonasphage</i> <i>Pseudomonas phage</i> <i>Staphylococcus phage</i>

2.3 Psoriasis:

Compared to AD, little is known about how the skin's microbiome plays a role in psoriasis. Psoriasis is an idiopathic inflammatory skin condition that affects 2% of the population globally. The signs of this disorder include hyperkeratosis, hyperproliferation of keratinocytes, immune cell infiltration of the skin, and angiogenesis. Similar to AD, psoriasis is brought on by a combination of environmental and inherited causes. The microbial population surrounding the lesions is more ecologically diverse overall than healthy skin. Firmicutes dominate in psoriatic lesions but actinobacteria are underrepresented when compared to healthy skin (Cho, 2012; Zákostelská et al., 2016). It is unclear whether these changes in the microbiome associated with psoriasis are a result of the condition or a factor in its development.

2.4. Rosacea:

Around the world, rosacea affects 3% of people. The majority of the patients have fair skin and Northern European ancestry. Clinical symptoms of the condition include flushing, persistent erythema, papules, pustules, telangiectasia, and inflammatory nodules, which are typically visible on the face. The imbalance between the host and skin microbiome that rosacea causes may be advantageous to species other than bacteria. The Demodex mite is evidently more prevalent on the skin of rosacea patients than on healthy skin. (Casas et al., 2012).

2.5. Seborrheic Dermatitis (SD):

Malassezia is thought to be the culprit for seborrheic dermatitis since it regulates the skin microbiome (SD). The first diagnosis of this chronic inflammatory skin disorder around puberty is typically due to an increase in cutaneous lipids caused by androgen-driven sebaceous gland development and sebum production. The illness usually affects those over 50 as well. Every ethnic group is susceptible to SD, which is diagnosed in men more often than in women. Between 1 and 5% of the population are thought to be affected by it. People with acquired immunity-deficient syndrome are among those at high risk of contracting AIDS. Erythematous patches with greasy scaling are the feature of the clinical appearance. The scalp, glabella, anterior hair line, brows, ears, and chest are among the areas that are often impacted (Gaitanis et al., 2012). The term "dandruff" is frequently applied to scalp seborrhea. It has a very high frequency of about 50% of the population and is mostly linked to *M. restricta* and *M. globosa* (Clavaud et al., 2007). Using antifungal medications therapeutically can improve a patient's health not, though, antibiotics. Regarding the underlying mechanisms of the pathogenicity, questions remain. A compromised skin barrier facilitates the progression of disease (Harding, 2002). The fungus secretes a lipase that is known to convert triglycerides into aggravating fatty acids that may result in scaling and hyperproliferation or to create arachidonic acid, which is also connected to inflammation (Gupta et al., 2004). The latest research suggests that the fungus, which is often a part of the skin's microbiome, can develop into a pathogenic condition if its growth is unregulated. What these control variables are and how they are suppressed remain a mystery.

3. Influence of the Urban Environment on the Microbiota:

The environment in which we live has a significant impact on the skin microbiota even though the skin mucosal surface is in close contact with the outside world. It's especially likely that people who live in urban areas and people who live in rural areas have diverse skin microbial populations. The study by Ying et al. on the skin bacterial community of normal people aged 12 to 60 years indicated that the skin microenvironment (sebaceous, wet, or dry) was the most significant determinant. This study established that the body site is the primary driver of variation in the relative abundance of distinct species within bacterial communities. The bacterial microbiota of the skin is significantly influenced by the area of living, whether urban or rural. Urban and rural populations appeared to have similar skin microbiome richness, but it has been found that intragroup variance in microbial community structure is much higher in rural patients than in urban people (Ying et al., 2015). Additionally, metropolitan populations frequently have higher *Trabulsiella* prevalence, particularly on the forehead, volar forearm, and backs of hands (glabella). Women also showed differences, with urban individuals having higher concentrations of *Cutibacterium* than rural individuals, whereas the opposite was true for *Corynebacterium*. All age groups are affected by the living environment, albeit the degree of this effect varies with age, notably in young children. Additionally, toddlers (ages 1-4) have a more pronounced impression of the terrestrial world than infants (under one year old) and kids their age. Teenagers, on the other hand, are influenced by their home environment. The disparities in exposure to soil, aquatic, and host-associated microbial sources between rural and urban populations may be responsible for these variations in skin microbial composition, given that urban workers frequently spend more time indoors. Cultural differences and lifestyle-related factors may potentially contribute to the reported variances in skin microbiomes (Lehtimäki et al., 2017; Ying et al., 2015). Recent research has looked at how development affects both domestic and human microbiomes. The profile of these ecosystems changed along an urbanisation gradient, according to a comprehensive chemical and microbiological study that examined numerous areas of the Amazon rainforest with the same latitude. Human, animal, and household samples were gathered at four different geographic sites: a remote village (Checherta), a rural village (Puerto Almendras), a large town (Iquitos), and low- and middle-class areas of a city (Manaus). This study found that pollution levels in households significantly rose along with population growth. Liquid chromatography with tandem mass spectrometry (LC-MS/MS) analysis of samples from each location showed that the amounts of household surface chemicals, detergents, personal care and cleaning products, and compounds derived from pharmaceuticals were greater in the more urban locations. The home surface chemical products available in the metropolis of Manaus were comparable to, but distinct from, those found in rural areas, regardless of socioeconomic standing (lower or middle class). This pattern matched the discrepancies in cleaning and cosmetics product availability between Brazil and Peru. Additionally, there were notable differences in microbial profiles between sample sites (McCall et al., 2020). Increased urbanization was found to alter the composition of household bacterial, fungal, and micro eukaryotic populations. Urbanization was specifically associated with an increase in the variety of skin and house fungi as well as an increase in the relative quantity of bacteria and fungi that are connected with

human skin. Potentially harmful fungus included *Aspergillus*, *Malassezia*, *Candida*, and *Eureptiles* among others urban skin and housing samples identified. Meanwhile, urbanization caused the bacterial population on human skin (hands, arms, and feet) to become less diverse and shift in composition. Urbanization significantly reduced the bacterial richness of the hands and arms in particular. Moreover, more frequent shoe wearing was linked to an increase in the relative abundance of pathogenic fungi and *Staphylococcus species* on the foot, but the variety of microeukaryotes on this skin surface reduced. *Corynebacterium*, *Micrococcus*, *Pseudomonas*, and *Enhydrobacter*, well-known skin bacteria, became more enriched on skin surfaces with urbanization, whereas the abundant supply of environmental bacteria (*Dermabacteraceae* and *Intrasporangiaceae*), as well as a wide variety of low-abundant bacteria and many other taxa that are typically not associated with humans, decreased or nearly disappeared. Indicating that these products may be at least largely to blame for the loss in cutaneous bacterial variety in urban contexts, detergents were demonstrated to have a negative relationship with skin bacterial diversity. A higher proportion of bacterial and fungal possibly hazardous taxa were found as urbanisation increased. This may account for the greater occurrence of common Western illnesses such as atopic dermatitis, acne, and *Staphylococcus aureus* infections. For instance, people from non-industrialized countries and members of indigenous tribes do not have acne vulgaris on their skin (McCall et al., 2020). Even though, 79–95% of Western have the disease. Acne supposedly didn't affect native people until they relocated to Westernized cities, demonstrating the influence of environment and lifestyle on the skin condition (Cordain et al., n.d., 2001).

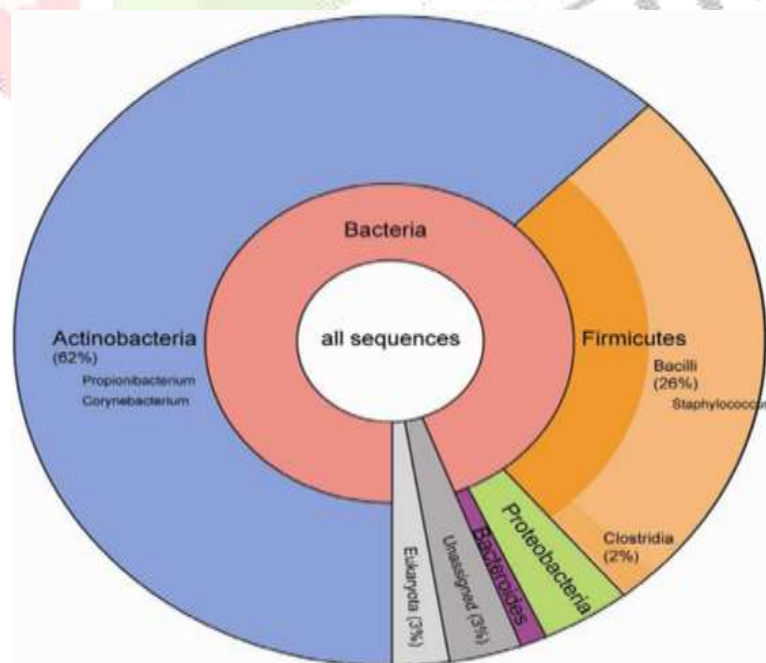
4. Antibiotics and the Microbiome:

Uncertainty over how modern medications affect the microbiome is very large. Numerous immunosuppressive or antibacterial dermatological treatments could have unintended effects on the microbiome. It has been demonstrated that antibiotic use not only causes a transitory drop in bacterial diversity but also a long-term decrease in microbiome members who are not the drugs' primary targets. Gram-negative bacterial populations dropped after therapy, despite the fact that vancomycin typically destroys Gram-positive bacteria. The indirect interactions between bacterial species that emerge from ecosystem-wide activities like metabolite exchange and waste product clearance are likely what have an impact on unwanted microorganisms (Jakobsson et al., 2010; Jernberg et al., 2007). Furthermore, even after antibiotic treatment is ended and even after the density of bacteria in the gut has been restored, the long-term alterations in the composition of the microbial community make it simpler for pathogens like vancomycin-resistant *Enterococcus* to colonise. The power of bloodstream invasion is increased as a result. Antibiotics for AD or UV radiation for psoriasis are examples of bactericidal therapies that may have long-lasting, unrecognised effects on the microbiota and the likelihood of disease recurrence. There is considerable debate over the effectiveness of probiotic treatments for skin disorders such as atopic dermatitis. A meta-analysis of seven Cochrane and non-Cochrane reviews revealed no convincing evidence that treatments like probiotics, maternal antigen avoidance, and various antigen-avoidance diets lowered the incidence of atopic dermatitis (Foisys et al., 2011; Staley, 1985). Despite the fact that aggregated data showed a decrease in eczema incidence with exclusive breastfeeding for at least six months and with

maternal probiotic supplements, these conclusions were based on small trials. The focus of these investigations was also on modifying the gut microbiome to affect skin health. Future studies into treatments for skin conditions brought on by microorganisms may focus on probiotic regimens that directly influence the skin microbiome (Foisy et al., 2011).

5. Metagenomic Approach

To identify cutaneous bacteria, skin swabs or biopsies were traditionally cultured. Less than 1% of bacterial species, however, can grow in the usual laboratory conditions, and many of those that can survive are outcompeted by organisms with a faster rate of development. Early microbiological surveys therefore had an oversupply of bacteria or fungi that were simple to grow, like *Staphylococcus* or *Malassezia* species. Recent advancements in DNA amplification and sequencing technologies that do away with the necessity for culture processes have made it possible to more comprehensively and objectively view the "microbiome," or the collection of the skin's microbiota and its genetic material (Staley, 1985). The term "metagenomics" describes a sequence-based, culture-free method of analysing any group of microorganisms, such as the skin microbiota. Think about bacterial. This method often involves directly PCR-amplifying the 16S ribosomal RNA (16S rRNA) gene from skin samples. The 16S rRNA gene is present in all bacteria and archaea but not in eukaryotes. Following high-throughput sequencing of the PCR results, it has both variable regions for taxonomic categorization and conserved regions that serve as binding sites for PCR primers. Sequences that share more than 97% of their similarities are typically classified as belonging to a single species. It is believed that strain changes within a single species are what cause sequence discrepancies. Additionally, the number of sequences belonging to a species reveals the species' relative abundance in the initial skin sample (Handelsman, 2004; Pace, n.d.; Turnbaugh et al., 2007).



This Pie chart showing microbial composition within the same example metagenome.

6.The Microbiome in Immune Development:

The body's primary barrier against infection is the skin's physical and immunological defences. Along with the gut, the skin is one of the organs that the immune system most frequently examines. In addition to distinguishing between self and other, the immune system also has to perform the more difficult task of identifying between good and bad germs. It is difficult to determine precisely what alerts the immune system to pathogenicity because all microbes share the same molecular patterns of lipopolysaccharides and peptidoglycans. The immune system is influenced and supported by skin and gut microorganisms, according to recent research. Studies on germ-free laboratory mice helped scientists first understand the significance of microbiota on immunological development. These mice exhibit decreased immunological marker epithelium expression, unfavourable T cell differentiation, and suboptimal mesenteric lymph node and gut-associated lymphoid tissue development. Research has also shown that alterations in gut microbiota have an impact on immune dysregulation illnesses. Similar to this, a recent study found that in germ-free mice lacking commensal skin microorganisms, cutaneous T cell numbers and cytokine production are abnormal. These findings offer compelling evidence that immunological activity at the epithelial and associated immune tissue levels are well-established in the skin, just as they are in the gut. Thus, the gut microbiome and the skin microbiome can both be researched using many of the same concepts and techniques (Falk et al., 1998). A good skin barrier consists of immune detection and epidermal keratinocytes, which produce antimicrobial peptides (AMPs) that maintain innate immunity. These AMPs are expressed more frequently when *Propionibacterium* species and other Gram-positive bacteria are present. In addition to AMPs, sebocytes can hydrolyze sebum triacyl glycerides to produce antimicrobial free fatty acids. Additionally, commensal bacteria including *S. epidermidis* and *P. acnes* hydrolyze triacyl glycerides (Lai & Gallo, 2009; Lee et al., 2008). The *Lactococcus*, *Streptococcus*, and *Staphylococcus* species are among the Gram-positive commensal bacteria that produce their own bactericidal components. Phenol soluble modulins (PSMs), which are peptides made by *S. epidermidis*, have selective activity against Group A *Streptococcus*, *E. coli*, and *S. aureus* but not against other *S. epidermidis*. It's interesting to note that while *S. epidermidis* PSMs primarily affect neutrophils and destroy bacteria, *S. aureus* PSMs show limited antibacterial activity and instead cause neutrophil lysis. The abundance of AMPs produced by bacteria can inhibit pathogen survival on healthy human skin by 2-3 logs in nanomolar concentrations. They also have a minor impact on innate immunity (Lai and Gallo, 2009; Lee et al., 2008). Microbiota not only activate and sustain innate immunity, but also influence adaptive immunity, but these interactions are more complex and little understood. The commensal *Bacteroides fragilis* generates regulatory T cells and anti-inflammatory cytokines, mainly IL-10, according to studies conducted in the stomach. Reviews of various studies on how the gut microbiota may affect the immune system have been published (Surana and Kasper, 2012). In order to better understand how skin microbiota may impact the innate and adaptive immune systems, research into how numerous autoimmune diseases—including lupus, vitiligo, and dermatomyositis, to name a few—present on the skin even if they are also systemic should be done right away.

7.Conclusion:

The environment and living things are both home to a wide variety of microorganisms with significant niche specialization. Several microbial ecosystems may be thoroughly studied using sequencing technology and bioinformatics, revealing their intricate structure and functioning. The health of the earth and its people may be monitored via microbiomes. Accurately anticipating the effects of perturbations or environmental changes on human health depends on an understanding of the interactions between our intrinsic and surrounding microbial ecosystems. Particularly, as the skin is the first line of defense against external aggressors, growing urbanization might disrupt the skin ecology and, as a result, human health. Moreover, newly discovered microorganisms may be useful as novel probiotics or postbiotics and offer therapeutic treatments for human illnesses including dermatological problems. Our knowledge of the various microbiomes is constantly being updated, with substantial insights being gained over the last decade.

Conflict of interest :- No Conflicts of interest

REFERENCE:

- Bay, L., Barnes, C.J., Fritz, B.G., Thorsen, J., Restrup, M.E.M., Rasmussen, L., Sørensen, J.K., Hesselvig, A.B., Odgaard, A., Hansen, A.J. and Bjarnsholt, T., Bojar, Richard A., and Keith T. Holland; (2004) ‘Acne and *Propionibacterium Acnes*’ *Clinics in Dermatology* , Vol. 22 No. 5 , pp.375–79.
- Buffie, C. G., and Pamer, E. G. 2013. Microbiota-mediated colonization resistance against intestinal pathogens. *Nature reviews. Immunology*, vol. 13 no.11, pp. 790-801.
- Byrd, Allyson L., Yasmine Belkaid, and Julia A. Segre. (2018) “The Human Skin Microbiome.” *Nature Reviews Microbiology* Vol. 16 no. 3, pp. 143–55.
- Callewaert, Chris, Katia Ravard Helffer, and Philippe Lebaron; (2020) “Skin Microbiome and Its Interplay with the Environment.” *American journal of clinical dermatology* Vol. 21, pp. 4–11.
- Capone, Kimberly A., Scot E. Dowd, Georgios N. Stamatas, and Janeta Nikolovski; (2011) “Diversity of the Human Skin Microbiome Early in Life.” *Journal of Investigative Dermatology* Vol. 131 pp. 10, pp. 2026–32.
- Casas, C., Paul, C., Lahfa, M., Livideanu, B., Lejeune, O., Alvarez-Georges, S., Saint-Martory, C., Degouy, A., Mengeaud, V., Ginisty, H. and Durbise, E; (2012) “Quantification of *Demodex Folliculorum* by PCR in Rosacea and Its Relationship to Skin Innate Immune Activation.” *Experimental dermatology* Vol. 21 no. 12, pp. 906–10.
- Cho I, Blaser MJ; (2012) ‘The human microbiome: at the interface of health and disease’ *Nature reviews. Genetics* vol. 13, pp. 260–270.

- Clavaud, C., Jourdain, R., Bar-Hen, A., Tichit, M., Bouchier, C., Pouradier, F., El Rawadi, C., Guillot, J., Ménard-Szczębara, F., Breton, L. and Latgé, J.P; (2013) “Dandruff Is Associated with Disequilibrium in the Proportion of the Major Bacterial and Fungal Populations Colonizing the Scalp.” *PLoS ONE* vol. 83.
- Cordain, L., Lindeberg, S., Hurtado, M., Hill, K., Eaton, S. B., & Brand-Miller, J; (2002) ‘Acne vulgaris: a disease of Western civilization’ *Archives of dermatology*, vol.138 no. 12, pp. 1584-1590.
- Costello, E.K., Lauber, C.L., Hamady, M., Fierer, N., Gordon, J.I. and Knight, R; (2009) “Bacterial Community Variation 0 Body Habitats across Space and Time.” *Science* vol. 326 no. 5960, pp. 1694–97.
- Cramer, Claudia et al; (2010) “Elder Siblings Enhance the Effect of Filaggrin Mutations on Childhood Eczema: Results from the 2 Birth Cohort Studies LISApplus and GINIpplus.” *J of Allergy and clinical Immunology* Vol. 125 no. 6, pp. 1254-1260.
- Gong, Z., Wang, W., El Omari, K., Lebedev, A. A., Clarke, O. B., and Hendrickson, W. A. (2023) Crystal structure of LGR ligand $\alpha 2/\beta 5$ from *Caenorhabditis elegans* with implications for the evolution of glycoprotein hormones. *Proceedings of the National Academy of Sciences*, vol. 120 no. 1, pp. e2218630120.
- Dominguez-Bello, Maria G., Elizabeth K. Costello, Monica Contreras, Magda Magris, Glida Hidalgo, Noah Fierer, and Rob Knight; (2010) “Delivery Mode Shapes the Acquisition and Structure of the Initial Microbiota across Multiple Body Habitats in Newborns.” *Proceedings of the National Academy of Sciences* vol. 107 no. 26, pp. 11971–75.
- Dorothy a. Somerville; (1969) “The effectt of age on the noemal bacterial flora of the skin.” *British Journal of Dermatology* Vol. 81, pp. 14-22
- Nast, A., Dréno, B., Bettoli, V., Bukvic Mokos, Z., Degitz, K., Dressler, C., Finlay, A.Y., Haedersdal, M., Lambert, J., Layton, A. and Lomholt, H.B; (2016) “Microbiome in Healthy Skin, Update for Dermatologists.” *Journal of the European Academy of Dermatology and Venereology* Vol. 30 no. 12, pp. 2038–47.
- Einstein, A., Podolsky, B., and Rosen, N. (1935). Can quantum-mechanical description of physical reality be considered complete?. *Physical review research* Vol. 47 no. 10, pp. 777.
- Faith, J. J., Guruge, J. L., Charbonneau, M., Subramanian, S., Seedorf, H., Goodman, A. L., and Gordon, J. I; (2013) The long-term stability of the human gut microbiota. *Science*. Vol. 341 no. 6141, pp. 1237439.
- Falk, P. G., Hooper, L. V., Midtvedt, T., and Gordon, J. I. (1998) ‘Creating and maintaining the gastrointestinal ecosystem: what we know and need to know from gnotobiology’ *Microbiology and Molecular Biology Reviews* vol. 62 no. 4, pp. 1157-1170.

- Fierer, N., Hamady, M., Lauber, C. L., and Knight, R. (2008). The influence of sex, handedness, and washing on the diversity of hand surface bacteria. *Proceedings of the National Academy of Sciences* vol. 105 no. 46, pp. 17994-17999.
- Findley, K., Oh, J., Yang, J., Conlan, S., Deming, C., Meyer, J. A., and Segre, J. A; (2013) 'Topographic diversity of fungal and bacterial communities in human skin. *Nature*' vol. 498 no. 7454, pp. 367-370.
- Fitz-Gibbon, S., Tomida, S., Chiu, B.H., Nguyen, L., Du, C., Liu, M., Elashoff, D., Erfe, M.C., Loncaric, A., Kim, J. and Modlin, R.L: (2013) "Propionibacterium Acnes Strain Populations in the Human Skin Microbiome Associated with Acne." *Journal of Investigative Dermatology*. Vol. 133 no. 9, pp. 2152–60.
- Foisy, M., Boyle, R.J., Chalmers, J.R., Simpson, E.L. and Williams, H.C., (2011) "The Prevention of Eczema in Infants and Children: An Overview of Cochrane and Non-Cochrane Reviews." *Evidence-Based Child Health: Cochrane Database Syst.* Vol. 6 no. 5, pp. 1322–39.
- Gaitanis, G., Magiatis, P., Hantschke, M., Bassukas, I.D. and Velegraki, A., (2012) "The Malassezia Genus in Skin and Systemic Diseases." *Clinical Microbiology Reviews* vol. 25 no. 1, 106–41.
- Gallo, Richard L: (2017) "Human Skin Is the Largest Epithelial Surface for Interaction with Microbes." *Journal of Investigative Dermatology* Vol. 137 no. 6 , pp. 1213–14.
- Gallo, R. L; (2017) 'Human skin is the largest epithelial surface for interaction with microbes' *Journal of Investigative Dermatology*, vol.137 no. 6, pp. 1213-1214.
- Gioti, A., Nystedt, B.R., Li, W., Xu, J., Andersson, A., Averette, A.F., Mřnch, K., Wang, X., Kappauf, C., Kingsbury, J.M. and Kraak, B; (2013) "Genomic Insights into the Atopic Eczema-Associated Skin Commensal Yeast *Malassezia Symptodialis*." *mBio* vol. 4 no. 1, pp. e00572-12.
- Grice, E.A., Kong, H.H., Conlan, S., Deming, C.B., Davis, J., Young, A.C., NISC Comparative Sequencing Program, Bouffard, G.G., Blakesley, R.W., Murray, P.R. and Green, E.D., (9009) "Topographical and Temporal Diversity of the Human Skin Microbiome." *Science* vol. 324 no. 5931, pp. 1190–92.
- Grice, E. A., Kong, H. H., Conlan, S., Deming, C. B., Davis, J., Young, A. C., and Segre, J. A; (2009) Topographical and temporal diversity of the human skin microbiome. *Science*, vol. 324 no. 5931, pp. 1190-1192.
- Grice, E. A; (2015) The intersection of microbiome and host at the skin interface: genomic-and metagenomic-based insights. *Genome research* Vol. 25 no. 10, pp. 1514-1520.
- Grice, Elizabeth A., and Julia A. Segre. (2011) "The Skin Microbiome." *Nature Reviews Microbiology*. Vol. 9 no. 4 , pp. 244–53.

- Griffiths, Christopher EM, and Jonathan NWN Barker. Null Mutations in the Filaggrin Gene (FLG) Determine Major Susceptibility to Early- Onset Atopic Dermatitis That Persists into Adulthood. *Journal of Investigative Dermatology*. Vol. 127 no. 3, pp. 564–67.
- Gupta, A.K., Batra, R., Bluhm, R., Boekhout, T. and Dawson Jr, T.L. (2004) “Skin Diseases Associated with *Malassezia* Species.” *Journal of the American Academy of Dermatology*. Vol 51 no. 5, pp. 785–98.
- Guo, X., Xu, W., Zhang, W., Pan, C., Thalacker-Mercer, A. E., Zheng, H., and Gu, Z; (2023) High-frequency and functional mitochondrial DNA mutations at the single-cell level. *Proceedings of the National Academy of Sciences*, vol. 120 no.1, pp. e2201518120.
- Handelsman, J. (2004) Metagenomics: application of genomics to uncultured microorganisms. *Microbiol. Mol. Biol. Rev.*, vol. 68 no. 4 , pp. 669-685.
- Hannigan, G.D., Meisel, J.S., Tyldsley, A.S., Zheng, Q., Hodkinson, B.P., SanMiguel, A.J., Minot, S., Bushman, F.D. and Grice, E.A., (2015) “The Human Skin Double-Stranded DNA Virome: Topographical and Temporal Diversity, Genetic Enrichment, and Dynamic Associations with the Host Microbiome.” *mBio* vol. 6 no. 5.
- Harding, C. R., Moore, A. E., Rogers, S. J., Meldrum, H., Scott, A. E., and McGlone, F. P. (2002) Dandruff: a condition characterized by decreased levels of intercellular lipids in scalp stratum corneum and impaired barrier function. *Archives of Dermatological Research*. Vol. 294, pp. 221-230.
- Huang, J. T., Abrams, M., Tloutan, B., Rademaker, A., & Paller, A. S; (2009) Treatment of *Staphylococcus aureus* colonization in atopic dermatitis decreases disease severity. *Pediatrics*, vol. 123 no. 5, pp. e808-e814.
- Iebba, V., Totino, V., Gagliardi, A., Santangelo, F., Cacciotti, F., Trancassini, M., and Schippa, S. (2016) Eubiosis and dysbiosis: the two sides of the microbiota. *New Microbiol.*, vol. 39 no. 1, pp. 1-12.
- Iinuma, K., Sato, T., Akimoto, N., Noguchi, N., Sasatsu, M., Nishijima, S., Kurokawa, I. and Ito, A., (2009) “Involvement of *Propionibacterium Acnes* in the Augmentation of Lipogenesis in Hamster Sebaceous Glands in Vivo and in Vitro.” *Journal of Investigative Dermatology* vol. 129 no. 9 , pp. 2113–19.
- Jakobsson, H.E., Jernberg, C., Andersson, A.F., Sjölund-Karlsson, M., Jansson, J.K. and Engstrand, L. (2010) “Short-Term Antibiotic Treatment Has Differing Long- Term Impacts on the Human Throat and Gut Microbiome.” *PLoS ONE* vol. 5 no. 3.
- Jernberg, Cecilia, Sonja Löfmark, Charlotta Edlund, and Janet K. Jansson. (2007) “Long-Term Ecological Impacts of Antibiotic Administration on the Human Intestinal Microbiota.” *International Society for Microbial Ecology*, vol. 1 no. 1, pp. 56–66.
- Kang, D., Shi, B., Erfe, M. C., Craft, N., and Li, H. (2015) ‘Vitamin B12 modulates the transcriptome of the skin microbiota in acne pathogenesis’ *Science translational medicine.*, vol. 7 no. 293, pp. 293ra103-293ra103.

- Kong, H.H., Oh, J., Deming, C., Conlan, S., Grice, E.A., Beatson, M.A., Nomicos, E., Polley, E.C., Komarow, H.D., Murray, P.R. and Turner, M.L; (2012) “Temporal Shifts in the Skin Microbiome Associated with Disease Flares and Treatment in Children with Atopic Dermatitis.” *Genome Research* vol. 22 no. 5, pp. 850–59.
- Kong, H.H., Oh, J., Deming, C., Conlan, S., Grice, E.A., Beatson, M.A., Nomicos, E., Polley, E.C., Komarow, H.D., Murray, P.R. and Turner, M.L; (2012) “Shifts in Human Skin and Nares Microbiota of Healthy Children and Adults.” *Genome medicine* Vol. 4 no. 10.
- Lai, Yuping, and Richard L. Gallo. (2009) “AMPed up Immunity: How Antimicrobial Peptides Have Multiple Roles in Immune Defense.” *Trends in Immunology* Vol. 30 no. 3, pp. 131–41.
- Lee, D.Y., Yamasaki, K., Rudsil, J., Zouboulis, C.C., Park, G.T., Yang, J.M. and Gallo, R.L; (2008) “Sebocytes Express Functional Cathelicidin Antimicrobial Peptides and Can Act to Kill *Propionibacterium Acnes*.” *Journal of Investigative Dermatology*. Vol. 128 no. 7, pp. 1863–66.
- Lehtimäki, J., Karkman, A., Laatikainen, T., Paalanen, L., von Hertzen, L., Haahtela, T., and Ruokolainen, L. (2017) ‘Patterns in the skin microbiota differ in children and teenagers between rural and urban environments. *Scientific reports* vol.7 no. 1, pp. 45651.
- Luna, Paula Carolina. 2020. “Skin Microbiome as Years Go By.” *American journal of clinical dermatology* vol. 21, pp. 12–17.
- Marples, Richard R. (1982) “Sex, Constancy, and Skin Bacteria. *Archives of dermatology*.” Vol. 272 pp. 317-320
- Markram, H., Muller, E., Ramaswamy, S., Reimann, M.W., Abdellah, M., Sanchez, C.A., Ailamaki, A., Alonso-Nanclares, L., Antille, N., Arsever, S. and Kahou, G.A.A; (2015) “The Influence of Age and Gender on Skin-Associated Microbial Communities in Urban and Rural Human Populations.” *PLoS ONE* vol. 10 no. 10.
- McCall, Laura Isobel et al. (2020) “Home Chemical and Microbial Transitions across Urbanization.” *Nature Microbiology*. Vol. 5 no. 1, pp. 108–15.
- McDowell, A., Gao, A., Barnard, E., Fink, C., Murray, P.I., Dowson, C.G., Nagy, I., Lambert, P.A. and Patrick, S. (2011) “A Novel Multilocus Sequence Typing Scheme for the Opportunistic Pathogen *Propionibacterium Acnes* and Characterization of Type I Cell Surface associated Antigens.” *Microbiology* vol. 157 no. 7, pp. 1990–2003.
- Cho, I., Yamanishi, S., Cox, L., Methé, B.A., Zavadil, J., Li, K., Gao, Z., Mahana, D., Raju, K., Teitler, I. and Li, H; (2012) “A Framework for Human Microbiome Research.” *Nature* vol. 486 no. 7402, pp. 215–21.
- Naoe, S., Tayasu, I., Sakai, Y., Masaki, T., Kobayashi, K., Nakajima, A., Sato, Y., Yamazaki, K., Kiyokawa, H. and Koike, S; (2016) “Antimicrobial Activities of Ozenoxacin against Isolates of *Propionibacteria* and

- Staphylococci from Japanese Patients with Acne Vulgaris.” *Journal of medical microbiology*. Vol. 65 no. 8, pp. 745–50.
- Nakatsuji, T., Chiang, H. I., Jiang, S. B., Nagarajan, H., Zengler, K., and Gallo, R. L. (2013) The microbiome extends to subepidermal compartments of normal skin. *Nature communications* vol. 4 no. 1, pp. 1431.
- Oh, J., Byrd, A. L., Park, M., Kong, H. H., and Segre, J. A. (2016). Temporal stability of the human skin microbiome. *Cell*, vol. 165 no. 4, pp. 854-866.
- Pace, N. R. 1997. A molecular view of microbial diversity and the biosphere. *Science*, vol. 276 no. 5313, pp. 734-740.
- Palmer, C. N., Irvine, A. D., Terron-Kwiatkowski, A., Zhao, Y., Liao, H., Lee, S. P., and McLean, W. I; (2006) “Common Loss-of-Function Variants of the Epidermal Barrier Protein Filaggrin Are a Major Predisposing Factor for Atopic Dermatitis.” *Nature genetics*, vol. 38 no. 4, pp. 441-446.
- Picardo, M., Ottaviani, M., Camera, E., and Mastrofrancesco, A. (2009) Sebaceous gland lipids. *Dermatoendocrinol*. Vol. 1, pp. 68–71.
- Saunders, Charles W., Annika Scheynius, and Joseph Heitman; (2012) “Malassezia Fungi Are Specialized to Live on Skin and Associated with Dandruff, Eczema, and Other Skin Diseases.” *PLoS Pathogens* vol. Vol. 8 no. 6 , pp. e1002701.
- Scholz, Christian F.P., and Mogens Kilian. (2016). “The Natural History of Cutaneous Propionibacteria, and Reclassification of Selected Species within the Genus Propionibacterium to the Proposed Novel Genera Acidipropionibacterium Gen. Nov., Cutibacterium Gen. Nov. and Pseudopropionibacterium Gen. Nov.” *International Journal of Systematic and Evolutionary Microbiology* vol. 66 no. 11, pp. 4422–32.
- Somerville, D. A. 1969. The normal flora of the skin in different age groups. *Br. J. Dermatol*, vol. 81 no. 4, pp. 248-258.
- Staley, J. (1985) “Measurement of In Situ Activities of Nonphotosynthetic Microorganisms in Aquatic and Terrestrial Habitats.” *Annu. Rev. Microbiol*. Vol. 39 no. 1, pp. 321–46.
- Surana, Neeraj K., and Dennis L. Kasper. (2012) “The Yin Yang of Bacterial Polysaccharides: Lessons Learned from B. Fragilis PSA.” *Immunological Reviews* vol. 245 no. 1, pp. 13–26.
- Fitz-Gibbon, S., Tomida, S., Chiu, B.H., Nguyen, L., Du, C., Liu, M., Elashoff, D., Erfe, M.C., Loncaric, A., Kim, J. and Modlin, R.L; (2013). “Pan-Genome and Comparative Genome Analyses of Propionibacterium Acnes Reveal Its Genomic Diversity in the Healthy and Diseased Human Skin Microbiome.” *mBio* vol. 4 no. 3.
- Turnbaugh, P.J. and Gordon, J.I; (2007) “The Human Microbiome Project.” *Nature* vol. 449 no. 7164 :pp. 804–10.

- Turnbaugh, P. J., Ley, R. E., Hamady, M., Fraser-Liggett, C. M., Knight, R., and Gordon, J. I; (2007) The human microbiome project. *Nature*, vol. 449 no. 7164, pp. 804-810.
- Telofski, L. S., Morello, A. P., Mack Correa, M. C., and Stamatias, G. N; (2012) The infant skin barrier: can we preserve, protect, and enhance the barrier?. *Dermatol Res Pract* .
- Xu, J., Saunders, C. W., Hu, P., Grant, R. A., Boekhout, T., Kuramae, E. E., and Dawson Jr, T. L; (2007) Dandruff-associated *Malassezia* genomes reveal convergent and divergent virulence traits shared with plant and human fungal pathogens. *Proceedings of the National Academy of Sciences*, vol. 104 no. 47, pp. 18730-18735.
- Zákostelská, Z., Málková, J., Klimešová, K., Rossmann, P., Hornová, M., Novosádová, I., Stehlíková, Z., Kostovčík, M., Hudcovic, T., Štěpánková, R. and Jůzlová, K; (2016) “Intestinal Microbiota Promotes Psoriasis-Like Skin Inflammation by Enhancing Th17 Response.” *PLOS ONE* vol. 11 no. 7, pp. e0159539.

